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Fourth Edition

Textbook of Female Urology and Urogynecology

Edited by

Linda Cardozo
David Staskin

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VOLUME ONE

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Preface

The success of the first three editions of the *Textbook of Female Urology and Urogynecology* and our desire to regularly update and provide a timely and relevant reference textbook in this rapidly evolving field stimulated us to produce this fourth edition. We hope we have again fulfilled our mission by presenting a book that serves as a foundation for established ideas, a review of the current state of the art, and a platform for introducing the dynamic concepts of the future.

We are both proud and humbled to present this fourth edition and take this opportunity to thank all those who contributed their time and effort—thanks also for choosing this textbook for your practices and your libraries. We are particularly grateful to our section editors and appreciate their commitment to producing an authoritative and comprehensive reference book that has demonstrated broad appeal to the wide range of health providers involved in the management of female pelvic floor problems.

We specifically selected these section editors and authors to present an international approach to the numerous female urogenital health issues in order to produce a good balance of knowledge, expertise, and writing skills without the polarization of ideas that can occur as a natural product of geography, training, and interests. Once again, we have included authors with international reputations and others who are newcomers to the field. We recognize that there is a significant overlap between female urology and urogynecology. However, there are also differences, and we hope that these are reflected by having a balance between the healthcare professionals who have written the individual chapters. In the future, readers will continue to evaluate the physicality of a traditional textbook versus a digitized edition, or a website that allows collaborative editing of its content and structure by its users, and this will influence our future as consumers of information and the choice of medium for future editors, authors, and readers.

We are indebted to the publisher, who facilitated production of all four editions. In addition, to quote from the preface of the third edition, “we are most grateful to our patients who place their trust in all of us every day and we hope that this textbook will contribute to their quality of care and to those who will treat them in the future.”

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Section I

Background Issues

1 History of Urogynecology and Female Urology

Jane A. Schulz, Harold P. Drutz, and Jack R. Robertson

INTRODUCTION

Having moved into the new millennium, accompanied by many new advances in the field of urogynecology and reconstructive pelvic surgery, it is appropriate to take time to reflect on the events of the last century and to make suggestions for future directions. With the significant increase in our postmenopausal female population, there is a growing demand for improved quality of life and management of pelvic floor dysfunction. No longer do we contemplate *whether* women will grow older but, rather, *how* they will grow older. The life expectancy for women has almost doubled through the twentieth century. In 1923, Professor Sir Arthur Keith, in his Hunterian lecture on “Man’s Posture: Its Evolution and Disorders” [1], stated:

> Every movement of the arms, cough or strain sets going a multitude of “water hammers” within the abdominal and pelvic cavities. Every impulse sets the bladder knocking at the vaginal exit … it is the continual repetition of small forces, more frequently than the sudden application of a great effort which wear down the vaginal defense.

Although it has long been recognized that factors such as childbearing and chronic increases in intra-abdominal pressure contributed to pelvic floor prolapse, only recently has there been growing demand to manage all of the resulting problems. Urinary incontinence is now the most common reason for admission to long-term institutionalized centers in Canada and the United States. Billions of dollars are spent every year on nappy (diaper) and pad products, but this does nothing to correct the underlying problem of incontinence.

Since the inception of medical writing, gynecological and urological conditions have been reported. The Kahun papyrus, circa 2000 BC, described diseases of women including diseases of the urinary bladder. The Ebers papyrus, 1550 BC, classified diseases by systems and organs. Section VI includes a prescription for the cure of a woman suffering from disease of her urine, as well as her womb. Urinary fistula is an example of the intimate relationship of the urinary and genital systems in women. Henhenit lived in the court of Mentuhotep II, about 2050 BC. Her mummy, found in 1935, revealed by radiography an extensive urinary fistula [2].

Reviewing the last century of progress in the new subspecialty of urogynecology and reconstructive pelvic surgery proved to be a tremendous, and somewhat daunting, task. Perhaps the quotation that best summarizes the events that have occurred is the opening sentence from Charles Dickens’ *A Tale of Two Cities*: “It was the best of times, it was the worst of times.” Undoubtedly, we have made tremendous progress in this burgeoning new field; however, a political battlefield was perpetuated with the division of the female pelvic floor between urologists, urogynecologists, gynecologists, and colorectal surgeons. This political feud is cleverly illustrated in the article of Louis Wall and John DeLancey with its well-known drawing of the competing urologist, gynecologist, and colorectal surgeon [3]. This is one of the many challenges that must be overcome in providing overall women’s healthcare as we move further into the twenty-first century. A multidisciplinary approach to managing female pelvic floor dysfunction must be advocated to provide women with appropriate care in the areas of urinary and fecal incontinence, urogenital aging, conservative management, and reconstructive pelvic surgery [4].

Voltaire, the French philosopher of the “Age of Enlightenment” said, “these truths are not for all men nor for all times.” From this, we must humbly accept the concept that the truths we believe in today regarding our management of women with pelvic floor disorders must be constantly reassessed and modified with scientific advancements and research. Similarly, the epigram by Alphonse Karr (1849) “plus ça change plus c’est la même chose” (the more things change, the more they stay the same) also reflects the changes during the past century especially in the field of surgical intervention, where in many cases we have continued to reinvent the wheel. Now, we will review the significant events in this field over the last century.

HISTORY OF THE INTERNATIONAL UROGYNECOLOGY ASSOCIATION

At the Federation International of Gynecology and Obstetrics (FIGO) meeting in Mexico City in 1976, two medical friends, Professor Axel Ingelman-Sundberg, of Stockholm Sweden, and Jack Rodney Robertson, of California, USA, met. It was time to form a new society. The objective was to further the urinary health of females. Both physicians were deeply involved in this work.

Axel Ingelman-Sundberg, renowned for his research, his pioneering in gynecologic surgery, and his teaching at the Karolinska Institute in Stockholm, Sweden, was the catalyst. Sweden had been a founding member of FIGO. Axel tried to persuade FIGO to make International Urinary Incontinence a subcommittee, but they declined. In his capacity as vice president of FIGO, Axel reserved a special room for the formation of the International Urogynecological Association (IUGA). He was elected the first president, to serve 5 years, 1976–1980, by the colleagues who registered as members. They were Abbo Hassan Abbo, MD, Sudan; Wolfgang Fisher, MD, East Germany; Bozo Kralj, MD, Yugoslavia; Oscar Contreras Ortiz, MD, Argentina; Donald R. Ostergard, MD, USA; Eckard Petrie, MD, West Germany; Jack R. Robertson, MD, USA; Mr. Stuart Stanton, MD, U.K.; Ulf Ulmsten, MD, Sweden; and David W. Waller, MD, UK. Ulf Ulmsten, then professor of obstetrics and gynecology in Aarhus, Denmark, was chosen secretary.

The next meeting followed in Sheffield, UK, in July 1977, in connection with the local gynecological meeting. At Bergen, Norway, in 1978, IUGA met along with the Scandinavian Congress of Obstetrics and Gynecology. In 1979 in Tokyo, IUGA met again with FIGO; this time IUGA was a special section of the program. In October 1980, IUGA met in New Orleans, organized by Jack Robertson, in connection with the newly formed Gynecological Urology Society (GUS), later to become the American Urogynecologic Society (AUGS).

The fifth IUGA meeting was held in Stockholm, September 1981, at the Wenner–Gren Center, famous for Nobel Prize presentations. The banquet was at the Royal Opera House, with a special program by the famous Swedish opera singer, Kerstin Dellert. Jack Robertson was elected president and served until 1985. Peter Sand, of Chicago, Illinois, became the general secretary. During this time, the association was growing in membership.

In the United States, Jack Robertson had found that women were being treated as second-class citizens, being examined with male instruments for their incontinence problems. An alarming number of women were incontinent after their hysterectomy surgery. Robertson devised a system of viewing the bladder using carbon dioxide instead of water. In 1968, he went to Germany and convinced the famous endoscope maker, Karl Storz, who had recently acquired the technique of fiber optics, to produce a female urethroscope to Robertson's specifications. Storz immediately liked the idea of not using water and made the first Robertson female urethroscope. Instead of just resting their instruments upon it, this was the first time doctors could view the female urethra and its pathology. This was the beginning of a pioneering path with Robertson giving seminars to physicians anxious to learn about the female urinary tract, which had not been included in their gynecological training. An immediate result was a sharp rise in the diagnoses of urethral diverticula.

The meeting was held at Santa Barbara, California, in 1982 organized by Jack Robertson and combined with the GUS, organized by Don Ostergard. In 1983, IUGA met in Mainz, Germany, and in 1984, IUGA met at the famous Breakers Hotel in West Palm Beach, Florida.

At the meeting in Budapest, Hungary, in 1985, physicians came from behind the Iron Curtain. It was vital for them to present their work at the meeting as they would rise in professional and, most importantly, pay level as a result. When one group from Poland presented a problem, the audience asked why ultrasound had not been used, which at that time would have been the obvious method of treatment. The physicians from Poland replied simply: “We do not have ultrasound.” Donald Ostergard was elected the third president and presided at the 1986 meeting at Yale University, organized by Ernest Kohorn. Don's memories include “a lot of work organizing individuals to take the financial risks to hold a meeting.”

An important event occurred at the 1986 Yale meeting. The *International Urogynecology Journal* was born. Oscar Contreras Ortiz was nominated editor in chief. Donald Ostergard became the first managing editor and, later, the editor in chief. He was followed by Linda Brubaker and now Peter

Dwyer and Paul Riss. The first issue, Volume I, was printed in September 1989 and contained the abstracts of the Riva del Garda meeting. The associate editors, section editors, and editorial board represent countries all around the world.

The 1987 meeting was in Ljubljana, Yugoslavia, organized by Bozo Kralj, of Slovenia, with 200 members worldwide. Bozo became the fourth president at the 1988 memorable meeting at Iguazu Falls, Argentina, hosted by Oscar Contreras Ortiz, where Hans Van Geelen says, “made every effort, and succeeded in strengthening social ties.” In 1989, Rodolfo Milani hosted the meeting in Riva Del Garda, Italy.

Next elected was Eckhard Petri of Germany, from 1990 to 1992, inaugurated at the Stockholm, Sweden, meeting organized by Ulf Ulmsten. Peter Dwyer says of this meeting: “One of the most low key of all the meetings, it was possibly one of the most enjoyable. It was basic but had good science. The chairman’s dinner was held in Ulf’s department at the Uppsala University cafeteria.” The 16th annual IUGA meeting was held in Sydney, Australia, in 1991, and the host and hostess were Jim and Peggy Gibson. They had a fabulous chairman’s reception that was held at the farm they owned at the time called “Stanton Hall.”

In 1992, IUGA combined with AUGS, in Boston, Massachusetts, with a lobster bake party at the famous aquarium. James Gibson, Australia, was elected sixth president. He presided the 1993 meeting in Nimes, France, which was coordinated with ICS in Rome. Gibson organized Organon to give IUGA $10,000 each year for 5 years for the best presentation at each meeting. In 1994, Harold Drutz hosted the meeting in Toronto, Canada, at which he was elected the seventh president. He presided at the Kuala Lumpur meeting in 1995 as well, hosted by Jim Gibson, which, he says, was one of the first meetings to make a profit.

In September 2–5, 1996, the meeting was in Vienna, Austria, organized by Paul Riss. This was a glorious site at which Oscar Contreras Ortiz, Buenos Aires, Argentina, was elected the eighth president. The 1997 meeting occurred in Amsterdam, arranged with the combined efforts of Hans Van Geelen, Harry Vervest, and Mark Vierhout. The meeting location was planned in Europe as FIGO was in Copenhagen. In 1998, Buenos Aires, Argentina, was the venue for IUGA, hosted by Oscar Contreras Ortiz. Linda Cardozo, London, UK, was the ninth president. In 1999, in Denver, Colorado, Willy Davila organized IUGA with Rick Schmidt of ICS to allow the first combined meeting of the two societies.

The 2000 IUGA meeting in Rome, Italy, organized by Mauro Cervini, chose Hans Van Geelen, from the Netherlands, as president. The largely attended meeting was enlivened by an audience with Pope John Paul II, celebrating the millennium year. The Pope blessed the International Urogynecology Association in his Papal address during the meeting. Hans Van Geelen recalls that at an early IUGA meeting the attendance was so small that the members could sit around one round table, discussing the clinical relevance of urodynamics. He, too, says, “in the beginning, hosting a meeting was a delicate task.”

In 2001, the IUGA meeting moved to the southern hemisphere again with Peter Dwyer as the host in Melbourne, Australia, combined with the Australian Continence Foundation. Axel Ingelman-Sundberg was awarded a lifetime achievement award, via a live television connection, at the 2001 meeting. The 2002 meeting was held in Prague, with Michael Halaska as the organizer. The river Moldau flooded the inner town, and Professor Halaska had to change the venue of the gala dinner and take out new insurance. In Prague, Peter Dwyer of Melbourne, Australia, was elected president. Peter comments that IUGA became not only a scientific society but developed a true camaraderie of friendship. He says that the young urogynecologists appreciated the emphasis on the clinic rather than the basic science (rats). Peter writes: “Presenting our own research internationally and getting ideas for our next projects was also very important, and the meetings were great fun.”

In 2003, IUGA was back in Buenos Aires, again organized by Oscar Contreras Ortiz. August 24–27, 2004, saw a spectacular meeting of IUGA in Paris, France, combined for the second time with the ICS. The chairman’s dinner held at Maxim’s Restaurant, honored Jack R. Robertson with a lifetime achievement award. The Palais Versailles was the unbelievable site of the gala dinner, hosted by Bernard Jacquetin for IUGA and Francois Haab for ICS. Paul Riss of Moedling, Austria, was elected to serve as president from 2004 to 2006. Copenhagen, Denmark, August 9–12, was the site of the 2005 IUGA meeting, organized by Gunnar Lose.

The two old friends, Axel Ingelman-Sundberg and Jack R. Robertson, met in Munich, Germany, in

August of 2004. The meeting in Copenhagen in 2005 was an exciting meeting at a unique venue with the first discussion of some of the newer mesh kits. In 2006, the annual IUGA meeting was in the beautiful historic city of Athens, with many social events being held at some of the ancient historic sites. Professor Oscar Contreras Ortiz received a prestigious lifetime achievement award. 2007 found us back across the Atlantic in Cancun Mexico with a stunning gala dinner at sunset on the beach. At the Cancun meeting, Professor Donald Ostergard received a lifetime achievement award. Despite difficult weather caused by a number of typhoons, many were still able to attend the 2008 meeting in Taipei, where Professor Harold Drutz received a lifetime achievement award from the IUGA for his ongoing contributions to the society (including the only Canadian to have been president of the society, in 1994–1996). The stunning venue of Lake Como, Italy, was the site for the 2009 meeting, where Professor Jim Gibson received a lifetime achievement award. 2010 saw another joint meeting of the ICS and IUGA hosted by Professors Drutz and Herschorn in Toronto, Canada.

The 2011 IUGA meeting moved back to Europe and was held in Lisbon, Portugal. 2012 led the IUGA meeting back to beautiful Brisbane, Australia. In 2013, Dublin hosted a wonderfully successful meeting and Linda Cardozo received a lifetime achievement award. In 2014, IUGA joined with AUGS in Washington, DC, to host a great meeting where 61 countries were represented.

UROGYNECOLOGY TRAINING PROGRAMS

Urogynecology training programs have grown internationally with support from the IUGA. Recognition and accreditation of urogynecology and pelvic floor reconstruction has also progressed significantly with formal subspecialty certification programs now in many countries. The detailed progress and trainees of some of the larger subspecialty training programs are given in the appendix.

PROGRESS IN THE TWENTIETH AND TWENTY-FIRST CENTURIES

Treatment

Marion Sims, in the United States, was one of the first to establish the relationship of urology and gynecology. Determined to cure vesicovaginal fistulas, he finally used silver wire and announced in 1852 the cure of 252 out of 320 attempts. Howard A. Kelly, the first professor of gynecology at the Johns Hopkins Medical School, believed that gynecology and urology were so closely related that a physician could not be trained in either field and ignore the other. In 1893, he invented a cystoscope and was the first person to insert ureteral catheters under direct vision. Kelly’s successor, Guy Hunner, described Hunner’s ulcer, which today is called interstitial cystitis. Succeeding Hunner was Houston Everett, whose contribution was the relationship of the urinary tract to cervical cancer. In 1914, Latzko perfected the cure of posthysterectomy vesical vaginal fistula. Next, Richard TeLinde added water endoscopy to the Hopkins female urology program. Most teaching programs at the time gave little or no exposure to female urology [2].

In 1892, Poussan proposed the concept of urethral advancement for the management of urinary incontinence [5]. He suggested, “introducing a bougie into the urethra, resecting the external meatus and portion of the urethra, and then after torsion of the canal to one hundred and eighty degrees, it is transplanted to a point just below the clitoris.” By the turn of the century, four main treatments for stress urinary incontinence were outlined:

1. Injection of paraffin into the region of the urethra
2. Massage and electricity
3. Torsion of the urethra
4. Advancement of the external urethral meatus

A century later, we are still trying to identify the best urethral bulking agent. Although it is no longer paraffin, research with Teflon (poly [tetrafluorothene]), silicone, collagen, autologous fat, hyaluronic acid, carbon particles, and various copolymers has failed to identify an ideal medium.

In his landmark paper in 1913, Kelly outlined operations for managing urinary incontinence in women [6]. These included the following:

- Puncture of the bladder and insertion of a catheter
- Closing the urethra and creating a vesicoabdominal fistula

- Closing the vagina and creating a rectovaginal fistula
- Compression of the urethra with an anterior colporrhaphy
- Periurethral injection of paraffin
- Advancement of the urethral meatus to the clitoris

Kelly suggested that “the torn or relaxed tissues of the vesical neck should be sutured together using two or three vertical mattress sutures of fine silk linen passed from side to side.” In his first publication, he described 16 patients as being well and 4 patients in whom the procedure was not successful, giving a success rate of 80%. However, further evaluation has revealed that the long-term success, using only these sutures to correct stress incontinence, falls to roughly 60% [7]. This decline is possibly related to gradual postoperative elongation of the smooth muscle in which the sutures were placed [8]. With coincident suburethral plication of the pubourethrovaginal ligaments of the urogenital diaphragm, the long-term results of a Kelly plication are significantly better [9].

Sling procedures were pioneered in the early 1900s by three European physicians. Goebell first suggested transplantation of the pyramidalis muscle in 1910 [10]. This was followed by Frankenheim who, in 1914, recommended using the pyramidalis or strips of rectus muscle as a suburethral sling by attaching the muscle to overlying fascia [11]. In 1917, Stoeckel suggested combining the techniques of Goebell and Frankenheim and adding plication of the vesical neck [12]. Throughout the twentieth century, there have been many variations of sling procedures described in the literature. In 1907, Giordano suggested the use of the gracilis muscle by wrapping it around the urethra [13]. Shortly thereafter, in 1911, Squier described the use of the levator ani muscles by placing them between the vagina and urethra [14], and, in 1923, Thompson recommended the use of strips of the rectus muscle, surrounded by fascia, to be passed in front of the pubic bones and around the urethra [15]. The next key event in the development of surgery to the anterior compartment was the development of the bulbocavernosus muscle fat pad graft by Martius in 1929 [16]. This has found wide use in fistula repairs and reconstruction of the anterior vaginal wall. In 1968, John Chasser Moir [17] introduced the concept of the gauze hammock operation as a modification of the original Aldridge [18] sling procedure described in 1942. Chasser Moir recognized that “operations of this type do no more than support the bladder neck and urethrovesical junction and so prevent the undue descent of parts when the woman strains or coughs.”

Victor Bonney, in 1923, stated, “incontinence depends in some way upon a sudden and abnormal displacement of the urethra and urethrovesical junction immediately behind the symphysis” [19]. This was followed in 1924 by a description from B.P. Watson of “the muscle sheet that normally supports the base and neck of the bladder” and his statement that “so far as the incontinence of urine is concerned, the important sutures are those which overlap the fascia at the neck of the bladder and so restore it to its normal position.” In reviewing Watson’s work with anterior colporrhaphy, he was able to obtain “perfect control” in 65.7% of cases, “improvement” in 21.9%, and “no success” in 12.4% [20]. These figures are in keeping with others that have been reported for anterior colporrhaphy. Therefore, it was apparent that hypermobility of the bladder neck was an issue and that the anterior colporrhaphy was not a satisfactory operation for stress incontinence.

The next landmark in genitourinary surgery occurred in 1949 with the publishing of the paper of Marshall, Marchetti, and Krantz on “The correction of stress incontinence by simple vesicourethral suspension.” They suggested that this operation was “particularly valuable for patients whose first procedure failed.” In their first 44 patients, they described 82% of patients with excellent results, 7% with improvement, and an 11% failure rate [21]. Shortly thereafter, in 1950, H.H. Fouracre Barns described the “round ligament sling operation for stress incontinence”; this technique was popularized by Paul Hodgkinson [22]. In 1961, John Burch first described his modification of the Marshall–Marchetti–Krantz procedure, which involved a retropubic colpourethropexy that took the anterolateral aspects of the vault of the vagina and attached them to Cooper’s ligament [23]. Burch recognized the potential complications of this procedure if done alone including the creation of an enterocele or rectocele, the development of ventral/incisional hernias, and even the possibility of a vesicovaginal fistula.

Diagnosis and Investigation

As the number of procedures offered for the treatment of stress incontinence increased, there were also significant advances in the urogynecological diagnostic procedures available. In 1882, Mosso and Pellacani described cystometry using a smoked drum and a water manometer [24]. An aneroid barometer for cystometric evaluation was developed by Lewis in 1939 [25]. Jeffcoate and Roberts, in 1952, introduced the concept of radiographic changes in the posterior urethrovesical angle [26]. These changes were further modified in 1956 by Bailey in England, who described seven variations in the urethrovesical angle on radiographic studies [27]. Later modifications were performed by Tom Green in the United States in 1962, when he described Green types 1 and 2 incontinence [28]. Identification of the posterior urethrovesical angle by lateral bead chain cystography was introduced by Hodgkinson in 1953 [29].

By 1956, Von Garrelts had introduced the concept of uroflowmetry [30]. In 1964, Enhorning, Miller, and Hinman combined cystometry with radiographic screening of the bladder [31]; this was followed a few years later in 1969 by Brown and Wickham's introduction of urethral pressure profilometry [32]. Another landmark occurred in 1971, when Patrick Bates, Sir Richard Turner-Warwick, and Graham Whiteside introduced synchronous cine pressure–flow cystography, with pressure and flow studies [33]. This was the beginning of the field of video urodynamics. Equipment was further expanded with the introduction of the microtip transducer in 1975 by Asmussen and Ulmsten, for measuring urethral closure pressure [34].

Further investigational advances occurred in the latter part of the twentieth century. These included the introduction of the Urilos monitor in 1974 by James et al. [35]. This device allowed evaluation of the symptom of dampness for whether the fluid lost was urine. In 1981, Sutherst et al. developed the pad-weighing test as an objective measure of the severity of urinary incontinence [36].

In 1961, Enhorning suggested that "surgical treatment for stress incontinence is probably mainly beneficial because it restores the neck of the bladder and the upper part of the urethra to the influence of intra-abdominal pressure" [37]. This introduced the concept of pressure transmission ratios and the idea that successful operations for stress urinary incontinence worked by restoring the urethrovesical junction to an intra-abdominal position. In 1956, Jeffcoate added further interpretation of our investigative techniques when he attempted to caution gynecologists by stating "the absence of the posterior urethrovesical angle is merely a sign of incompetence of the internal sphincter. The presence of an angle is a function of the involuntary muscle at the urethrovesical junction, not of the muscle of the pelvic floor" [38]. And so the simplistic approach of static cystourethrograms began to be questioned. Green had suggested that if one saw a radiographic diagnosis of type 1 incontinence, this could readily be repaired with an anterior colporrhaphy; the type 2 stress incontinence required a retropubic urethropexy. A number of authors, including Drutz in 1978 [39], have confirmed the limited accuracy of static cystourethrograms.

By 1953, Paul Hodgkinson had recommended "that if on anteroposterior straining radiograph, the urethrovesical junction is depressed 4 cm below the lower border of the symphysis, I believe the objective of the operation can be accomplished through anterior colporrhaphy" [28]. A decade later, Hodgkinson commented on the frequency of detrusor dyssynergia, with grade 1 defined as a detrusor contraction in response to coughing and heel jouncing and grade 2 a spontaneous automatic detrusor contractility when recumbent. Hodgkinson recognized the importance of discovering this condition prior to performing any surgery for stress urinary incontinence [40].

Success Rates

As we approached the 1970s, we began to recognize that operative failures in the treatment of stress urinary incontinence involve three areas [41] as follows:

1. Incorrect diagnosis and the fact that bladder instability (and not just simple stress incontinence) may have been the cause of the incontinence.
2. The wrong operation may have been chosen and some operations probably give better long-term results.
3. The concept of technical failure.

We recognized that the vaginal approach to primary stress incontinence probably only gave a 50%–60% success rate, whereas the suprapubic approach gave success rates of at least 80%. Morgan, in 1973, discussed indications for primary retropubic urethropexy: these included minimal pelvic floor relaxation, chronic chest disease, occupations involving heavy lifting patients who were heavily involved in athletics, and obesity [42]. In 1970, Hodgkinson stated that “the most durable operation for stress incontinence is a retropubic urethropexy and the least durable is a vaginal repair.” Hodgkinson quoted a 92.1% success rate with his own 404 patients that had retropubic urethropexy [40]. The other movement in the 1970s was of the urologists and gynecologists toward endoscopic bladder-neck suspensions such as the Pereyra, Raz, and Stamey suspensions; numerous variations including the Gittes and Cobb–Raagde were described in the literature. In the 1990s, we have now realized that the long-term results of these needle suspension procedures are also not as good as the retropubic procedures.

The 1990s have also seen the advent of minimally invasive sling procedures for stress urinary incontinence. The first of these, the tension-free vaginal tape and the concomitant integral theory of the pathophysiology of incontinence were described by Ulmsten and Petros in the early 1990s [43,44]. There are now multiple variations of this procedure including the transobturator approach. Success rates are reported to be similar to that of the Burch repair [45]. More recently, single-incision midurethral slings have been advocated. The long-term success of these new procedures is yet to be established.

The great champion of pelvic floor exercises, Arnold Kegel, reported pre- and postoperative benefits of the properly performed exercises [46]. Unfortunately, many patients are placed on this regimen only after an unsuccessful surgical procedure. Robertson, with Bergman and Elia, in 2004, has described an enhancement of Kegel exercises, when done in a magnetic field, combined with DeLancey’s “knack procedure,” to give support to the urethra when it is most needed [47].

THE WAY AHEAD

Now in the twenty-first century, we must consider what lies ahead. The main fields of responsibility as urogynecologists and reconstructive pelvic surgeons include the following:

- Education
- Surgery
- Uropharmacology
- Neurophysiology
- Behavior modification
- Collagen
- Ultrasonography/magnetic resonance imaging (MRI)
- Stem cells
- Graft materials

Regarding education, we need to focus on education of our colleagues in obstetrics and gynecology, family practice, geriatrics, and community health care, of allied health professionals such as nursing and physiotherapy, and of the public. The awareness must be increased that incontinence is not a normal effect of aging; the many myths including “everyone gets it” and “it can’t be treated” must be dispelled. Urogenital aging must be stressed as part of menopause management, and conservative management in the community should be promoted. The other aspect of education is the training of new subspecialists in the field of urogynecology and reconstructive pelvic surgery. Board certification is now available in Australia and in the United States. IUGA is now establishing international standards for training in conjunction with FIGO and WHO.

Within the field of surgery for pelvic floor problems, we need to reevaluate what we do. Over 200 operations have been described for stress incontinence. Randomized controlled trials, with adequate patient numbers and follow-up of at least 2 years, are required for evaluation of new and existing procedures. The role of bulking agents is still controversial and the ideal medium has yet to be discovered. A variety of fascia and mesh is available for use in pelvic floor reconstructive procedures; however, the long-term durability and consequences of these are still unknown. This includes many new mesh devices and kits for pelvic floor reconstruction. Concerns have been raised about the ethics of some of these newer mesh devices [48]. New pharmacologic agents continue to be produced; well-designed, placebo-controlled trials are mandatory for their evaluation. Neurophysiology is another developing area; work is being done to determine if there are certain factors in labor that lead to irreversible changes to the pelvic floor. Other questions that have been raised include whether abnormalities in the electromyographic patterns predict success or failure of different treatments. We continue to develop new modes of conservative management including behavior modification and devices; further studies are needed to clarify the specific areas of use for these therapies.

The role of collagen in pelvic floor disorders is a fascinating area. We need effective, qualitative, and quantitative assays to determine whether there are certain defects of collagen in patients with pelvic floor dysfunction. Also, we need to establish whether there may be potential genetic markers that may be screened for to determine certain “at-risk” patients. Perhaps there exists a select group of patients that should be counseled to have delivery by cesarean section; this group may also require the use of synthetic materials in reconstruction of their pelvic floor. We need to look at the relationship of collagen to estrogen and the general effects of urogenital aging to see if they are independent factors. Research into genetic components of pelvic floor prolapse is exciting. At Mount Sinai Hospital in Toronto, Dr. May Alarab and her associates have shown that genes that both promote the buildup of extracellular matrix and cause its degradation are different in premenopausal women with prolapse compared to controls.

We are in the midst of a revolution in imaging and diagnostic technology. The development of 3D ultrasound [49] and the progress with MRI have allowed a new approach to evaluating defects associated with stress urinary incontinence and pelvic floor disorders. Progress in the field of ultrasound has been hampered by a lack of standardization of terminology; this was recognized by the German Association of Urogynecology, who attempted to make recommendations for standardization of methodology [50]. The fact that different methods are used (such as abdominal, perineal, introital, vaginal, and rectal) has further impeded progress in this field. Recent papers have investigated the urethra and surrounding tissues with intraurethral ultrasonography; the authors have proposed that sphincter measurements can be a prognostic factor in patients who underwent operations for stress urinary incontinence [51]. Beco stated that “Doppler and colour studies will play and increasing role in the evaluation of urethrovesical disorders” (J. Beco, personal communication, November 1996). With new developments in MRI and especially dynamic MRI, these techniques will also play a growing role in investigation and research. New ways of investigating urethral function are also appearing with the introduction of the MoniTorr device and measurement of urethral retro-resistance [52].

The difficulties of introducing new graft materials into pelvic floor reconstructive surgery have highlighted the need for careful research and long-term follow-up with all innovative technologies. Stem cell research may introduce a natural type of treatment for stress urinary incontinence that replaces bulking agents.

There is an increasing focus on quality of life tools as a research outcome. National and international societies must continue to promote and support research in the field to advance pelvic floor health for women.

CONCLUSIONS

At the International Continence Society meeting in 1986, Sir Richard Turner-Warwick gave an address in which he defined the urogynecologist as “neither the general urologist nor the general obstetrician and gynecologist, but someone who has special training and expertise in genitourinary problems in women” [53]. Today, we should expand this definition to include urogynecology and reconstructive pelvic surgery. Such a physician implies a surgeon with specialized training in the conservative and surgical management of women with urinary and/or fecal incontinence, persistent genitourinary complaints, and disorders of pelvic floor supports.

As Marcel Proust said, “We must never be afraid to go too far, for the truth lies beyond.” We must humbly accept that the “truths” that we identify today certainly will have to be changed in the future. However, if we work collaboratively to produce well-designed scientific research, we should be able to establish truths that stand the test of time in our ongoing quest to improve the quality of life for women with pelvic floor problems.

ACKNOWLEDGMENTS

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reconstructive pelvic surgery: Where do we go from here? *Int Urogynecol J* 1996; 7: 348–353.

We thank professors Stanton, Cardozo, Ostergard, and Drutz for providing information on their trainees.

APPENDIX

Trainees of Professor Stuart Stanton and Their Current Practice Locations

Australia
Michelle Atherton
Emmanuel Karantanis
Mark Krieger

Brazil
Marina Silva

Canada
Colin Birch
Jane Schulz
David Wilkie

Germany
Kaven Baessler
Thomas Dimpfl

Hong Kong
Shek Chong Poon

Israel
Menachem Alcalay
Benny Abramov
Avi Benshushan
Inbar Benshachar
Moshe Barzilai
Alex Condrea
Gabi Gillon
Ronen Gold
David Gordon
Ilan Gruenwald
Zvi Klein
Haim Krissi
Rami Langer (deceased)
Yuval Lavy
Elad Leron
Shachar Madjar
Menachem Neuman
Shlomo Shimonovitz
Elan Ziv

Japan
Kumiko Kato

Philippines
Anna Franco
Lisette Prodigalidad

Saudi Arabia
Medun Al Naim

Singapore
Yue Kim Chin
William Han
Paul Tseng

Switzerland
Annette Kuhn

Taiwan
Paul Chou

Turkey
Cavat Ozoy

United Kingdom
Linda Cardozo
Charlotte Chaliha
Sarah Creighton
Jeremy Elkabir
Michelle Fynes
Emma Gordon
Keiyh Hertogs
Paul Hilton
David Holmes
Andrew Macaulay
Paddyanne Macbride
Ash Monga
Kingsley Norton
Sarah Reynolds
Ranee Thakar

United States
Micky Baggish
Amanda Clark
James Dunaway
Beth Goodson
Corinne Jabs
Marge Kahn
Gretchen Lentz
Serge Marinkovic
Carlos Medina
Fritz Montz
Charlie Nager
Peggy Norton
Deidre Robinson
Sandra Rose (Valaitis)
Lewis Wall
Ann Wiskind

Trainees of Professor Linda Cardozo, Their Work as a Research Fellow, and Their Current Practice Locations

(Professor Cardozo was Professor Stanton’s first trainee.)

1983–1985	*Dr. Eboo Versi*: Studied urinary symptoms and urodynamic findings in climacteric women. Associate professor of urogynecology, Harvard Medical School, Boston, USA. Now working in the pharmaceutical industry.
1985–1987	*Mr. Andrew Tapp*: Compared physiotherapy to surgery in the treatment of genuine stress incontinence. Now consultant obstetrician and gynecologist, Shrewsbury.
1987–1989	*Mr. Christian Barnick*: Studied electromyography of the urethral sphincter in various groups of women. Now consultant obstetrician and gynecologist at the Homerton Hospital, London.
1988–1990	*Mr. Christopher Benness*: Assessed the efficacy of vaginal estradiol pellets in the management of postmenopausal urinary urgency (MD 1995). Now consultant at Royal Prince Alfred Hospital, Sydney, Australia with subspecialty accreditation in urogynecology.
1989–1991	*Mr. Alfred Cutner*: Studied the effect of pregnancy on the lower urinary tract (MD 1993). Now consultant gynecologist at the University College Hospital, London.

1990–1991	*Mr. Gilbert Burton*: Studied toilet training habits (MD 1994). Now consultant at North Shore Hospital, Sydney, Australia, with subspecialty accreditation in urogynecology.
1990–1992	*Mr. Brian Wise*: Evaluated maximal electrical stimulation in the management of detrusor instability (MD 1996). Now consultant obstetrician and gynecologist, Ashford, Kent.
1991–1994	*Mr. Cornelius Kelleher*: Studied the effect of urinary incontinence and its management on the quality of life of women (MD 1996). Now consultant obstetrician and gynecologist at St Thomas's Hospital, London.
1992–1994	*Mr. Vikram Khullar:* Evaluation of ultrasound and Doppler blood flow measurements in the assessment of incontinent women (MD 1999). Subspecialty trainee urogynecology, King's Healthcare Trust, 1997–2000. Currently the consultant in urogynecology at St Mary's Hospital, London.
1993–1995	*Mr. Simon Hill*: Investigated the management of women with nocturia. Currently consultant obstetrician and gynecologist and medical director at Blackburn District General Hospital.
1994–1996	*Mrs. Carmel Ramage (Gleeson)*: Combined project with Professor Christopher Fry, Institute of Urology, London, assessing the Na^+ ion pump in the detrusor muscle. Currently consultant obstetrician and gynecologist, Bradford.
1994–1996	*Mr. Stavros Athanasiou*: Undertook ultrasound assessment of the pelvic floor in women with prolapse and incontinence (MD 1998). Returned to practice with a university appointment in Athens, Greece.
1995–1997	*Mr. Philip Toozs-Hobson*: "Three dimensional ultrasound assessment of damage to the urethral and anal sphincters following childbirth" (MD 2002). Now consultant obstetrician and gynecologist at Women's Hospital, Birmingham.
1995–1998	*Mr. Kelvin Boos*: Studied devices for the management of genuine stress incontinence (MD 2001). Appointed consultant obstetrician and gynecologist, Brighton. Now returned to Ireland.
1996–1999	*Mr. Andrew Hextall*: Studied the effect of estrogens on urinary symptoms in postmenopausal women (MD 2001). Now consultant obstetrician and gynecologist, West Hertfordshire.
1997–1998	*Mr. Alex Yip*: Overseas fellow returned to Singapore to both academic and private practice.
1997–2000	*Mr. John Bidmead*: Studied physiotherapy and novel surgical techniques for stress incontinence. Subspecialty trainee, 2000–2002. Consultant urogynecologist, King's College Hospital.
1999–2000	*Ms. Katie Clifford*: Fellow on secondment from St Mary's Hospital, currently a consultant at Imperial, London.
1999–2002	*Mr. Dudley Robinson*: Studied the use of antidiuretics in the management of incontinence. Subspecialty trainee, 2002–2004 (MD 2006). Consultant urogynecologist at King's College Hospital.
2000–2002	*Mrs. Jane Rufford (Bailey)*: Studied minimally invasive surgery, surgery for stress incontinence. Currently consultant gynecologist (part time) at King's College Hospital.
2001–2004	*Mr. James Bamforth*: Studied the effect of prolapse on quality of life in the elderly. Subspecialty trainee urogynecology. King's College Hospital (2004–2006). Now consultant obstetrician and gynecologist, Bournemouth.
2002	*Mr. Piet Hinoul*: Overseas fellow from Belgium returned initially to clinical urogynecology, now working in a senior medical post with Johnson & Johnson.
2002–2005	*Mr. Matthew Parsons*: Studied the use of a computerized bladder diary (MD 2009). Now consultant obstetrician and gynecologist, Birmingham Women's Hospital.
2004–2007	*Ms. Maria Vella*: Studied incontinence in women with cystic fibrosis. Currently a trainee, South East Thames. Now consultant obstetrician and urogynecologist, Bury St Edmonds.
2005–2008	*Mr. Rufus Cartwright*: Studied the oxybutynin patch and its effect on quality of life (MD 2010). Currently a trainee at North Thames. Undertaking further research for a PhD on an MRC grant.
2005–2006	*Ms. Sushma Srikrishna*: Studied patient-orientated goals in relation to pelvic floor reconstructive surgery. Subspecialty trainee, 2006–2008. Currently consultant obstetrician and urogynecologist, King's College Hospital.
2006–2007	*Mr. Arther Tseng*: Visiting fellow in Singapore, now a consultant urogynecologist in Singapore.
2007–2009	*Ms. Arasee Rangenathan*: Studied the effect of new drugs on the bladder and urethra. Now consultant obstetrician and gynecologist, Sidcup Hospital.
2008	*Mr. Luigi Erricello*: Overseas fellow from Italy now practicing in Italy.
2008–2010	*Mr. Ismaiel Abu-Mahfouz*: Studied ultrasound bladder wall thickness. Returned to Jordan.
2009–2010	*Mrs. Monika Vij*: Returned to West Midlands, now a subspecialty trainee in urogynecology, Bristol.
2009	*Mr. Marco Torella*: Visiting fellow in Italy, now working in Italy.
2010–onward	*Ms. Heleni Mastoroudes*: Studying the management of rectoceles. Returned to clinical training in the South East Thames rotation.

2010	*Mr. Guy Mozogo*: Visiting fellow in France, returned to clinical practice.
2010–onward	*Mr. Ilias Giarenas*: Studying invasive investigative techniques for women with lower urinary tract symptoms, currently subspecialty trainee in urogynecology at King's College Hospital, studying combination therapy for the overactive bladder.
2011	*Ms. Isabelle Freilling*: Visiting fellow from Sweden, returned to clinical practice.
2012	*Mr. Ki Hoon Ahn*: Visiting fellow from Korea, returned to clinical practice.
2012–2013	*Mr. Lanka Abeywickrama*: Clinical research fellow, returned to clinical practice in West Midlands.
2013–onward	*Mr. Ganesh Thiagamoorthy*: Studying common interventions used in association with pelvic floor surgery, current fellow.
2013–onward	*Mr. Martino Zecche*: Currently in a fellow post.
2013	*Ms. Maria Grazia Matarazzo*: Visiting fellow in Italy, now returned to clinical practice in Italy.

Trainees of Professor Donald Ostergard and Their Practice Locations

1978–1979	*Tom McCarthy*: UCSF Medical School to private practice (now deceased).
1979–1980	*Narender Bhatia*: Professor at UCLA Medical School, director of the Urogynecology Fellowship Training Program with over 35 fellows trained, Long Beach, CA.
1980–1981	*David Hebert*: Tulane Medical School to private practice, Los Angeles.
1981–1982	*Alfred Bent*: Professor in several medical schools, director of the Fellowship Training Program with over 30 fellows trained, retired in Halifax, Nova Scotia.
1981–1982	*David Richardson*: Professor, director of Fellowship Training Program, Detroit, MI.
1982–1983	*Richard Scotti*: Professor in several medical schools, director of the Fellowship Training Program with over 20 fellows trained (now deceased).
1982–1983	*Jerry Benzl*: Private practice, Mission Viejo, CA.
1983–1984	*Larry Francis*: Private practice, San Bernardino, CA.
1983–1984	*Larry Cutner*: Private practice, Long Beach, CA.
1984–1985	*Larry Bowen*: Private practice, Sacramento, CA.
1984–1986	*Peter Sand*: Professor, Fellowship Program director with approximately 10 fellows trained, Chicago, IL.
1985–1986	*Jody Blanco*: Professor, Cornell, NY.
1986–1987	*Nicolette Horbach*: Professor to private practice, Arlington, VA.
1986–1987	*Jeff Cornella*: Professor, director of the Fellowship Training Program with over 15 fellows trained, Phoenix, AZ.
1987–1988	*Robby Summitt*: Professor, now private practice, Memphis, TN.
1987–1988	*Toni Harris*: Academic, University of California, Davis, CA.
1988–1989	*Joe Montella*: Professor, University of Philadelphia, Philadelphia, PA.
1988–1989	*Lisa Hirsch*: Private practice, Newport Beach, CA.
1989–1990	*Scott Farrell*: Academic practice, has trained several fellows, Halifax, Nova Scotia.
1989–1990	*Hilary Cholhan*: Professor, director of the Fellowship Training Program with over seven fellows trained. Now private practice, Buffalo, NY.
1990–1991	*Jorge Peacher*: Private practice, San Antonio, TX.
1990–1991	*Karl Luber*: Private practice, faculty, Fellowship Training Program, San Diego, CA.
1991–1992	*Michael Weinberger*: Academic to private practice, Los Angeles, CA.
1992–1994	*Janine Jensen*: Academic to private practice, Long Beach, CA.
1991–1993	*Steve Swift*: Professor, director of the Fellowship Training Program with approximately 15 fellows trained, Charleston, SC.
1993–1995	*Victoria Handa*: Professor, Johns Hopkins University; director of the Fellowship Training Program, Baltimore, MD.
1994–1996	*Michelle Germain*: Private practice, Baltimore, MD.
1995–1998	*Karen Noblett*: Professor, director/faculty of the Fellowship Training Program, University of California, Irvine, CA.
1996–1999	*Jack Devine*: Private practice, Akron, OH.
1998–2001	*Andrew Cassidenti*: Clinical professor at USC, private practice, Mission Viejo, CA.
1999–2002	*Stacey Wallach*: Professor, University of California, Davis, CA.
2001–2004	*Laurie Kane*: Private practice, Delaware.

2002–2005	*Melissa Huggins*: Private practice, Providence, RI.
2004–2007	*Tam Le*: Private practice, faculty, Fellowship Training Program, Los Angeles, CA.
2005–2008	*Leanne Kon*: Private practice, Los Angeles, CA.
2007–2008	*Alex Shapiro*: Private practice, Denver, CO.
2008–2009	*Jill Hall*: Private Practice, Oxnard, CA.
2008–2011	*Hiren Patel*: Academic, University of California, Irvine, CA.
2009–2011	*Gina Sternschuss*: Private practice, Upper Michigan.
2011–2013	*Lioudmila Lipiskaia*: Academic, Buffalo, NY.
2011–2012	*Ali Azadi*: Academic to private practice, Louisville, KY.
2013–2014	*Christina Truong*: Academic, UCLA, Torrance, CA.

Trainees of Professor Harold Drutz and Their Practice Locations

1980–1981	*Abrahim Shamai*: Rambam Hospital Israel.
1986–1989	*Thomas Mainprize*: Fellowship director in Calgary, then chair of the Department of Obstetrics and Gynecology, Saskatoon, Canada.
1990	*Jae Yup-Hong*: University of Korea, Seoul, Korea.
1989–1990	*Kevin Baker*: University of Ottawa, Ottawa, Canada.
1989–1990	*Douglas Torraville*: Corner Brook, Newfoundland, Canada.
1990–1991	*Marie-Claude Lemieux*: Head of obstetrics and gynecology, Maisonneuve, Rosemont, Montreal, Canada.
1991–1992	*Elaine Demarcousa*: New York City, USA.
1991–1992	*Clive Spence Jones*: London, UK
1992–1993	*Cathy Flood*: Created the division of urogynecology at the University of Alberta and was the director from 1993 to 2008, fellowship director of urogynecology, Edmonton, Canada.
1992–1994	*Patricia Lee*: Head urogynecologist at the Sunnybrook Hospital, Toronto, Canada.
1993–1994	*Paul Hardiman*: Hammersmith, UK.
1994–1996	*J. Barry MacMillan*: Head of urogynecology, University of Western Ontario, London, Canada.
1994–1996	*Robert Verhoest*: New York, USA.
1996–1998	*Bunan Alnaif*: Trainee from Canada and Iraq, now practicing in Vanderbilt, USA.
1996–1998	*Fons Amaye-Obu*: New York, USA, and Nigeria.
1997–1998	*Ian Currie*: Buckinghamshire, UK.
1997–1999	*Kevin Smith*: Reading, UK.
1998–1999	*Jane Schulz*: Divisional director of urogynecology, Edmonton, Canada.
1999–2000	*Corrinne Jabs*: Regina, Canada.
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2 Epidemiology: United States

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INTRODUCTION

Epidemiology, the study of the relationships of various factors determining the frequency and distribution of diseases in a community [1], as applied to the study of urinary incontinence (UI), has advanced over the past several years. However, most of these studies are cross-sectional. A need exists for more longitudinal studies to evaluate the incidence, remission, risk factors, and prevention of this disease process. The methodologies to evaluate the epidemiology of UI vary greatly. Furthermore, there is no consensus on the definition of UI among investigators dealing with this subject. Consequently, there is conflicting information, especially in the prevalence rates. Another major issue in studying UI is the fact that incontinence itself is a condition with many varied types, which can be transient and which can occur in many different segments of the population. Students of the epidemiology of UI must therefore account for all these variables when evaluating data from these studies.

PREVALENCE OF UI

Prevalence of UI is defined as the probability of being incontinent within a defined population group during a specific period. In 1983, Diokno et al. created the first comprehensive epidemiological study of incontinence in the United States [2]. The Medical, Epidemiologic, and Social Aspects of Aging (MESA) study showed the prevalence of incontinence among women 60 years and older living in the community to be 38%.

A recent cross-sectional analyses using data from the 2008 Nurses' Health Study among participants age 62–87 years revealed a prevalence of urine leakage at least once per month to be 38%, 7% fecal incontinence alone, and 7% dual incontinence [3].

UI prevalence in nursing homes is even higher. Offermans et al. [4] reported the prevalence rates based on analyzing 16 reported studies. The prevalence rate was reported to range from 43% to 77% (median 58%).

The prevalence of UI in women increases with age. A postal survey was conducted by Thomas et al. [5]. Incontinence was subdivided into regular UI for a loss twice or more per month and occasional for less than twice per month. Table 2.1 shows the prevalence rates for regular and occasional incontinence in women aged 15 to more than 85 years.

Several studies have investigated incontinence in women of different races and found intriguing results. Lower rates of stress and mixed incontinence were reported by African-American women when compared with white women [3,6]. Hispanic and Asian-American women have been shown to have equivalent urodynamic stress incontinence rates to white women, whereas the African-American women had higher rates of detrusor overactivity than the other three groups [7]. African-American women were found to have statistically significant smaller bladder capacities, smaller maximum cystometric capacities, and higher maximum urethral closure pressures compared to Caucasians [8]. Fenner et al. looked at the incontinence rates in African-American and Caucasian women in southeastern Michigan. They observed similar racial differences in prevalence, type, and quantity of urine loss but failed to find support for the belief that risk factors for UI differed between Caucasian and African-American women [9].

INCIDENCE AND REMISSION

Incidence is the probability of becoming incontinent during a defined period of time. Determining the incidence of a condition or disease is helpful in determining the onset of the condition as well as in understanding the risk factors of the condition. The MESA survey established the incidence rate of UI in the United States [10]. The incidence rate among women who were continent during the initial baseline interview and became incontinent a year later was 22.4%. For those who remained continent at the 1-year follow-up visit, the incidence in the second year of follow-up was 20.2%. Hagglund et al. found a mean 4% annual incidence rate of UI reporting on a Swedish community of 10,500 inhabitants aged between 22 and 50 years [11]. An annual incidence rate of 6.3% for people greater than or equal to 40 years old was found in McGrother et al.'s study in the United Kingdom [12]. Two thousand twenty-five women older than 65 years in rural Iowa were evaluated by Nygaard and Lemke. The 3-year incidence rate for urge incontinence and stress incontinence were 28.5% and 28.6%, respectively [13]. Maserejian et al. reported the incision of UI based on the Boston Area Community Health Survey (BACH) of 3201 women age 30–79 years. They reported the incidence of UI at least monthly to be 17.1% and weekly 8%–9%. Among women with weekly baseline UI, 41.7% continued to report weekly UI, 14.1% monthly UI, and 44.2% had complete remission [14].

The MESA survey also analyzed the remission rate for UI. The remission rate—that is, women who were incontinent at the baseline (first) interview and became continent during the second interview a year later—was 11.2%. A similar rate (13.3%) of incontinent respondents at the second interview reported being continent a year later at the third interview. Hagglund et al. reported a 4% mean annual remission rate in the same Swedish community mentioned earlier [11]. Nygaard and Lemke's 3-year remission rates for urge and stress incontinence were 22.1% and 25.1%, respectively [13]. Townsend et al. looked at remission rates in 64,650 women 36–55 years of age participating in the Nurses' Health Study II. They reported remission rates of 13.9% at 2-year follow-up. However, when the group was further delineated by age group, they found significantly higher remission rates in women 36–45 years of age when compared to those 46–55 years of age (17.1% vs. 11.9%) [15].

Table 2.1 Prevalence of Urinary Incontinence in Women

Years	Regular UI (%)	Occasional UI (%)	Total UI (%)
15–24	4.0	11.9	15.9
25–34	5.5	20.0	25.5
35–44	10.2	20.7	30.9
45–54	11.8	21.9	32.9
55–64	11.9	18.6	30.5
65–74	8.8	14.6	22.4
75–84	16.0	13.6	29.6
>85	16.2	16.2	32.4

Source: Offermans MP et al., *Neurourol Urodyn*, 28(4), 288, 2009.

These findings suggest a proportion of women affected by UI will improve over time without intervention. Because UI can be affected by many factors such as acute illness, seasonal changes, and fluctuating medical illnesses, it can be assumed that when questioned longitudinally many women would report varying degrees and prevalence of incontinence. Implying that for many patients, UI is not necessarily a progressive condition but rather a dynamic process that may come and go with or without medical or surgical intervention. Further studies are needed to determine factors that may predict which respondents tend to have remission and which tend to persist or progress. It is also important to consider the possibility of spontaneous remission when reviewing "cure" rates reported in treatment trials and to discuss the possibility of remission/recurrence when counseling patients.

TYPES AND SEVERITY OF UI

Prevalence and Incidence of Types of UI

In epidemiological studies, as in clinical investigations, the type of UI must be defined. In general, incontinence is considered to be of the stress type when the urine loss was experienced at the time of physical exertion (such as coughing, laughing, sneezing). Urge incontinence is defined as involuntary loss of urine preceded by a sudden urge to void. When the urine loss is associated with both stress and urge, it is considered to be of the mixed type. Because of the difficulty in identifying the overflow type, when the urine loss is associated with neither the stress nor the urge type, the incontinence is labeled "other." However, when the survey respondents were taken one step further into urodynamic testing, the type of incontinence has been classified into the various urodynamic types according to the pathophysiological abnormality.

Interestingly, when urodynamic testing is performed on women with UI, there is often a discord between subjective and objective findings [16–18]. Cundiff et al. evaluated 535 women over a 10-year period via detailed history and physical exam, urinary diary, and urodynamics. They found that by utilizing symptoms alone, a misdiagnosis would be made in 13% of women reporting only stress incontinence and 59% of women reporting only urge incontinence [19]. Some of this can likely be explained by the artificial nature of office urodynamics and other technical issues, but patient's poor understanding of the different types of UI and incomplete history taking may also be implicated.

The age of onset may be an important factor in the type of UI experienced. Kinchen et al. found the median age of American women reporting stress incontinence was 48 years, mixed incontinence was 55 years, and urge incontinence was 61 years [20]. Luber et al. evaluated 642 incontinent women and discovered that stress incontinence was more common in younger women aged 30–49 years (78%) versus those aged 50–89 years (57%). Urge incontinence predominates in the older population (67%) versus women under the age of 50 years (56%) [21].

According to Nygaard et al., the rate of urge incontinence tends to rise with age, while the rate of stress incontinence decreases somewhat in the oldest age groups, possibly due to lower activity levels [13] (Figure 2.1).

The MESA survey conducted by Diokno et al. [2] in Washtenaw County, Michigan, reported the prevalence of the types of clinical incontinence encountered among their respondents. The most common type reported by these women aged 60 years and older was the mixed stress and urge type (55.5%), followed by the stress type (26.7%), the urge (9.0%), and other types (8.8%).

A meta-analysis of published studies of UI epidemiology in the world suggested that stress incontinence is the most common form [22]. Stress incontinence accounted for almost half of the total worldwide prevalence of UI and mixed incontinence constituted 29% of the total prevalence. The analysis showed that urge incontinence was less common, consistent with the U.S. and European surveys.

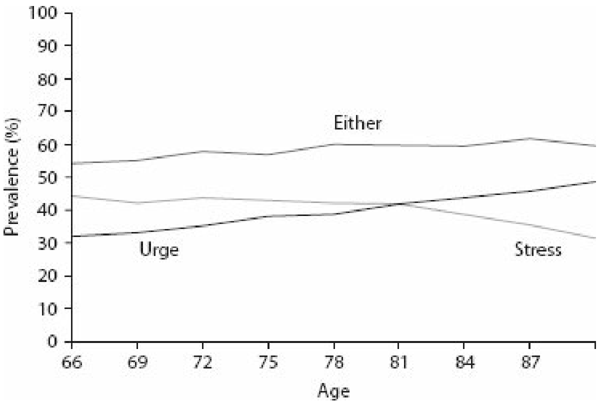
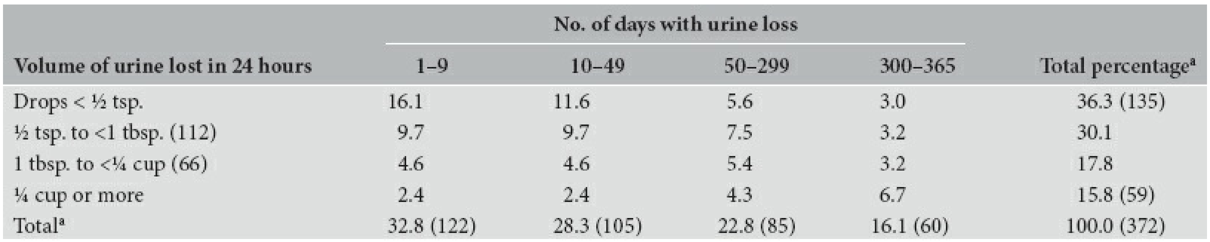


Figure 2.1 Prevalence of incontinence by age groups at baseline. Each age represents the midpoint of a three-year age range. Because of the small number of women above age 90, the graph ends with age range 86–88 years. "Urge" and "stress" refer to women who answered affirmatively to the urge and stress incontinence questions, respectively. "Either" refers to women who reported any incontinence (either urge or stress). (Data adapted from McGrother CW et al., *Br J Urol Int*, 93, 763, 2004.)

Table 2.2 Percentage of Severe Incontinence, as Judged by Volume and Frequency of Urine Loss, in 60-Year-Old Women



Volume of urine lost in 24 hours	No. of days with urine loss 1–9	10–49	50–299	300–365	Total percentage[a]
Drops < ½ tsp.	16.1	11.6	5.6	3.0	36.3 (135)
½ tsp. to <1 tbsp. (112)	9.7	9.7	7.5	3.2	30.1
1 tbsp. to <¼ cup (66)	4.6	4.6	5.4	3.2	17.8
¼ cup or more	2.4	2.4	4.3	6.7	15.8 (59)
Total[a]	32.8 (122)	28.3 (105)	22.8 (85)	16.1 (60)	100.0 (372)

Source: Diokno AC et al., *J Urol*, 136, 1022, 1986.

*Note:*Respondents with mild incontinence were those who reported low frequency (1–9 days/year) and/or small volume (<½ teaspoon/day for <300 days/year); those with severe incontinence were those who reported high frequency (≥300 days/year) and/or large volumes (>¼ cup/day on ≥50 days/year); those respondents with intermediate volume and/or frequency were considered to have moderate incontinence.

[a] Number of patients in parentheses.

Prevalence and Incidence of Severity of UI

In epidemiological studies, severity has been categorized by the frequency of incontinent episodes, by the volume of urine loss, or by the frequency of difficulty in controlling the flow of urine. The Diokno MESA study [2] reported the severity of UI among its 60-year-old respondents in terms of the number of days per year that urine loss was experienced and the volume of urine loss per day. As shown in Table 2.2, if severe or significant UI is considered to be the loss of at least a quarter cup of urine per day on 50 or more days/year, and frequency of incontinence is 300 or more days/year regardless of volume, then 20.4% of women respondents age 60 years and older at the time of the MESA survey had severe incontinence.

The patterns of change in the severity of UI in the MESA survey were also analyzed [10]. Based on the severity levels described in Table 2.2, continent respondents who became incontinent were most likely to develop a mild form of incontinence. About half of those who were classified originally as mildly incontinent remained so and very few became severely incontinent. Among those who reported moderate incontinence, most remained moderately incontinent or changed to mildly incontinent, with very few advancing to severe incontinence. Among women who were severely incontinent at baseline, most remained severely incontinent.

Kinchen et al. revealed that over 50% of incontinent respondents have urine loss at least once per week [20]. The severity of incontinence symptoms influences a woman's willingness to discuss the symptoms with a physician. Fewer than 20% of women report discussing incontinence with a physician within the past year when symptoms are mild. The proportion increases to 42% of women when symptoms are severe [23].

Prevalence of Voiding Frequency

The prevalence of voiding frequency is receiving greater attention as more and more studies are being conducted for conditions related to bladder dysfunction. For example, pharmacological interventions and behavioral techniques aimed at improving bladder function usually affect the frequency of voiding day and night. It is therefore imperative that a comparative standard is available on which to base any observations related to frequency of voiding prior to, during, and after an intervention.

The MESA study has established the distribution of voiding frequency among the elderly (60 years and older) living in a community, who are likely to be the subjects of pharmacological and behavioral interventions aimed at controlling abnormal voiding [2]. It appears that the normal daily frequency of urination in this age group is no more than eight times, as 88% of all our asymptomatic respondents reported that range. To be more specific, 47.3% of asymptomatic women reported that they voided six to eight times, 34.8% voided four or five times, and 5.5% voided one to three times daily. FitzGerald et al. reevaluated the definition of urinary frequency by evaluating 300 asymptomatic women aged 18–91 (median 40 years) who volunteered from a large metropolitan community. These women completed a 24-hour log of fluid intake and volumes voided. They found a median of eight voids in 24 hours with 95% of subjects recording less than 13 voids per 24 hours. Their conclusion was that using greater than or equal to eight voids per 24 hours as the definition of "frequency" may be inappropriate, suggesting that "frequency" may be greater than or equal to 13 voids in 24 hours [24]. Since the information came from a self-selected group of volunteers that reside in a large metropolitan area, their findings may not represent the true frequency of voiding in the general community.

In an investigation by the Bladder Diary Research Team, 161 asymptomatic women from 19 to 81 years of age were recruited at four independent research sites. Each subject completed a 3-day bladder diary to establish normative values based on age and 24-hour urine volumes. They found that there was a statistically significant increase in frequency with increased age and 24-hour volume. They also found a mean of 7.1 voids per 24 hours, with a range of 2–13, and that 95% of subjects recorded less than 10.4 voids per 24 hours [25]. The same group looked at 92 asymptomatic males from 20 to 84 years of age. They found a mean frequency of 6.6 with a range of 3–14 and 95% voiding less than 9.5 times per 24-hours [26]. While the numbers are slightly lower than those from the MESA study, they bolster their conclusion that utilizing eight voids as the definition of frequency may be incorrect and may need to be adjusted based on age and 24-hour urine volume.

In terms of nocturia—which was defined as the frequency of being awakened from sleep and getting up to void—93% of asymptomatic women voided no more than twice at night? In contrast, 25% of women with irritative symptoms and 24% of women with difficulty in emptying the bladder voided three or more times each night [2]. These data suggest that abnormal bladder function has a significant effect on the frequency of voiding. Incontinent women are voiding much more frequently than continent women. FitzGerald et al. [24] recorded nighttime voids in 44% of their population. While 8% voided greater than or equal to two times per night, 36% voided once during the night. The number of nighttime voids was dependent only on the patient age.

QUALITY OF LIFE

UI has a significant impact on a woman's quality of life. Fultz et al. examined 174 respondents who were moderately to extremely bothered by stress incontinence symptoms. Of these women, 54.4% reported that their symptoms had a moderate to extreme impact on physical activities and 42.7% perceived such impact on confidence, 38.6% on daily activities, and 36.5% on social activities [3]. The odds of moderate-to-extreme bother/burden decreased with age and increased with symptom severity.

The relative risk of admission to a nursing home is two times greater for incontinent women according to Thom et al. [27]. Over half of all female nursing home residents are reported to have "difficulty controlling urine," and over half need assistance in using the toilet [28].

PREVALENCE OF URODYNAMIC MEASURES AMONG CONTINENT AND INCONTINENT ELDERLY WOMEN

To establish the urodynamic characteristics of both continent and incontinent elderly women living in a community, a series of urodynamic tests were conducted on those MESA respondents who volunteered to undergo such tests [29,30]. This study provided information on the prevalence of the various parameters in the urodynamic tests that are of interest in the evaluation of incontinent patients but for which there are no well-established data from control subjects. The MESA survey data established the sensitivity and specificity of the various urodynamic tests, from which it was concluded that such tests—including uroflow, cystometrography, static urethral profilometry, and stress cystography—should be used, not to screen and diagnose UI but, rather, to confirm clinical manifestation. Recent studies confirmed the lack of concordance between clinical manifestations and urodynamic findings [16–18].

The MESA survey studied a random sample of noninstitutionalized ambulatory elderly women, both continent and incontinent; an initial clinical evaluation was followed by a series of urodynamic evaluations. A total of 258 self-reported continent and 198 self-reported incontinent women underwent the clinical evaluation comprising history taking, physical examination (including pelvic examination), and urinalysis. From these groups, 67 continent and 100 incontinent women underwent urodynamic testing including an initial noninstrumented uroflow test, followed by catheterized postvoid volume measurements, followed by filling cystometry, static and dynamic urethral profilometry, provocative stress test, and lateral stress resting and straining cystogram.

UROFLOWMETRY

The uroflow measures of peak flow rate (PFR) and average flow rate (AFR) were analyzed according to the voided volume at increments of 100 mL. When volume was controlled, the mean PFR and AFR did not differ significantly between respondents who were continent and those who were incontinent. The flow rates did not differ between women with competent sphincters and those with urethral incompetence. The continuity of the urinary stream was not associated with continence status or with the clinical type of incontinence (i.e., urge, stress, etc.).

Postvoid Residual Volume

A postvoid residual volume of 0–50 mL was found in 78.1% of continent and 86.5% of incontinent women, 9.7% and 8.4% had residuals of 51–100 mL, 2.4% and 1.6% had residuals of 101–150 mL, and 9.7% and 3.5% had residuals of 151 mL or more, respectively. There was no statistical difference between continent and incontinent women with regard to prevalence of a residual urine volume greater than 50 mL. These data give rise to questions regarding the postvoid residual volume in relation to the diagnosis of overflow incontinence: the determining factor for overflow incontinence may be the same factor as for urge and/or stress incontinence, and the abnormal postvoid residual volume may be coincidental or a contributory factor rather than a primary reason for the incontinence.

Bladder Capacity

Among the women volunteers, 79% of continent volunteers and 64% of incontinent volunteers had a bladder capacity of 300 mL or more; however, this difference in bladder volume between continent and incontinent subjects was not significant. The mean cystometric bladder capacities among 60- to 64-year-old continent and incontinent subjects were 381.8 and 442.7 mL, respectively; for 65- to 69-year-old subjects, they were 421.6 and 370.0 mL; for those aged 70–74 years, they were 410.3 and 414.2 mL; for those aged 75–79 years, they were 350.3 and 426.8 mL; and for those aged 80 years old or more, they were 318.3 and 408.3 mL, respectively. These results refute the notion that the bladder capacity of the elderly is smaller than normal, if we consider a bladder capacity of 300 mL or more to be normal.

Uninhibited Detrusor Contraction

The diagnosis of uninhibited detrusor contraction was based on the definition by the International Continence Society. The overall prevalence of uninhibited detrusor contraction in women was 7.9%; the prevalence of uninhibited detrusor contraction among continent respondents was 4.9%, whereas for incontinent subjects, it was 12.2%. The difference between the two prevalence rates was not significant. However, comparison of the bladder capacity between female respondents showed that the capacity in women with uninhibited detrusor contraction was 364 mL, whereas in those without uninhibited contractions, it was 404 mL; the difference was statistically significant at $p < 0.05$. This may explain the increased frequency, urgency, and smaller voided volumes of patients with detrusor overactivity.

Static and Dynamic Urethral Pressure Profilometry

The mean functional urethral length (FUL) did not change significantly as the age of the subjects increased, but the values of the maximum urethral pressure (MUP) and the maximum closure pressure (MCP) showed a significant progressive reduction as age increased ($p = 0.002$ and $p = 0.0003$, respectively). This progressive reduction of MUP and MCP reinforces the belief that elderly women are more predisposed to stress urine loss.

The parameters of urethral pressure profilometry for supine subjects did not show any significant difference between continence and incontinence. However, for standing subjects, significant differences were observed between continent and incontinent groups with respect to MUP, which was significantly ($p = 0.0025$) lower in the incontinent compared with the continent group. Likewise, the MCP and the FUL were significantly reduced in standing but not in supine incontinent subjects when compared with the continent group.

The results of dynamic profilometry were reported as either positive (zero or positive reading), corresponding to incontinence, or negative (corresponding to continence). There was no significant difference between incontinent and continent subjects in the supine position, but there was between the groups in the standing position. Despite this significant difference, there was a great deal of overlap between the results for the continent and incontinent groups, invalidating a diagnosis based on this test alone. However, these findings lead credence to weakened pelvic floor muscle support for incontinent woman in the standing position.

Lateral Stress Cystography

Comparison between continent and incontinent subjects and between those with different types of incontinence, with regard to urethral axis, posterior urethrovesical angle (PUV), and distance of urethrovesical junction to the urogenital diaphragm (UGD), showed that incontinent respondents had a significantly (*p* = 0.001) wider PUV angle than did continent respondents; however, no significant difference was observed between stress and nonstress types of incontinence. There was no difference in the urethral axis and the position of the bladder neck in relation to the UGD between the groups according to continence status or clinical type of incontinence. There was a significantly greater mean PUV angle among incontinent subjects with an incompetent sphincter than among continent subjects with a competent sphincter (*p* = 0.004); however, neither the measurements of the urethral axis nor the location of the UGD differed between these two groups.

PROVOCATIVE STRESS TEST

A provocative cough stress test was found to be significantly correlated to continence and incontinence status and, more specifically, to the stress type of urine loss with or without urge loss (*p* = 0.0005). The result of the stress cystogram, when correlated with the stress test, showed a strong association (*p* = 0.009). A urethral axis of 30° or more is more likely to give rise to a positive stress test than is an axis less than 30°. The stress test can be performed as part of the initial office evaluation and does not require special equipment: there is no morbidity, it is inexpensive and (more importantly) it has extremely high specificity; it should be a part of everyone's initial evaluation. However, a negative test in someone who is experiencing UI does not rule out its existence, as sensitivity of the test often is only 40%.

Medical Correlates of UI

Several medical conditions have been associated with UI in women. Difficulties with physical mobility, lower urinary tract symptoms, bowel problems, and diabetes are more common in women with incontinence. Other factors associated with UI include a family history of incontinence, vaginal childbirth, and estrogen hormone use. Many of these associations were identified through the MESA survey [31].

Patients who used wheelchairs or walking aids had a diagnosis of arthritis or who had fallen in the past year were defined as having mobility difficulties in the MESA survey. In women with mobility problems, urge incontinence was more common than any other type.

Regarding urinary tract and bowel problems, women with UI had a history of more urinary tract infections, dysuria, hesitancy, urgency, and slow stream than continent women. In addition, those who had more fecal incontinence or constipation had a higher rate of UI. Women with stress incontinence were the least likely of all urinary incontinent patients to lose control of their bowels.

Diabetes effects more than 12% of adults older than 40 and the prevalence increases to 19% of adults older than 60 [32]. Diabetic women have a 30%–70% increased risk of UI [31,33,34]. The risk of urge incontinence was increased about 50% among women with diabetes, while they had no increased risk of stress UI [6]. The mechanism for the incontinence is unclear. Possibilities include hyperglycemia [35] and microvascular complications causing altered innervation to the bladder [36]. Most prior studies on diabetic people with incontinence were conducted on elderly patients with type 1 diabetes who may have had other neurological or urological reasons for their incontinence. A recent cross-sectional analysis of a younger cohort of type 1 diabetics from the Epidemiology of Diabetes Intervention and Complication study demonstrated twofold greater odds of urge incontinence and 50% greater odds of stress incontinence compared to a matched cohort from the National Health and Nutrition Examination Survey [37]. Furthermore, UI was found to be more prevalent than neuropathy, retinopathy, or nephropathy. Data from the prospective, observational Nurses' Health Study cohort of more than 70,000 married registered nurses found type 2 diabetes to be a strong independent risk factor for UI [38,39]. In addition, the study found that the risk of incontinence increases with the duration of type 2 diabetes allowing the investigators to conclude that simply delaying the onset of diabetes could have important public health implications. Data from the Diabetes Prevention Program in prediabetic women showed that total weekly incontinence at three years was lowest in women randomized to the intensive lifestyle (34%) compared with metformin (48%) or placebo (46%) [40]. Weight loss accounted for the largest impact on incontinence in this study and underscores the difficulty the role of many confounding factors such as parity, stroke, diabetes, age, and body weight play in drawing causative conclusions. Further research is needed to define the role diabetes plays in UI and the impact intervention may have on decreasing its incidence. Females with incontinence more often reported a parent or sibling with UI than continent women. It was also noted that UI patients had a higher rate of personal UI during adolescence versus continent patients.

There is an increased risk of later UI after a vaginal delivery, even after the first delivery [41]. An increased risk of surgery for the stress UI is also seen after a vaginal delivery [42]. During pregnancy, there is an increased prevalence of incontinence, especially in the third trimester, which usually resolves shortly after delivery [43]. Possible etiologies are hormonal changes during pregnancy, damage to the pelvic muscles, and nerve injury during labor and delivery [44]. It is difficult to identify the specific parturition risk factors, as there are many potential, interrelated factors that occur during a single pregnancy and delivery. Most observational studies have demonstrated that cesarean sections are protective against incontinence versus vaginal deliveries [45,46]. The EPINCONT study of more than 15,000 Norwegian women demonstrated overall incontinence rates of 10% of nulliparous, 16% of cesarean section, and 21% in vaginal delivery only women [47]. However, the protective role of cesarean section diminished when adjusted with increasing age. An interesting study of identical twins at the annual Twins Day Festival in Twinsburg, Ohio, found that vaginal delivery more than doubled the report of stress UI compared to cesarean section [48]. In 2007, a systematic review of the literature by Press found that cesarean section reduced the risk of postpartum stress UI from 16% to 9.8% in six cross-sectional studies and from 22% to 10% in 12 cohort studies [49]. From these data, they calculated that between 10 and 15 cesarean sections would need to be performed to prevent one woman from developing SUI. Less is known about the cesarean section timing (before labor, in labor but without pushing, or in labor and pushing) and its effect on incontinence. A study of Israeli women 1 year after their first delivery found similar stress UI rates in women undergoing vaginal deliveries (10%) and cesarean for obstructed labor (12%) compared to planned cesareans (3%) [50].

Historically, estrogen, either vaginal or oral, was thought to improve incontinence episodes in postmenopausal women. The trigone and urethra are covered by nonkeratinized squamous epithelium, and these tissues contain estrogen receptors [51] and respond to estrogen [52]. There have been many uncontrolled trials demonstrating subjective improvement in incontinence, while a few randomized controlled trials showed no significant difference between control and treatment groups [53,54]. The Heart Estrogen Replacement Study found intriguing UI outcomes when comparing a regimen of conjugated estrogen and medroxyprogesterone acetate with placebo [55]. Incontinence improved in 26% of women given placebo compared to 21% assigned to combined estrogen/progestin, whereas 27% worsened in the placebo group compared to 39% receiving hormonal replacement. They concluded the effect of estrogen might be cancelled by the progesterone, as progestin has been shown to decrease intraurethral closing pressure.

In the United States, approximately 31% of adults are obese and 33% are overweight, with the most rapid increase among those in the younger (18–29 years) age range [56]. Numerous epidemiological studies have demonstrated an association between obesity and stress UI. Women with a median body mass index (BMI) of 28.2 had a higher incidence of UI than those with a BMI of 25.5 (normal range) [57]. Odds ratios as high as 1.6 per 5-unit increase in BMI have been demonstrated [56]. The additional weight is believed to result in higher pressures on the bladder and causes an increase in urethral hypermobility. In a urodynamic evaluation study of subjects from the Program to Reduce Incontinence by Diet and Exercise trial, BMI had a stronger association with intra-abdominal pressure than with intravesical pressure [58]. The authors suggested that increasing weight might push women closer to their threshold for UI episodes even if their intrinsic continence mechanisms are comparable. Randomized nonsurgical weight reduction studies suggest losing 5% or more of body weight can lower UI episodes by as much as 70% [56]. In fact, reduction in UI frequency has been suggested to be a powerful motivator for lifestyle modification. UI following gastric bypass surgery has resulted in similar reductions, which correlate significantly with decrease in BMI [56,59]. The BACH survey reported that the waist circumference at baseline and increasing waist circumference over 5-year follow-up were the most robust predictors of UI incidence. They also reported that for incontinent at baseline, persistence of UI was associated with depression symptoms and alcohol consumption [14]. Nygaard et al. also reported the association between depression and incontinence in middle-aged women [60].

Patterns of Reporting of UI

According to a nationwide, two-staged, cross-sectional postal survey conducted by the NFO World group [61], 41.6% of incontinent women believed their incontinence was a natural part of growing older and 47.0% accepted it as a part of their life.

Approximately 86% of women reported being bothered by symptoms of UI, with 25.6% reported being moderately bothered, 14.5% very bothered, and 8.5% extremely bothered. Only 44.9% of these incontinent women had ever talked to a physician about it. Those who were more bothered by their symptoms were more likely to have talked to a physician (not bothered, 25.2%; slightly bothered, 37.1%; moderately to extremely bothered, 56.5%). Older women were also more likely to talk to a physician than younger women (53.5% vs. 39.8%).

Of the incontinent women who spoke with a physician, 2.9% first talked with a family practitioner, 35.1% with an obstetrician–gynecologist, 10.9% with an internist, and 4.4% with an urologist. Of all women who initially spoke with an internist or family practitioner, 19.0% were later referred to a urologist and 17.3% to a gynecologist.

Coping Strategies to Control UI

Patient self-care practices were also evaluated by the NFO World group [61]. Of all the women surveyed (bothered and nonbothered by UI), 42.1% currently used panty liners, 33.5% used the toilet frequently even when they did not have an urge to urinate, and 29.5% sought out a toilet immediately upon arriving at an unfamiliar location. Of the incontinent women, 23.3% limited their fluid intake and pelvic floor muscle exercises were performed by 19.9% of all UI women and by 20.3% of women with stress symptoms only. Only 6.3% of all the women are currently being treated with prescription medications and 2.1% have had surgery for their UI.

CONTINENT SURGERY AND ITS OUTCOMES

An estimated 126,000 continence surgeries are performed annually in the United States [62]. A review of the literature demonstrates that the median proportion of women cured or improved by surgery at 1–2 years was 78% for anterior repair, 86% for retropubic suspension, and 91% for sling procedures [63]. However, the NFO World group panel evaluated the prevalence and outcomes of continence surgery in community-dwelling women via a postal survey [64]. Four percent of community-dwelling women and 8% of women 60 years or older had a history of continence surgery. The initial satisfaction of surgery was high but then decreased as time progressed. Of those who had surgery within the past 3 years, 64% were currently satisfied, where only 41% were satisfied if their surgery was 3–5 years ago. Seventy-three percent of the women who had surgery reported incontinence in the preceding month, 58% in the preceding week, and 53% who used pads. Of those with recurrent UI, 83% complained of stress incontinence. One-third of the women had their surgery within the last 5 years.

PREVALENCE OF PELVIC ORGAN PROLAPSE

Pelvic organ prolapse is often a concurrent problem with UI. The prevalence of pelvic prolapse was evaluated by Hendrix et al. in 2002 by analyzing women who enrolled in the Women's Health Initiative Hormone Replacement Therapy Clinical Trial [65]. In women with a uterus, the rate of uterine prolapse was found to be 14.2%, cystocele was 34.3%, and rectocele was 18.6%. For women who had a hysterectomy, the rate of a cystocele was 32.9% and a rectocele was 18.3%. Hispanic women had the highest risk for uterine prolapse and African-Americans had the lowest risk. Finally, parity and obesity were strongly associated with an increased risk of uterine prolapse, cystocele, and rectocele. Nygaard detected no difference in prevalence by racial/ethnic group regarding pelvic floor disorders. The prevalence of women experiencing pelvic organ prolapse was 2.9% [66].

ECONOMIC BURDEN OF UI

The direct and indirect financial impact of UI on our health-care system is significant. Hu et al.

estimated the total cost of UI was $19.5 billion (year 2000 dollars) [67]: $14.2 billion was due to community residents and $5.3 billion due to institutional residents. The direct costs for community residents, which included absorbent products, laundry, treatment, and consequences (UTIs, etc.), were $13.66 billion. Indirect costs, which involved lost productivity secondary to missing work, for community residents was estimated to be $553 million, with a $393 million loss for women and $159 million loss for men. For the institutionalized individual, the direct cost is $5.32 billion.

PREVENTION OF UI IN THE COMMUNITY

One of the ultimate goals of any epidemiological study is to improve population health through prevention based on lessons learned. The MESA epidemiological project in the first 20 years has contributed to the knowledge on prevalence, incidence, remission rates, and correlates of UI. The team members also established the efficacy and safety of behavioral modification program (BMP) in managing geriatric incontinence. It became clear that the next step (armed with this information) is to apply the BMP not only for treatment but also for prevention of UI.

Diokno et al. then embarked on a randomized controlled study using BMP taught to groups of women who were incontinent or having no more than five UI episodes in the last 365 days based on the MESA questionnaire. A 2-hour class presentation of BMP was given to the intervention group of 164, whereas the control group of 195 did not receive any instruction. At the end of 12 months, the primary outcome measure was the number of days UI occurred based on the MESA questionnaire. Secondary measures included voiding frequency and the intervoid interval based on a 3-day voiding diary. At 12 months, the treated group was statistically significantly better than the control group in continence status ($p = 0.01$) (Figure 2.2), pelvic muscle strength (Figure 2.3) (pressure score $p = 0.0003$ and displacement score $p < 0.0001$), improved voiding frequency ($p < 0.0001$), and intervoid interval ($p < 0.0001$) [68].

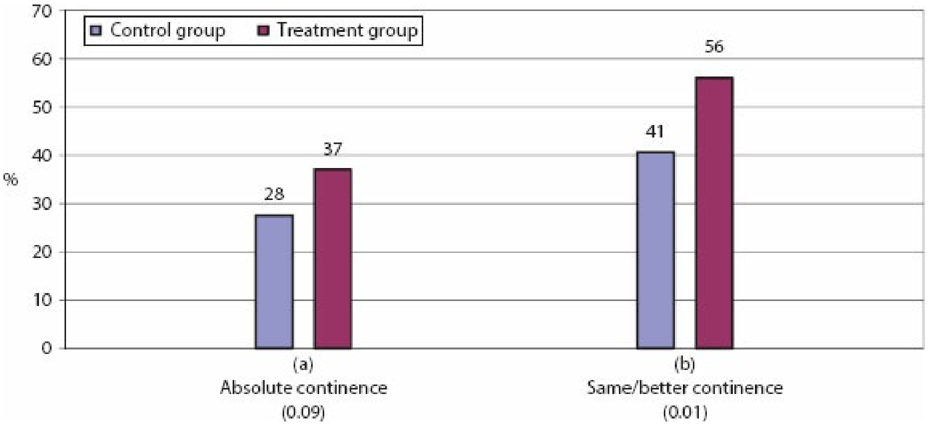


Figure 2.2 Continence in control and treatment groups at 12-month exit. At baseline, two groups reported identical 39% absolute continence and 0 urinary incontinence (UI) days with 61% of participants reporting 1–5 UI episodes in a year. (a) Absolute continence criterion: Percentage of participants that remained or became absolute continent at exit. (b) same (0 or 1–5 UI days) or improved continence criterion: Percentage of participants with the same or improved continence level at exit. The bars represent percent of participants. Values in parentheses represent control vs. treatment *p*-values. (From Diokno AC et al., *J Urol*, 171, 1165, 2004. With permission.)

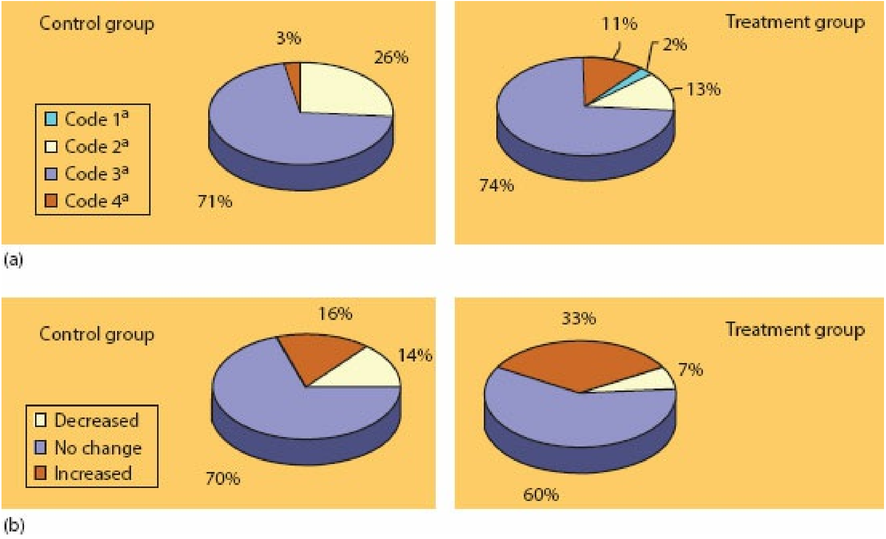


Figure 2.3 Pelvic floor muscle strength scores in treatment and control groups. (a) Portion at each strength level. At 12-month exit, treatment group had higher digital pressure scores than controls, suggesting stronger pelvic floor muscles (*p*-value = 0.0003). (b) Changes in pressure scores at 12-month exit vs. baseline (p-value = 0.0008). More treatment than control participants had improved score at exit compared with baseline. [a]Pressure codes: 1, no pressure; 2, flick and incomplete circumferential pressure points; 3, full but loose circumferential pressure to being snug; 4, circumferential compression to overriding of fingers. (From Diokno AC et al., *J Urol*, 171, 1165, 2004. With permission.)

CONCLUSION

UI is a prevalent condition that can affect women of all ages. The incidence is especially high in the elderly population. UI is associated with many medical conditions. Urodynamic testing can help explain the mechanism of UI. Many women with UI think that it is a part of the normal aging process and do not talk to their physicians about this condition. Despite the advancement in medical and surgical treatment of UI, many women's satisfaction rates with treatment are not as high as some physicians perceive it. Recent randomized controlled trial of BMP for preventing UI in older women demonstrated feasibility and efficacy in improving continence status, pelvic muscle strength, and voiding control for as long as a year after treatment.

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3 Epidemiology: South America

Paulo C.R. Palma, Miriam Dambros, Fábio Lorenzetti, and Fabio Thadeu Ferreira

INTRODUCTION

Worldwide, urinary incontinence (UI) is a common problem that can affect 17%–45% of adult women. The high cost in terms of personal well-being [1] and financial expenditure for both individuals and society [2,3] makes this syndrome a major public health concern. The most prevalent type is stress incontinence, being responsible for 48% of all cases. Next to stress incontinence, urge incontinence is the second most prevalent cause of incontinence (8%–17%) [4,5]. Mainly due to shame, taboo, and unawareness of treatment possibilities, only a minority of women suffering from incontinence seek professional help. In daily practice, patients usually seek help only when urine loss leads to significant mental, physical, and social problems, as well as discomfort, often after many years of suffering. The prevalence of UI is the probability of being incontinent within a defined population at a defined point in time, estimated as the proportion of incontinent respondents identified in a cross-sectional survey [6]. The World Health Organization (WHO) defines health not only as the absence of disease but also as a "state of physical, emotional and social well being" [7]. According to the old International Continence Society definition, UI causes hygienic and social problems [8], and results in quality-of-life (QoL) impairment, depression, and sexual problems [9]. UI has a significant impact on the QoL of 20% of women [10]. Epidemiological studies dealing with UI are sparse and methodologies varied. In South America, very little research has been done on this subject, and, as a consequence, there is conflicting information, especially in respect to South American prevalence rates.

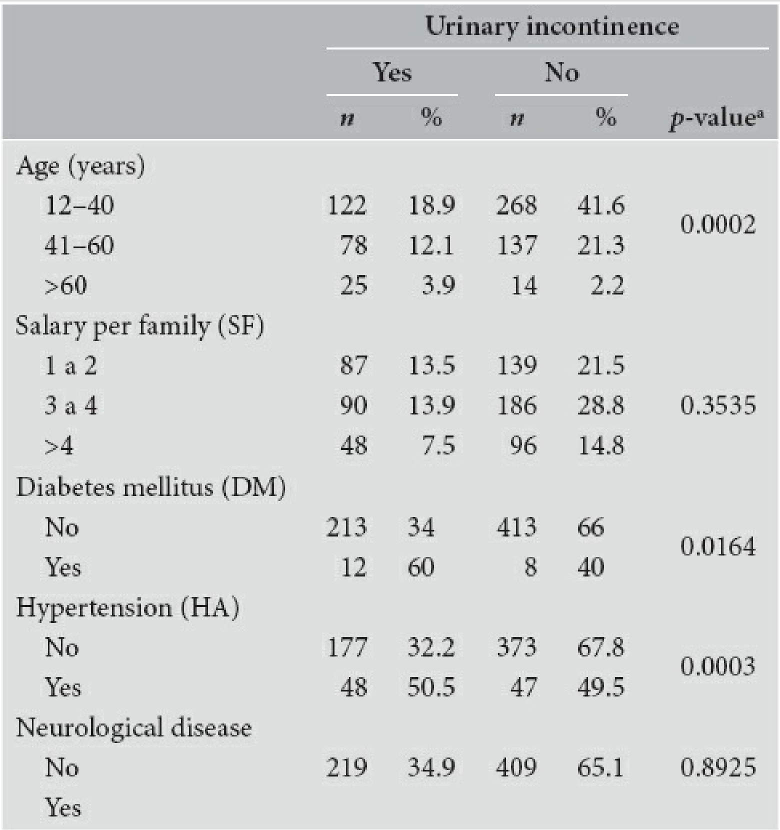
ETIOLOGICAL FACTORS

It is generally believed that the main etiological factor leading to UI is one or more vaginal deliveries, with an increase in risk with greater parity [11]. Possible etiologies for UI include distension or disruption of the muscles, ligaments, and nerves responsible for bladder control that occurs during vaginal delivery [12]. Other authors, however, have found that the occurrence of UI during pregnancy in nulliparous women has a stronger association with persistent incontinence after delivery than with parity [13]. This would suggest a more significant effect from pregnancy itself than the process of vaginal delivery. Women who are not exposed to vaginal childbirth by having all their babies by cesarean section (CS) offer the opportunity to check the relative relevance of pregnancy itself, as compared with vaginal delivery, as a risk factor for UI.

Tamanini et al. evaluated women to identify prevalence, associated factors, and risk factors for UI as well as the impact on the QoL in women seeking for cancer prevention screening. The method of choice was cross-sectional analysis of 646 women who sought cancer prevention screening in Oncologic Hospital in October 2005. The prevalence, severity, and impact of UI on the QoL were assessed by means of International Consultation on Incontinence Questionnaire (ICIQ-SF) [14]. Mean age was 37.7 years (ranging from 12 to 79). General UI prevalence rate reached was 34.8%. The ICIQ-SF final score from the whole population sample was 3.1 (ranging from 0 to 21) increasing to 8.9 in the incontinent group. Age, literacy, diabetes, and hypertension were associated with UI and were considered and identified as risk factors along with frequency of pregnancies (Table 3.1). Family wages per month (<4), neurological diseases, and parity and its mode (vaginal delivery or CS) were not considered risk factors in this study. Elderly women (older than 60 years) had three times the odds of UI compared to those younger than 40 years. Women with hypertension had 1.7 the odds of UI compared to those with no hypertension. UI was highly prevalent among this sample of population of our area. Furthermore, UI caused moderate impairment on the QoL (Table 3.2) of women who sought cancer screening. UI should be considered a major public health problem in the studied area. Risk factor identified were age (Figure 3.1), literacy, diabetes, hyperlipidemia, absence of physical exercises, intense manual labor, frequent urinary infections, hypertension, and frequency of pregnancy and vaginal delivery with episiotomy [15]. Overall, elderly women with hypertension are at a high risk of UI [16].

Latin America has one of the highest rates of CS in the world, with a tendency toward a further increase. Recent estimates indicate that the incidence of CS varies between 16.8% and 40% in most Latin American countries [17] and that this rate is higher in private hospitals than in public hospitals. In addition, the incidence of CS is greater in those Latin American countries with a higher per capita gross domestic product. Although strategies to reduce CS rates have been proposed, very few have been assessed through randomized controlled trials.

Table 3.1 Demographic Data on Continent Patients (ICIQ-SF Final Score = 0) as well as Incontinent Patients (3 ≥ ICIQ-SF Final Score ≤ 21) (n = 646)



	Urinary incontinence				
	Yes		No		
	n	%	*n*	%	*p*-value[a]
Age (years)					
12–40	122	18.9	268	41.6	0.0002
41–60	78	12.1	137	21.3	
>60	25	3.9	14	2.2	
Salary per family (SF)					
1 a 2	87	13.5	139	21.5	0.3535
3 a 4	90	13.9	186	28.8	
>4	48	7.5	96	14.8	
Diabetes mellitus (DM)					
No	213	34	413	66	0.0164
Yes	12	60	8	40	
Hypertension (HA)					
No	177	32.2	373	67.8	0.0003
Yes	48	50.5	47	49.5	
Neurological disease					
No	219	34.9	409	65.1	0.8925
Yes					

Table 3.2 Impact of QoL on Urinary Incontinence Using the ICIQ-SF Final Score (n = 225)

Impact of QoL	**Score**	***n***	**%**
None	0	45	20
Slight	1–3	75	33.3
Moderate	4–6	45	20
Severe	7–9	20	8.9
Very severe	10	40	17.8

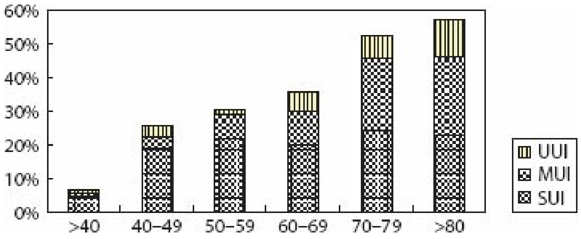


Figure 3.1 Prevalence of UI by age. (Based on data from Liu B et al., *Int J Clin Exp Med*, 7(3), 686, March

15, 2014.)

URINARY INCONTINENCE, QUALITY OF LIFE, AND SEXUAL FUNCTION

Recently, many studies have measured the QoL in incontinent patients, using a number of different self-administered condition-specific and generic QoL questionnaires. The impact of UI on patients' lives does not appear to be directly related to the volume of urine loss, although it does appear to be related to the overall burden of symptoms [18].

An open prospective study was carried out at our institution, enrolling patients with UI. The aim was to look at the relationship of UI and QoL issues, particularly with respect to altered sexual function. The study population consisted of 30 women aged between 31 and 51 years (mean 43 years). The duration of symptoms ranged from 12 to 53 months. All the patients were multiparous and 60% of women had incomplete elementary education. Two sexual function questionnaires were completed by respondents. The female sexual function index identifies problems related to sexual response and possible dysfunctions, as well as issues related to libido, excitement, lubrication, orgasm, pleasure, and pain. The Impact of Urinary Incontinence on the Sexual Response/RJ questionnaire [19,20] identifies the effects of UI on sexual function, social problems, and self-esteem. It also evaluates adaptive changes to cope with urinary symptoms, and sexual behavior before and after the onset of UI.

Of the 30 women participating in the study, 26 (86%) were married and all had only one partner, 19 (63%) were catholic, and 18 (60%) had incomplete elementary education. Concerning the effects of UI on daily life (Table 3.3), the major problems identified were the bad smell caused by urinary leakage, the need to use pads for 13 patients (43%), and the involuntary loss and wetness for 12 (40%). In addition to the results in Table 3.3, the study also showed that there were significant effects of UI on self-esteem, 11 patients (37%) having the feeling of being less valued, with 17 (57%) women having a worsening of their sexual lives as a result of their urinary symptoms. Twenty-three patients (76%) related that they had urinary loss during sexual intercourse. Among these, 17 (74%) claimed it as a negative influence on their sexual life. Of the 23 patients, 6 (26%) did not complain, 2 (9%) considered it a mild interference, 4 (17%) evaluated it as moderate, and 11 (48%) indicated it as a severe interference. Regarding the frequency of sexual intercourse before and after the onset of incontinence, 17 patients (57%) expressed altering patterns. Sexual activity changed from weekly to monthly in seven patients (41%), from daily to weekly in five (29%), from daily to monthly in three (18%), from monthly to annual in one (6%), and from weekly to no relationship in one (6%). Differences in sexual function before and after the onset of incontinence were established. Ten variables related to sexuality were studied: desire, excitement, vaginal lubrication, general caresses, genital caresses, oral sex in the partner and in the patient, vaginal penetration, anal penetration, and orgasm. Six variables were significantly different following the onset of urinary leakage, with a worsening of sexual desire, genital caresses and general caresses, vaginal penetration, anal penetration, and orgasm. Abdo and colleagues studied the sexual lives of 1502 healthy Brazilian women and concluded that in 34.6% the greatest complaint was a lack of desire and in 29.3% was orgasmic dysfunction [21]. These results demonstrated a reasonable degree of sexual dysfunction among the general Brazilian population although this appears to be greater in the presence of UI.

Table 3.3 Most Frequent Problems Identified in Urinary Incontinence

Problem	**Frequency (%)**
Bad smell and use of tampon	13 (43)
Involuntary loss and wetness	12 (40)
Surgery indication	2 (07)
Stress incontinence	1 (03)
Urinary frequency	1 (03)
Urine loss in the presence of the husband	1 (03)

PREVALENCE OF CLIMACTERIC, UROGENITAL, AND SEXUAL SYMPTOMS IN A POPULATION OF BRAZILIAN WOMEN

A cross-sectional, descriptive, population-based study [22] was also carried out at the State University of Campinas on 456 women aged 45–60 years, living in Campinas, SP, Brazil, in 1997. Data were collected via home interviews, using structured validated. The results showed that climacteric symptoms in the population were highly prevalent and similar to those described in developed Western countries. Figure 3.2 shows the most prevalent symptoms identified. Hot flushes, sweating, and insomnia as expected were significantly more prevalent in peri- and postmenopausal women. The severity of vasomotor and psychological symptoms did not vary according to the menopause phase. Decreased libido was the most frequent sexual complaint. It was observed that some climacteric complaints were interrelated.

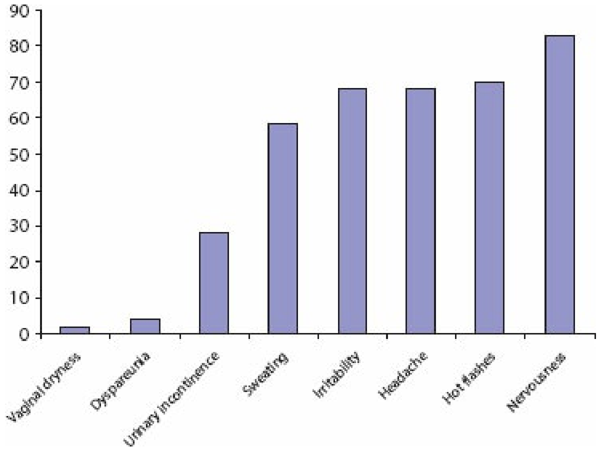


Figure 3.2 The most climacteric and urogenital prevalent symptoms found in the study of Pedro et al. [22].

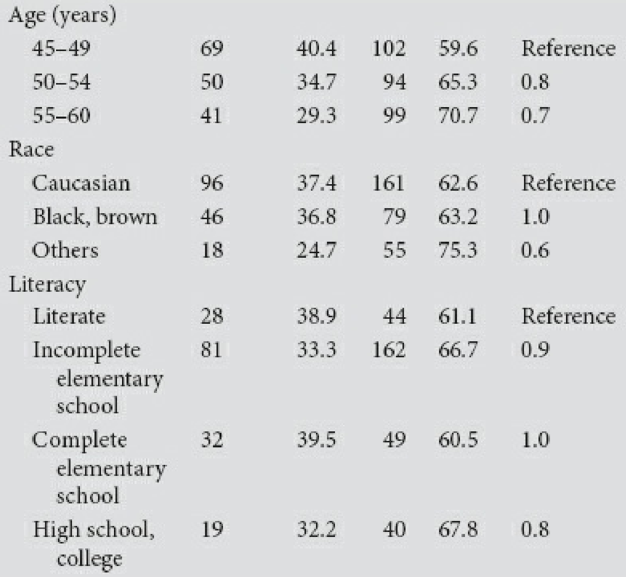
PREVALENCE OF STRESS URINARY INCONTINENCE AND ITS ASSOCIATED FACTORS IN PERIMENOPAUSAL WOMEN

A descriptive, exploratory, population-based study with secondary analysis of a population-based household survey on the perimenopause and menopause was conducted among women living in a Brazilian city [23]. Through a sampling process, 456 women between 45 and 60 years old were selected. Thirty-five percent of the interviews complained of stress urinary incontinence (SUI). None of the sociodemographic factors studied was associated with the risk of SUI (Table 3.4).

In addition, parity did not significantly alter SUI risk. Other factors, such as previous gynecological surgeries, body mass index, smoking habits, menopausal status, and hormone replacement therapy, were not associated with the prevalence of SUI. There were no racial variations in the prevalence of SUI. In the international literature, most prevalence studies are conducted among Caucasian women, and only few studies have assessed racial differences in the prevalence of UI. In the few studies that have included other racial groups, a significantly larger percentage of Caucasian women appear to report UI compared to African–American or Hispanic females [24]. Urodynamic diagnosis showed that SUI was more frequent in Caucasian women compared to African-Americans. However, more research with regard to racial differences in the prevalence of UI is necessary to make significant conclusions regarding interracial differences in incontinence.

Table 3.4 Background Data for All Patients Assessed by Guarisi et al.

	Stress urinary incontinence				
	Most times or sometimes (n = 160)		Never (n = 295)		Prevalence ratio
	n	%	n	%	



Age (years)					
45–49	69	40.4	102	59.6	Reference
50–54	50	34.7	94	65.3	0.8
55–60	41	29.3	99	70.7	0.7
Race					
Caucasian	96	37.4	161	62.6	Reference
Black, brown	46	36.8	79	63.2	1.0
Others	18	24.7	55	75.3	0.6
Literacy					
Literate	28	38.9	44	61.1	Reference
Incomplete elementary school	81	33.3	162	66.7	0.9
Complete elementary school	32	39.5	49	60.5	1.0
High school, college	19	32.2	40	67.8	0.8

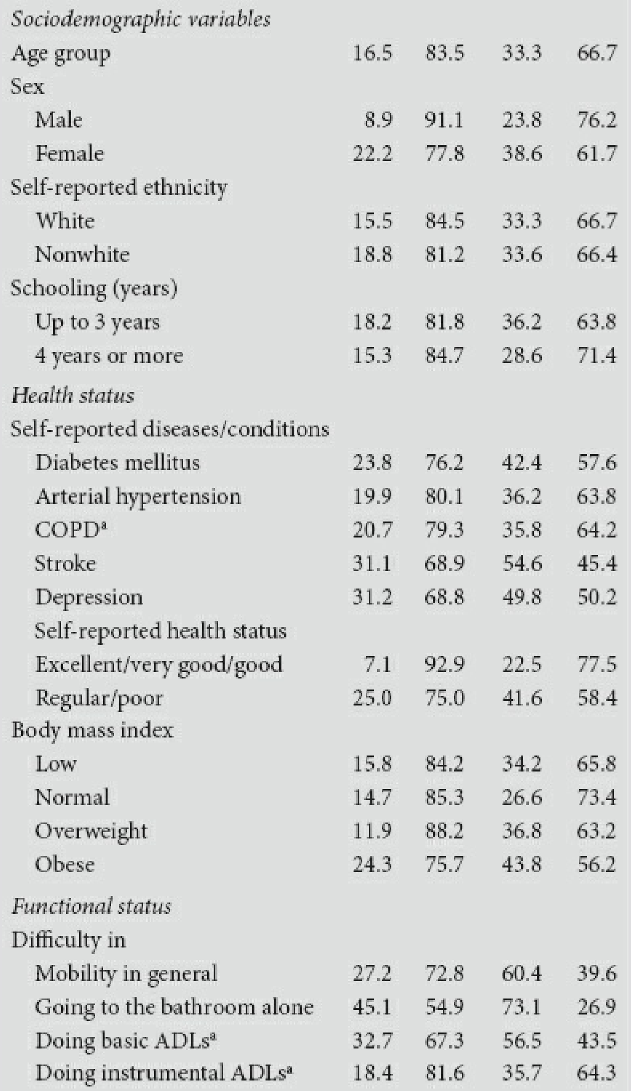
Source: Data adapted from Guarisi T et al., *Rev Saúde Publica*, 35(5), 428, 2001.

URINARY INCONTINENCE AMONG ELDERLY PEOPLE IN THE MUNICIPALITY OF SÃO PAULO, BRAZIL

Over the period from 1980 to 2025, the population aged 60 years and over in Latin America and the Caribbean is expected to at least double in size and, in more than half of these countries, to triple in size, before reaching the year 2025 [25]. This rapid and accentuated aging of the population will have a significant impact on social, economic, and health demands. Prominent among the health demands will be those relating to chronic diseases and their incapacitating sequelae and other complaints such as UI, which are all included among the so-called giants of geriatrics, given their negative consequences on QOL among elderly people [26].

Table 3.5 Distribution of Elderly People according to the Presence of Urinary Incontinence, Sociodemographic Variables, Health Status, and Functional Status

60–74 years		75 years and over	
Yes	No	Yes	No



Sociodemographic variables				
Age group	16.5	83.5	33.3	66.7
Sex				
Male	8.9	91.1	23.8	76.2
Female	22.2	77.8	38.6	61.7
Self-reported ethnicity				
White	15.5	84.5	33.3	66.7
Nonwhite	18.8	81.2	33.6	66.4
Schooling (years)				
Up to 3 years	18.2	81.8	36.2	63.8
4 years or more	15.3	84.7	28.6	71.4
Health status				
Self-reported diseases/conditions				
Diabetes mellitus	23.8	76.2	42.4	57.6
Arterial hypertension	19.9	80.1	36.2	63.8
COPD[a]	20.7	79.3	35.8	64.2
Stroke	31.1	68.9	54.6	45.4
Depression	31.2	68.8	49.8	50.2
Self-reported health status				
Excellent/very good/good	7.1	92.9	22.5	77.5
Regular/poor	25.0	75.0	41.6	58.4
Body mass index				
Low	15.8	84.2	34.2	65.8
Normal	14.7	85.3	26.6	73.4
Overweight	11.9	88.2	36.8	63.2
Obese	24.3	75.7	43.8	56.2
Functional status				
Difficulty in				
Mobility in general	27.2	72.8	60.4	39.6
Going to the bathroom alone	45.1	54.9	73.1	26.9
Doing basic ADLs[a]	32.7	67.3	56.5	43.5
Doing instrumental ADLs[a]	18.4	81.6	35.7	64.3

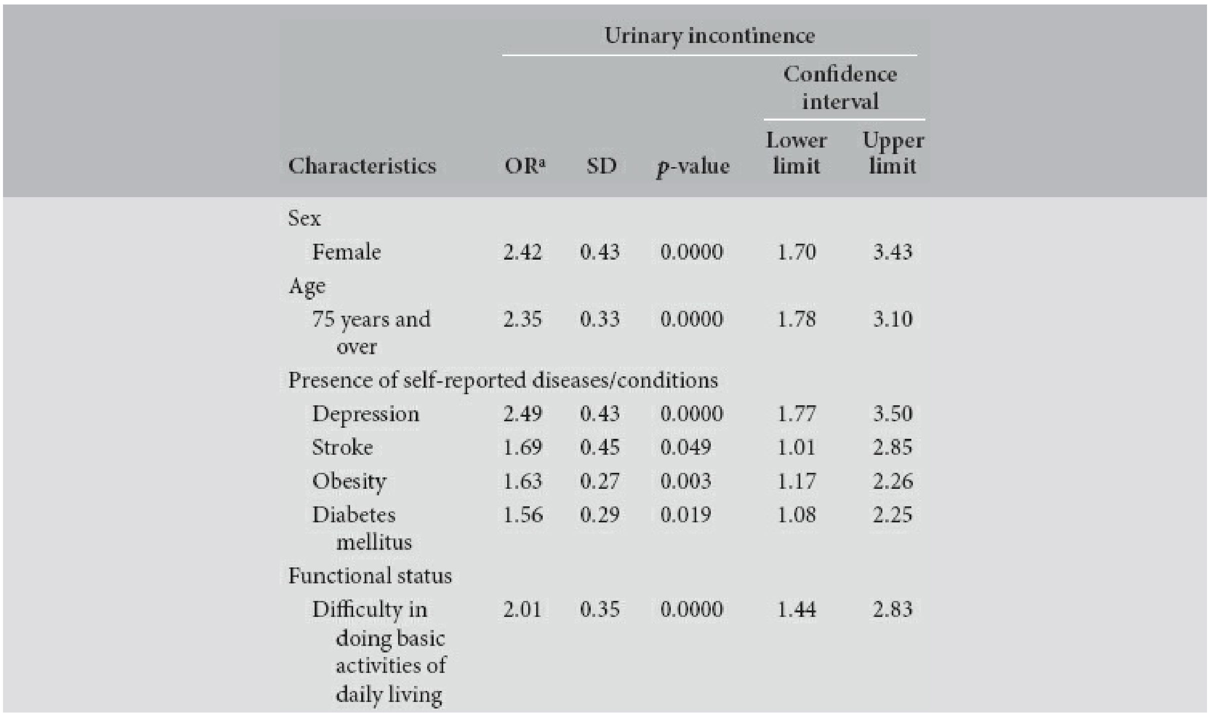
Note:Municipality of São Paulo, 2000.

[a] ADLs, activities of daily living; COPD, chronic obstructive pulmonary disease.

The Pan-American Health Organization and WHO [27] coordinated a multicenter study named Health, Well-being and Aging (SABE study) in elderly people living (over 60 years old) in seven countries of Latin America and the Caribbean. In Brazil, the study population carried out in São Paulo in the year 2000. The total Brazilian sample was 2143 people. The data were collected simultaneously, by means of home interviews, using a standardized instrument consisting of 11 thematic sections: personal data, cognitive assessment, heath status, functional status, medications, use of and access to services, family and social support networks, work history and sources of income characteristics of the home, and flexibility and mobility tests (Table 3.5).

The prevalence of self-reported UI was 11.8% among men and 26.2% for women. It was verified that among those reporting UI, 37% also reported stroke and 34% depression (Table 3.6). It was found that the greater the dependence that the elderly people presented, the greater the prevalence of UI was. The associated factors found were depression (odds – ratio = 2.49), being a female (2.42), advanced age (2.35), and important functional limitation (2.01). UI is a highly prevalent symptom among the elderly population of the municipality of São Paulo, especially among women. The adoption of preventive measures can reduce the negative effects of the UI.

Table 3.6 Final Model from Univariate and Multivariate Analysis for the Presence of Urinary Incontinence, according to Sociodemographic, Clinical, and Functional Characteristics of the Elderly People in the Municipality of São Paulo, Brazil, 2000



Characteristics	Urinary incontinence OR[a]	SD	p-value	Confidence interval Lower limit	Upper limit
Sex					
Female	2.42	0.43	0.0000	1.70	3.43
Age					
75 years and over	2.35	0.33	0.0000	1.78	3.10
Presence of self-reported diseases/conditions					
Depression	2.49	0.43	0.0000	1.77	3.50
Stroke	1.69	0.45	0.049	1.01	2.85
Obesity	1.63	0.27	0.003	1.17	2.26
Diabetes mellitus	1.56	0.29	0.019	1.08	2.25
Functional status					
Difficulty in doing basic activities of daily living	2.01	0.35	0.0000	1.44	2.83

[a] Adjusted OR (95% confidence interval) = odds ratio (95% confidence interval) adjusted using the logistic regression method, one by one for all variables and in the final model only for the significant variables.

CONCLUSION

UI is a highly prevalent condition in South America, as it is in many other parts of the world. Very few studies have concentrated on South American populations alone but those that have show a significant impact of UI on the QoL of sufferers.

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4 Epidemiology: Europe

Ian Milsom and Maria Gyhagen

INTRODUCTION

Urinary incontinence (UI), overactive bladder (OAB), and other lower urinary tract symptoms (LUTS) are highly prevalent conditions with a profound influence on well-being and quality of life as well as being of immense economic importance for the health service [1–4]. Millions of women throughout the world are afflicted [2,3], and there has been a growing interest in these symptoms in recent years as a consequence of the increased awareness of the human and social implications for the individual sufferer. Population studies have demonstrated that UI is more common in women than men and that approximately 10% of all women suffer from UI [2,3]. Prevalence figures increase with increasing age, and in women aged ≥70 years, more than 20% of the female population are affected. Inappropriate leakage of urine is perceived by many women but is not always reported to the doctor. However, an increasing awareness of the problem has in recent years attracted more patients to seek advice. In elderly women, UI may lead to possible rejection on the part of a relative and may be an important factor in the decision whether or not to institutionalize an elderly person. UI and other LUTS not only cause considerable personal suffering for the individual afflicted but are also of immense economic importance for the health service [4]. The annual cost of UI in Sweden, for example, has been reported to account for approximately 2% of the total health-care budget [1].

UI

This chapter describes the results of epidemiological studies performed in Europe. The reported prevalence of UI among women varies widely in different studies due to the use of different definitions, the heterogenicity of different study populations, and population sampling procedures. In addition, different definitions of UI have been applied. UI has been defined in the joint report from the International Urogynecological Association/International Continence Society as any involuntary leakage of urine [5]. However, some authors have chosen to restrict prevalence figures according to the frequency of involuntary urinary leakage—for example, based only on daily, weekly, monthly, or annual urinary leakage. Thus, for the reasons given earlier, it is difficult to compare the results of different population studies. However, when reviewing the literature, there is considerable evidence to support the theory that the prevalence of UI in women increases with age, but there are divergent opinions regarding the pattern of this increase [3,6–34].

In a review [3] of population studies from numerous countries, the prevalence of UI ranged from approximately 5% to 70%, with most studies reporting a prevalence of any UI in the range of 25%–45%. For daily incontinence, prevalence estimates typically range between 5% and 15% for middle-aged and older women.

Thomas et al. [6] investigated the prevalence of UI in two London boroughs by a postal survey (Figure 4.1a). The reported prevalence of UI increased from 5.1% in girls aged 5–14 years to 16.2% in 85-year-old women. There was, however, little or no change in prevalence rates up to 35 years of age. The prevalence rates then increased to approximately 10% in the 35–44 years age group. There was no significant increase at the time of the menopause, but a further increase to approximately 16% occurred in women ≥75 years. On the other hand, Iosif et al. [7] and Jolleys [14] (Figure 4.1b) reported a maximum prevalence of UI at the time of the menopause. Hannestad et al. [27], in a large Norwegian study, demonstrated an increased prevalence during the perimenopausal years, with prevalence rates being lower both before and after the time of the menopause (Figure 4.2a).

Conditions in Sweden are extremely favorable for epidemiological studies, in particular longitudinal studies. The Swedish population register, with its personal number system, provides up-to-date information on the total population and can be used to obtain random and, in some cases, representative subgroups of the total population for the purpose of epidemiological studies. There are several large population-based studies from Sweden describing the prevalence of UI in women. Figure 4.3a illustrates the results from two independent studies of UI in women. In both studies, prevalence was restricted to women who had urinary leakage at least once per week. Although the study performed by Samuelsson and coworkers [25] was undertaken in a rural area and that by Simeonova et al. [26] was carried out in an inner city, there are strong similarities between the results of the two studies, with a linear increase in the prevalence of UI that continues over the perimenopausal years.

In contrast, another Swedish population study [23] (Figure 4.3b) failed to demonstrate any increase in the prevalence of UI between women aged 46 and 56 (prevalence 12% for both cohorts). The majority of 46-year-old women were premenopausal, whereas the majority of 56-year-old women were postmenopausal. There were no differences in prevalence rates between pre- and postmenopausal women within the respective birth cohorts (Figure 4.4a). Thus, there was no evidence to suggest that the prevalence of UI increased at the time of the last menstrual period. The 5th International Consultation on Incontinence after an evaluation of the available literature came to the conclusion that the menopause per se did not influence the prevalence of UI. However, this is not necessarily synonymous with the fact that the reduction in circulating estrogens is not associated with an increase in the prevalence of UI in women after the menopause.

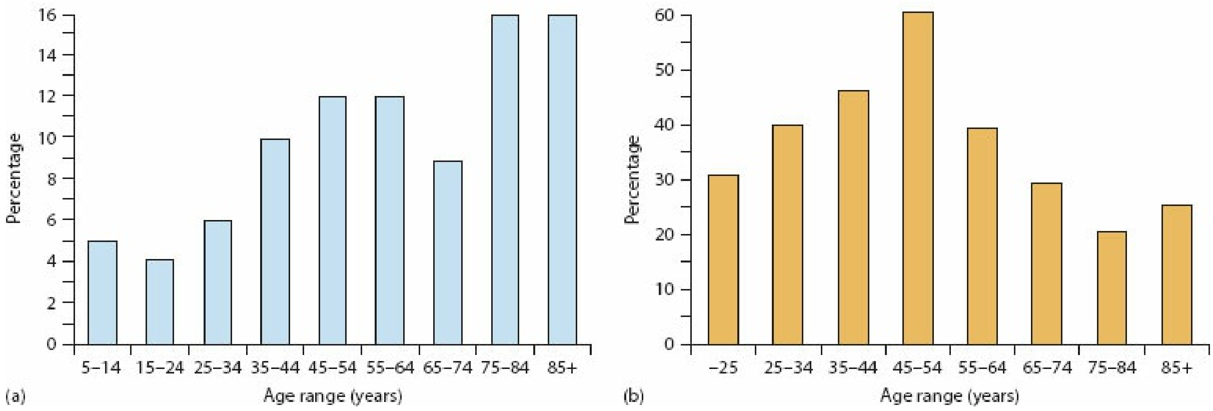


Figure 4.1 Comparison of the prevalence of female urinary incontinence in two British studies. (a) The study by Thomas et al. [6] was performed in 9323 British women, and (b) the study by Jolleys [14] was performed in 833 British women.

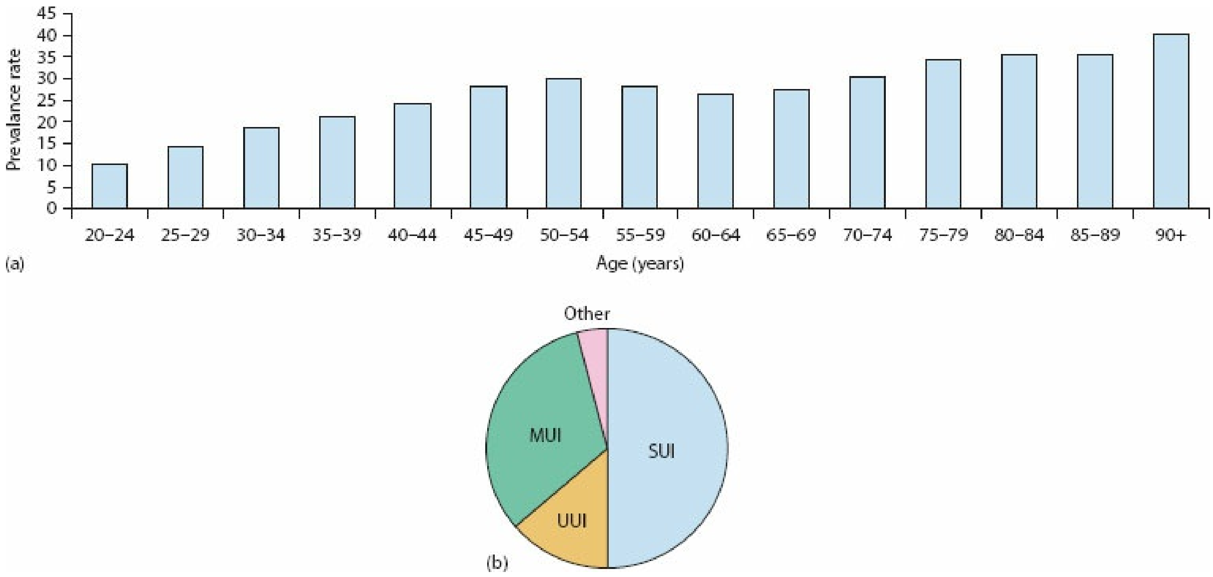


Figure 4.2 Prevalence of urinary incontinence in Norwegian women grouped (a) by age and (b) type of

incontinence. Abbreviations: MUI, mixed urinary incontinence; SUI, stress urinary incontinence; UUI, urge urinary incontinence. (Based on data from Hannestad YS et al., *J Clin Epidemiol*, 53, 1150, 2000.)

The prevalence of UI in women has been compared with the prevalence in men of the same age in two large Swedish studies [23,35]. As can be seen from the results illustrated in Figure 4.3b, there is a higher prevalence of UI in women than in men in all the age groups studied. In general, the prevalence of UI is approximately three times more common in women than in men.

The majority of the population studies referred to in this chapter have been performed by means of postal questionnaires. In several of the studies, attempts have been made to determine the proportion of women suffering from the different types of urinary leakage, i.e., stress urinary leakage (SUI), urge urinary leakage (UUI), and mixed urinary leakage (MUI). The distribution of the various types of incontinence in the large Norwegian study by Hannestad et al. [27] is shown in Figure 4.2b. In the literature, SUI tends to dominate among younger women, while the number of women with urge incontinence and mixed incontinence increases with age.

Further studies [27,30–35] have added important information on the prevalence of incontinence in women younger than 30 and older than 80 years of age, particularly for prevalence of incontinence by type. These studies are consistent with previous studies reporting that older women are more likely to have mixed and urge incontinence, while young and middle-aged women generally report stress incontinence. Overall, approximately half of all incontinent women are classified as stress incontinent. A smaller proportion are classified as mixed incontinent and the smallest fraction as urge incontinent. A recent study that included the entire adult age range by Hannestad et al. [27] demonstrated a fairly regular increase in prevalence of mixed incontinence across the age range and a decrease in prevalence of stress incontinence from the 40–49-year-old age group through the 60–69-year-old age group. There is no hard evidence for different prevalences of UI among Western countries. However, comparing prevalence between countries based on separate studies is difficult due to differences in methods and definitions, as well as language, cultural, and social differences. One of the few studies to estimate the prevalence of UI in more than one country found similar prevalences of any UI (41%–44%) in 3 of the 4 countries examined (France, Germany, and United Kingdom) but a lower prevalence (23%) in the fourth country (Spain) [28]. There was no apparent reason for the lower prevalence in Spain.

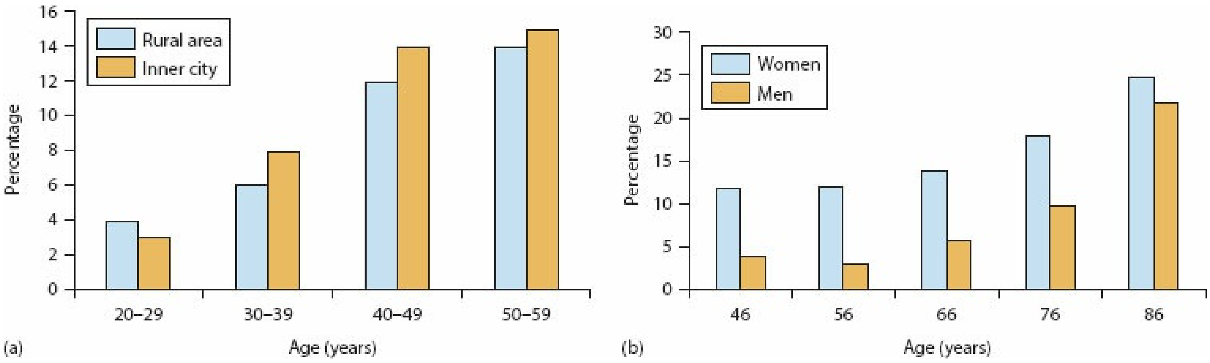


Figure 4.3 Comparison of the prevalence of urinary incontinence: (a) in two population-based studies of Swedish women in a rural area (Samuelsson et al. [25]) and in an inner city (Simeonova et al. [26]) and (b) in two population-based Swedish studies in women (n = 7459) [23] and men (n = 7763) [35] of the same ages.

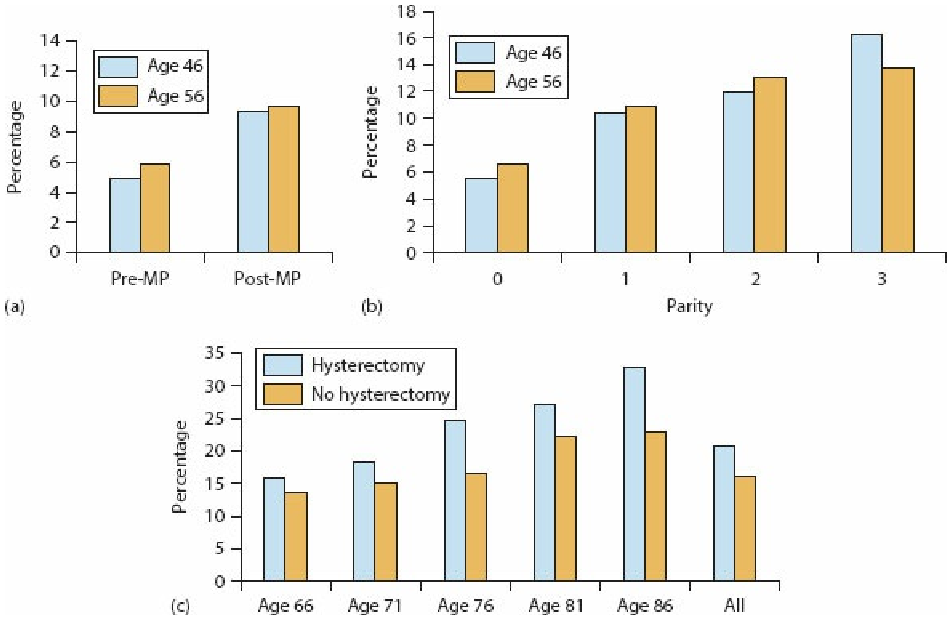


Figure 4.4 Prevalence of urinary incontinence: (a) in a random sample of 46- and 56-year-old women grouped according to menopausal status, (b) in a random sample of 46-year-old (n = 1530) and 56-year-old (n = 1638) women grouped according to parity, (c) in a random sample of 66-, 71-, 76-, 81-, and 86-year-old women grouped according to history of hysterectomy. (Data from Milsom I et al., *J Urol*, 149, 1459, 1993.)

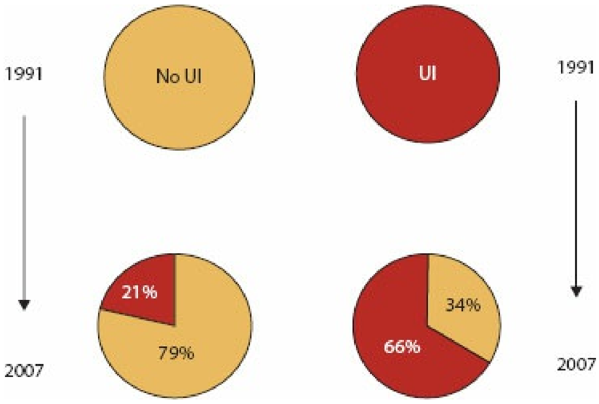


Figure 4.5 The incidence and regression of urinary incontinence in the same women assessed in 1991 and 2007. (From Wennberg A et al., *Eur Urol*, 55, 783, 2009. With permission.)

UI is, however, not static but dynamic and many factors may contribute to incidence, progression, or remission. There are only a few studies describing progression as well as remission, in the short term, of UI in the general population as well as in selected groups of the population. The mean annual incidence of UI seems to range from 1% to 9%, while estimates of remission are more varying, 4%–30% [36–38].

Wennberg et al. [36] studied the prevalence of UI in the same women (aged ≥20 years) over time in order to assess possible progression or regression. A self-administered postal questionnaire with questions regarding UI, OAB, and other LUTS was sent to a random sample of the total population of women in 1991. The same women who responded to the questionnaire in 1991 and who were still alive and available in the population register 16 years later were reassessed using a similar self-administered postal questionnaire. The overall prevalence of UI increased from 15% to 28% ($p < 0.001$) from 1991 to 2007, and the incidence rate of UI was 21%, while the corresponding remission rate was 34% (Figure 4.5).

Thus, in summary, when reviewing the literature, there is considerable evidence to support the theory that the prevalence of UI increases in a linear fashion with age as shown in Figure 4.6, which includes pooled data from 19 epidemiological studies where UI was reported to occur at least once per week.

FACTORS INFLUENCING THE PREVALENCE OF UI

Risk factors described in the literature are shown in Table 4.1 [3,30–32,39–41]. For the majority of these risk factors, there are at present no controlled trials demonstrating that intervention reduces the incidence, prevalence, or degree of severity of UI.

The influence of various factors on the prevalence of UI was evaluated by means of a postal questionnaire in women aged 46–86 years resident in the city of Gothenburg, Sweden [23]. Age, parity, and a history of hysterectomy were all correlated to the prevalence of UI, which increased in a linear fashion from 12.1% in women 46 years of age to 24.6% in women aged 86 years of age. The prevalence of UI was greater in parous women compared to nulliparous women, and prevalence increased with increasing parity (Figure 4.4b). UI was more prevalent in women who had undergone a hysterectomy (Figure 4.4c). The prevalence of UI was unaffected by the duration of previous oral contraceptive usage, and there was no evidence to suggest that the prevalence of UI increased at the time of the last menstrual period (Figure 4.4a).

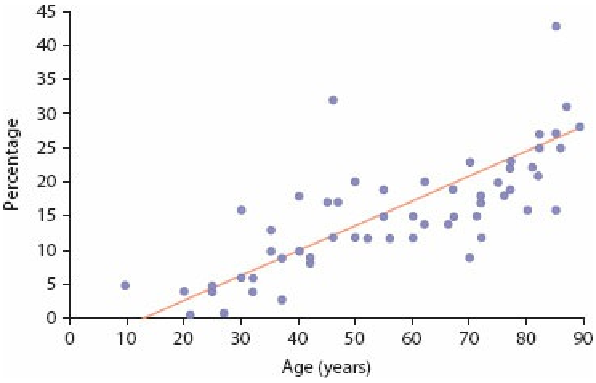


Figure 4.6 Prevalence of female urinary incontinence (≥1/week), which affected the woman's way of life (summary of 19 population studies). (Based on Hellström AL et al., Health economics, in Treatment of urinary incontinence, The Swedish Council on Technology Assessment in Health Report on Urinary Incontinence, SBU, Stockholm, Sweden, 2000.)

Several studies suggest that the risk of UI "runs in the family" [3,29,40–43]. Family history studies have found a twofold to threefold greater prevalence of stress UI among first-degree relatives of women with stress UI compared to first-degree relatives of continent women. In the Norwegian Nord-Trøndelag health survey Epidemiology of incotinence in the country of Nord-Trondelag (EPINCONT), daughters of mothers with UI had an increased risk of stress incontinence, mixed incontinence, and urgency incontinence [29]. In general, the risk was somewhat higher for sisters of a woman with UI than for daughters.

Table 4.1 Risk Factors for Urinary Incontinence in Women
Age
Sex
Smoking
Chronic bronchitis, asthma
Ethnic group
Obesity
Pregnancy
Vaginal delivery
Collagen defect
Hysterectomy
Dementia
Stroke, Parkinson's disease, etc.
Physical activity
Medication

Constipation
Diuretics
Enuresis
Chronic illness

Studies from the Swedish twin register indicated that heritability contributes to the liability of developing UI. The authors presented evidence that for both disorders genetic and nonshared environmental factors equally contributed 40% of the variation in liability [40,41]. Although study methodology and the magnitude of the risk estimates vary, studies on familial transmission of incontinence are in agreement [29,40,41] in which having a first-degree female family member with stress UI increases the risk for an individual becoming afflicted by the same disorder.

Many studies have assessed the influence of pregnancy and in particular vaginal delivery on the risk of developing UI. The prevalence of UI in nulliparous women of childbearing age has been reported to be 10%–15% [42–44]. UI preceding pregnancy in nulliparous has been shown to be a strong indicator for increased prevalence of UI 4–12 years postpartum [45,46]. Pregnancy in itself, independent of labor and delivery practices, seems to be a risk factor for postpartum UI [47,48] especially if the incontinence started during the first trimester [49]. During pregnancy, the prevalence of UI increases with gestational age [50] so that more than half of all women report UI during the third trimester [51–53]. Stress UI and mixed UI increased the most during pregnancy compared to before pregnancy, whereas urge UI did not change during the same period [54]. During the first 3 months, postpartum UI prevalence was 30% and most women had stress UI [55]. In uncomplicated courses of pregnancy and labor, UI usually declines rapidly during the first 3 months following childbirth, indicating that most symptoms are part of a normal pregnancy and delivery [47]. Several studies have also demonstrated that postpartum UI is a risk factor for UI after longer (7 months to 6 years) terms of follow-up [48,56–58].

The first delivery is considered to increase the prevalence of UI the most, and recent studies have demonstrated a further increase for each delivery [23,59–62]. Many cross-sectional and several longitudinal studies show a protective effect of CS for UI [63–66]. BMI is considered to be an established risk factor for UI [61], whereas the association between UI and age is complicated by confounders [67].

OAB and Other LUTS

In recent years, several epidemiological studies have also been conducted in order to better understand the prevalence and the impact of OAB and other LUTS. OAB is defined as the presence of urgency and frequency (either daytime or nighttime), with or without UI [5]. OAB is often divided into OAB without UI (OAB_{dry}) and those with OAB and UI (OAB_{wet}). The reported prevalence of OAB in females varied between 7.7% and 31.3%, and in general prevalence rates increased with age [68–72]. OAB has been shown to be associated with other chronic debilitating illnesses such as depression, constipation, and diabetes as well as neurological illnesses. OAB is commonly associated with other LUTS, which was well illustrated by the cluster analysis performed by Coyne et al. [73].

The prevalence of OAB symptoms was estimated in a large European study involving more than 16,000 individuals [68]. Data were collected using a population-based survey (conducted by telephone or face-to-face interview) of men and women aged ≥40 years, selected from the general population in France, Germany, Italy, Spain, Sweden, and the United Kingdom using a random, stratified approach. The main outcome measures were prevalence of urinary frequency (>8 micturitions/24 hours), urgency and urge incontinence, proportion of participants who had sought medical advice for OAB symptoms, and current or previous therapy received for these symptoms. The main results of this study are illustrated in Figure 4.7a with the prevalence of OAB symptoms grouped according to age and sex and in Figure 4.7b grouped according to age, sex, and nationality.

The progression or regression of OAB and other LUTS was studied by Wennberg et al. [36] in the same women (aged ≥20 years) followed over a period of 16 years (from 1991 to 2007). The overall prevalence of OAB, nocturia, and daytime micturition frequency of eight or more times per day increased by 9%, 20% ($p < 0.001$), and 3% ($p < 0.05$), respectively from 1991 to 2007. The incidence of OAB was 20% and the corresponding remission rate was 43%. Women with OAB symptoms were classified as OAB dry or wet depending on the presence or absence of concomitant UI. The prevalence of OAB dry did not differ between the two assessment occasions (11% and 10%, respectively), but the prevalence of OAB wet increased from 6% to 16% ($p < 0.001$). Among the women with no OAB in 1991, the prevalence in 2007 were 8% and 12% for OAB dry and wet, respectively. There was a progression from OAB dry to wet in 28%. Remission from OAB dry or wet to no OAB occurred in 50% and 26%, respectively (Figure 4.8).

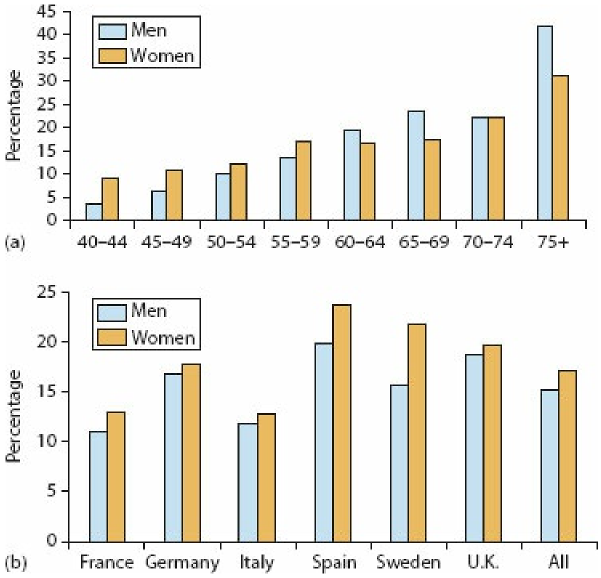
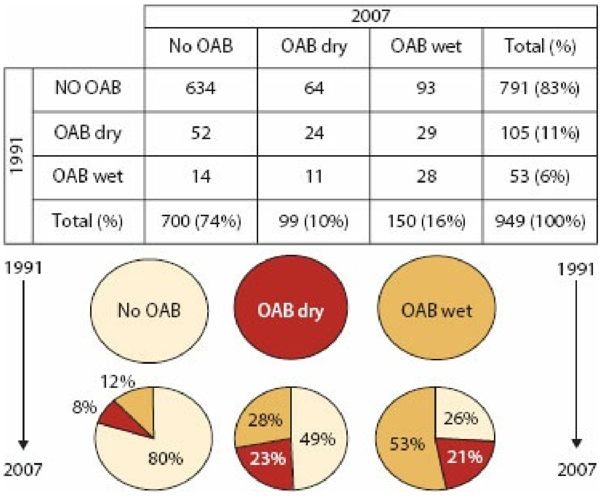


Figure 4.7 Prevalence of overactive bladder symptoms (a) grouped according to age and sex and (b) in a random sample of the total population aged ≥40 years from six European countries. (Adapted from Milsom I et al., *Br J Urol Int*, 87, 760, 2001.)



		2007			
		No OAB	OAB dry	OAB wet	Total (%)
1991	NO OAB	634	64	93	791 (83%)
	OAB dry	52	24	29	105 (11%)
	OAB wet	14	11	28	53 (6%)
	Total (%)	700 (74%)	99 (10%)	150 (16%)	949 (100%)

Figure 4.8 The percentage distribution of overactive bladder symptoms in the same women assessed in 1991 and 2007. (From Wennberg A et al., *Eur Urol*, 55, 783, 2009. With permission.)

SOCIOECONOMIC CONSIDERATIONS

The economic consequences of UI and other LUTS have recently been reviewed [4], and there are now numerous reports to support the statement that UI and LUTS have a huge bearing on health-care costs [1,4,74–77]. Prevalence rates vary throughout the world, but a recent review indicated that urge UI rates were particularly high in the Nordic countries [77] and in particular Sweden (Figure 4.9). The economic consequences of UI in Sweden in 1990 were assessed by Ekelund et al. [1]. The estimated annual cost for UI in Sweden at that time was 1.8 billion Swedish crowns. The Swedish health-care budget for 1990 amounted to 93 billion Swedish crowns. Based on the results of this evaluation, the annual costs of UI in Sweden accounted for approximately 2% of the total health-care costs. Ten years later, the annual estimated costs had increased from 1.8 billion Swedish crowns to 2.8–4.4 billion Swedish crowns [78].

Mean life expectancy in the industrialized world is increasing, and in some countries 25% of all persons are at present ≥65 years of age. Thus, the number of women requiring treatment for UI is expected to increase in the future. Another important factor to consider, apart from the numerical increase in the number of elderly women, is the fact that many elderly women of today suffer in silence, accepting these symptoms as a normal part of the aging process. Women who are at present 30 and 40 years of age have other demands on their physical condition and will undoubtedly not accept what their older counterparts accepted later in life.

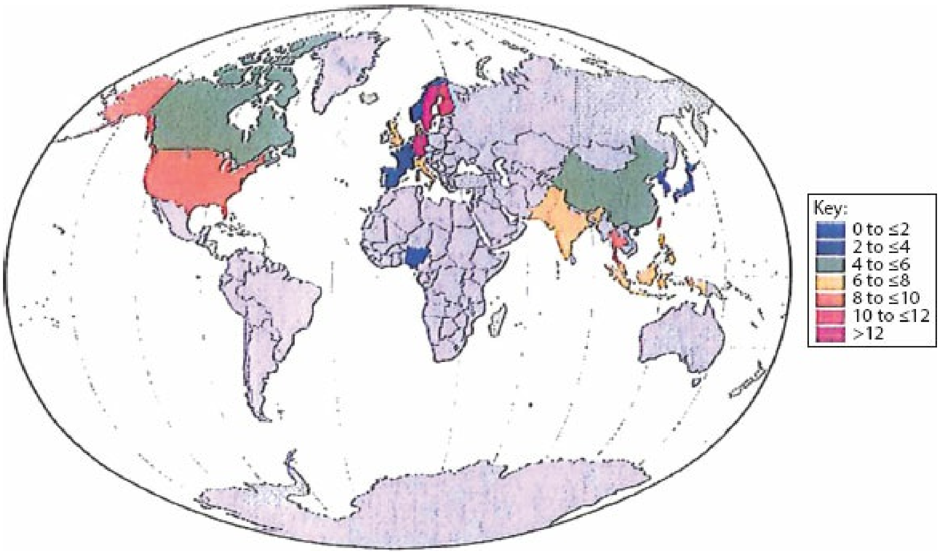


Figure 4.9 World map illustrating urgency urinary incontinence (UUI) prevalence rates for adult women for 2013. Prevalence rates reported in each captured study were adjusted for the current age distribution of the country's population obtained from the International Data Base of the U.S. Census Bureau. Age-adjusted prevalence rates were averaged when more than one study had been performed in a single country. For studies that reported separate rates for UUI, mixed urinary incontinence (MUI), and stress urinary incontinence, the UUI prevalence rate was calculated based on the sum of UUI and MUI rates. (From Milsom I et al., *Eur Urol*, 651, 79, 2014. With permission.)

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5 Epidemiology: Australia

Christopher Benness

BACKGROUND

Australia is a developed nation of 24 million people [1] with a small, disadvantaged indigenous population (2.5% of population are Aboriginal). It is a young nation, with its European settlement being less than 250 years ago. Most of the population arrived in various waves of immigration, initially from Europe but more recently from Asia, resulting in a multicultural society. The Australian health system has considerable private sector involvement complementing universal health coverage by the government. Most of the population live in cities on the coastal fringe with good access to healthcare. However, providing high-quality healthcare to the many remote centers in Australia is a challenge.

Australia was one of the first countries to designate urogynecology as a subspecialty area of obstetrics and gynecology. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists has had accredited subspecialists in this area since 1990. Certification in urogynecology requires 3 years training in an accredited unit, following completion of general obstetrics and gynecology training, and passing a written and oral examination [2]. There are currently 35 accredited urogynecologists in Australia and nine training units.

URINARY INCONTINENCE: PREVALENCE

Urinary incontinence is known to be a common condition in women [3], to be multifactorial in pathogenesis [4], and to significantly affect the quality of life of many of its sufferers [5]. It imposes a significant burden on affected individuals, those who care for them, and the health services [6]. The prevalence of a condition is one of the main epidemiological indices and is defined as the proportion of a population having a disease at a point in time. The prevalence of urinary incontinence in Australia has been explored by a variety of authors and studies in the past 30 years, looking at a range of different populations. Chiarelli et al. in 2005 applied the results of a systematic review of the medical literature to the Australian population [7]. They estimated that the prevalence of urinary incontinence in Australian women was 19.3% and that of fecal incontinence in women was 5.3%.

In 1983, Millard conducted a postal survey of 3000 people using a 38-question, self-administered questionnaire [8]. A multistage, cluster-sampling technique was used to select participants. Replies were received from 1256 people (42%) of whom 651 were females. Thirteen percent of the male and 34% of the female respondents had some degree of urine loss. The frequency of urinary loss is shown in Table 5.1. The mean duration of all leakage problems was 8.8 years: 18% reported leakage for less than a year, while 23% had had problems for 15 or more years. The circumstances in which the respondents experienced leakage are shown in Table 5.2 (more than one answer was allowed). The severity of urine loss as quantified by the respondents is shown in Table 5.3. In most cases, the incontinence occurred infrequently and was of minor severity. Nocturnal enuresis was present in 26 women (4%). Thirty-one percent of the women who reported urinary leakage had sought help from a health professional. As other studies have demonstrated [9], parity was a significant factor in the pathogenesis of urinary incontinence, with the prevalence doubling from 20% to 40% with the first child.

In 1999, Chiarelli et al. reported on urinary incontinence prevalence data from the Women's Health Australia project [10]. This longitudinal study involves three cohorts of women: young (age 18–23 years), middle-aged (aged 45–50 years), and older (70–75 years) at the time of the baseline survey. The women were selected randomly from the Australian Medicare database. During 1996, approximately 14,000 women in each of the three groups completed baseline surveys (respectively, 48%, 54%, and 41% of those of each group who were invited to take part). Among other health questions, the participants were asked whether they had leaked urine in the last month "never," "rarely," "sometimes," or "often." The advantages of this study were its large sample size and the representative nature of the sample.

The prevalence of urinary incontinence in young women in this study was 12.8% (95% CI 12.2–13.3); in middle-aged women, it was 36.15% (CI 35.2–37.0), and in older women 35% (CI 34.1–35.9). Parity was significantly associated with the prevalence of incontinence in young women but was less strongly correlated in the other age groups. There was a strong association between any degree of constipation and urinary leakage. In middle-aged women, those with high body mass index (BMI > 25) and constipation were those most likely to experience leakage of urine. Hysterectomy alone had a lower odds ratio for leakage, whereas women who reported a prolapse repair were more likely to leak. Neither current use of hormone replacement therapy nor duration of use was associated with urinary incontinence. At all ages, women who reported leaking urine had scores on the SF36 inventory suggesting a lower quality of life compared with continent women.

A follow-up study related to the Women’s Health Australia project was reported in 2003 [11]. The cohorts had aged by 5 years. The majority of all age groups reported mixed stress and urge leakage with almost 80% of incontinent women over 50 years of age having mixed incontinence. Risk factors for incontinence severity that were identified were raised BMI, high parity, and smoking >20 cigarettes per day.

Table 5.1 Frequency of Incontinence Episodes

	Percentage of respondents		
Frequency	**Male**	**Female**	**Overall**
Often wet	2	4	3
Once a day	2	4	3
Once a week	1	3	2
Once or twice a month	0	4	2
Rarely	8	18	13
Never wet	87	66	76

Table 5.2 Circumstances in Which Respondents Experienced Leakage

	Percentage of respondents	
Frequency	**Males (*n* = 79)**	**Females (*n* = 214)**
Coughing or sneezing	5	61
Straining or lifting	5	12
Urge	27	35
Giggle	9	30
No warning or provocation	1	7
Postmicturition dribble	59	8
With urinary infections	8	10
Other	8	9
Total[a]	122	172

[a] Respondents may have more than one type of incontinence.

Table 5.3 Severity of Urine Loss in Respondents

	Percentage of respondents		
Urinary Loss	**Males (*n* = 79)**	**Females (*n* = 214)**	**Overall**
Always wet	0	2	2
Flooding	0	2	1
Moderate loss	8	5	5
Slight loss	25	41	37
Just a spot	66	49	54

A further longitudinal study based on a cohort of women aged 70–75 years has been reported [12]. These women are part of the Australian Longitudinal Study of Women's Health and a follow-up after 9 years is outlined. Over this time, 14.6% (95% CI 13.9–15.3) of previously continent women became incontinent. Longitudinal models demonstrated an association between incontinence and dementia, falls, BMI, constipation, lower urinary tract infection, and urogenital prolapse. A weaker association was found with stroke and hysterectomy.

The results of a population survey in South Australia were published in 2000 [13]. This was a cross-sectional survey of men and women with 3010 interviews, conducted by trained female interviewers, from 4400 randomly selected households. The prevalence of all types of urinary incontinence in women was 35.3% and in men was 4.4%. Urinary incontinence increased after pregnancy according to parity and age. The highest prevalence (51.9%) was reported in women aged 70–74 years. The prevalence of fecal incontinence in women was 3.5%. Pregnancy (>20 weeks), regardless of mode of delivery, greatly increased the prevalence of major pelvic floor dysfunction, defined as any type of incontinence, symptoms of prolapse, or previous pelvic floor surgery. Multivariate logistic regression showed that, compared with nulliparity, pelvic floor dysfunction was significantly associated with cesarean section (OR 2.5, 95% CI 1.5–4.3), spontaneous vaginal delivery (OR 3.4, 95% CI 2.4–4.9), and at least one instrumental delivery (OR 4.3, 95% CI 2.8–6.6). Other associations with pelvic floor morbidity were age, BMI, coughing, osteoporosis, arthritis, and reduced quality of life scores.

RELATIONSHIP BETWEEN INCONTINENCE AND AGE GROUP

The prevalence of urinary incontinence and its relationship to age group in the Millard study [8] is shown in Figure 5.1 and Table 5.4. There is a rise with increasing age, peaking at 50% in the perimenopausal group (age 45–59 years) with some decline following this. The high prevalence (40%) in those over 70 years is similar to that found in other studies [11]. Urinary stress incontinence was most prevalent in middle-aged women (aged 45–59 years), while urge leakage increased with advancing age and peaked in the over 70s age group. These findings are similar to those of another Australian questionnaire-based study [14] of 542 community-dwelling women aged 24–80 years. The overall prevalence of any urinary incontinence was 41.7% (95% CI 37.2–45.8) with a response rate of 93.4%. Of the 210 women reporting urinary incontinence, 16% reported stress incontinence only, 7.5% reported urge incontinence only, and 18% reported mixed incontinence. Logistic regression revealed a significant association of obesity and parity with stress incontinence. Increasing age, being overweight, and previous hysterectomy were associated with urge incontinence.

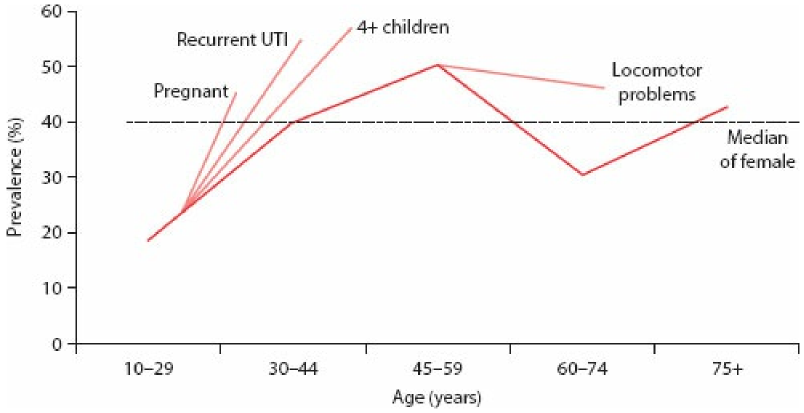
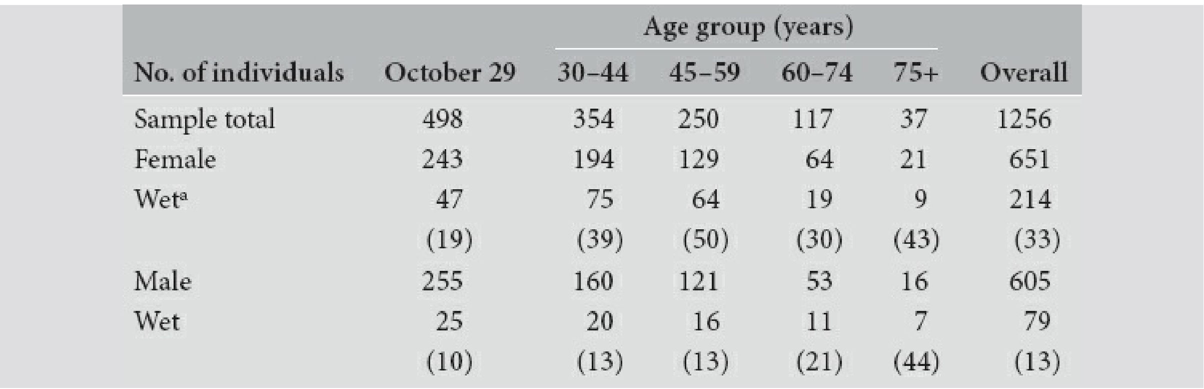


Figure 5.1 Prevalence of incontinence according to age.

Table 5.4 Prevalence of Incontinence and Its Relationship to Age Groups



		Age group (years)				
No. of individuals	October 29	30–44	45–59	60–74	75+	Overall
Sample total	498	354	250	117	37	1256
Female	243	194	129	64	21	651
Wet[a]	47	75	64	19	9	214
	(19)	(39)	(50)	(30)	(43)	(33)
Male	255	160	121	53	16	605
Wet	25	20	16	11	7	79
	(10)	(13)	(13)	(21)	(44)	(13)

[a] Percentages in parentheses.

Female adolescents with chronic lung disease have been shown by Nixon et al. to have a higher prevalence of urinary incontinence [15]. They assessed 55 adolescents, aged 12–19 years with cystic fibrosis. Forty-seven percent had experienced some urinary incontinence with twenty-two percent experiencing leakage at least twice per month.

INCONTINENCE IN PREGNANCY

An Australian study of the prevalence of urinary incontinence in pregnancy was reported by Chiarelli and Campbell [16]. This was a cross-sectional descriptive study using a structured interview. Women in the postnatal ward of a large teaching hospital were approached (336) and 304 participated (90%). Overall, 64% reported stress urinary incontinence during pregnancy. In the last month of pregnancy, 57% reported stress incontinence while 42% had urge incontinence. Of those experiencing incontinence, 18% reported severe urine loss. The leakage had started during the first trimester in 8%, in the second trimester in 18%, and in the last trimester of the most recent pregnancy in 47%. For 20% of those with leakage, it had begun in a previous pregnancy, and in 6%, it had begun after the birth of a previous child. For 49%, leakage was not at all bothersome, 31% found it a little bothersome, 16% quite bothersome, and 4% extremely bothersome.

Data analysis showed continence status to be significantly associated with delivery mode, parity, and chronic cough. Women who had had previous deliveries were 2.5 times more likely to be incontinent of urine than those who had no previous deliveries or had only cesarean sections. Those who reported previous forceps delivery were 10 times more likely to be incontinent than those with no prior delivery.

CHILDHOOD INCONTINENCE

In the Millard study [8], 21% of respondents recalled bed-wetting as a child and this was equal in males and females. It was more common in higher socioeconomic families. Of these childhood bed-wetters, 11% still wet the bed as adults. They were also at increased risk of developing urge incontinence in adult life.

The prevalence of childhood enuresis in Australia has been studied by Hawkins [17] in 1962 and by Bower et al. [18] in 1996. The former took a sample of 1000 children from one general practice and found a prevalence of nocturnal enuresis (of one or more nights per week at school age) of 18%. The Bower study used a self-administered questionnaire distributed to parents of children 5–12 years of age. Of the 3111 parents approached, 2292 (74%) responded. Nocturnal enuresis occurred in 18.9% of the children and 5.5% had daytime incontinence, while 4.4% had both day and night wetting. Sixty percent of the children with enuresis were male. Only one third of the families with enuretic children had sought professional help. A positive family history was more common in the enuretic children (70%) compared with the dry children (44%).

INCONTINENCE IN INSTITUTIONS

A Sydney study of 1659 residents of nursing homes found that urinary incontinence affected 77%, and that 25% of nursing staff time was spent dealing with urinary leakage [19]. The long-term care of looking after such residents is expensive and is estimated to cost more than Aus$500 million each year.

Also, the importance and association of incontinence and the increasing prevalence of falls in the elderly has been clearly documented [20]. The odds ratio of sustaining a fall is 1.45 (95% CI 1.36–1.54) in the presence of any type of urinary incontinence.

Table 5.5 Prevalence of Urinary Symptoms in Aboriginal Group

Symptom	**Frequency (%)**
Frequency	39
Urgency	40
Stress Incontinence	48
Urge incontinence	30
Stress and Urge Incontinence	23
Recurrent UTIs	5

ABORIGINAL POPULATION

The indigenous Australian population comprise a small part of the population but have a higher prevalence of most medical disorders than other Australians. A prevalence study of lower urinary tract symptoms was undertaken in rural, community-dwelling Aboriginal women [21]. A questionnaire was administered by a female practitioner, in a face-to-face interview, to 151 rural Aboriginal women. The women interviewed were recruited from the community and had not presented for medical attention. The mean age of the group was 39 years (range 16–69). With 35% having had five or more confinements, 87% were parous. Forty percent of the women were peri- or postmenopausal. Fifty-six percent reported symptoms of urinary incontinence. The prevalence of urinary symptoms in this group is shown in Table 5.5. Of the total group, 48% reported stress urinary incontinence, 30% had urge incontinence, and 23% complained of both stress and urge incontinence. Of those with stress incontinence, it occurred frequently in 30%. Urge incontinence occurred frequently in 38% of those with this problem. Among all the women surveyed, 46% were troubled by their urinary symptoms and 89% of them wanted treatment. Thirty-one percent had sought medical advice, but most had not found it helpful.

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6 Epidemiology: Asia

S.S Vasan and Reena Mallesh

INTRODUCTION

Urinary incontinence (UI) is a major clinical problem that has a profound effect on the quality of life and activities of daily living [1–3]. Women with UI report fear, shame, and humiliation and worry about the odor of urine from pads and wet underclothing [4]. UI is physically debilitating and socially incapacitating and is associated with loss of self-confidence, feelings of helplessness, depression, and anxiety [3].

Many adults suffer from UI, and the financial, physical, emotional, psychological, and social impacts are demoralizing and distressing [5–7]. UI has become a costly public health problem [6]. In the United States, it is estimated that direct health costs of UI among older people amount to more than $26 billion per year, an average of $3565 for each incontinent older person [8]. No estimate of health care costs of this kind is available in Asia.

UI is a general problem among older people [5]. Postmicturition dribble and continuous leakage are both common forms that arise in later life. Many incontinent older people in Asia and elsewhere do not talk about their UI or report it to physicians. This is partly due to their limited understanding of UI and also because they fear social rejection. Indeed, UI is underreported and underdiagnosed across all age groups [9–13]. Thus, no accurate estimate of UI is available for people across the age spectrum. Almost all studies, however, confirm that prevalence increases with age [5–11,14–16] and that prevalence is higher among women than among men at all ages [5,7,11,17–19]. The prevalence among older people living in institutions also is higher than among their community-dwelling counterparts [5,7,20,21].

The Agency for Health Care Policy and Research in the United States has estimated that 15%–35% of people aged 60 years and above living in the community have experienced some degree of UI [5,22–25]. Burgio and Locher [23] reported that 20%–30% of older people aged above 65 living in the community suffer from UI. It is also estimated that at least 50% of nursing home residents are incontinent [17,20,23,24,26]. Yarnell and St. Leger [27] reported that between 40% and 60% of nursing home residents are incontinent. According to Tobin [28], the higher prevalence of UI among people living in residential care facilities is related to their increased average age and to the increased prevalence of physical and mental morbidity.

Studies of the prevalence of UI suggest that it is widespread among women of all ages [29]. The probability of incontinence increases with age [30–32], and the nature of incontinence changes from stress incontinence to urge incontinence [33] with increasing age. This is due to an increased prevalence of multiple disorders and organ dysfunction in the elderly. This change has significant implications for clinical management [34]. While stress incontinence is typically managed with pelvic floor muscle training, with or without neuromuscular electrostimulation and surgery, management of urge incontinence might also include a bladder training program, transcutaneous electrical stimulation aimed at the spinal micturition reflex center, and drug therapy [35,36].

EPIDEMIOLOGY OF UI

Throughout Asia, UI remains a sensitive and taboo subject, and there is a need for more open discussion. For the sufferer, UI brings stigmatization, social embarrassment, loss of self-esteem, and loss of face, all of which prompt widespread underestimation and underdiagnosis [13]. There have been few systematic studies of the prevalence and impact of UI among older people in Asian countries.

This chapter reviews the prevalence and severity of UI within Asia with a discussion of the epidemiology of UI together with a systematic review of prevalence within the community [37–39]. Some of the factors assessed include

- Age/gender segments within the population

- Risk factors for incontinence
- Analysis of incontinence prevalence estimates
- Recommendations for studies to reliably determine the prevalence of incontinence within the Asian population

In one of the first pioneering studies done in Asia [40], the prevalence and risk factors of UI in a community-residing older population in Japan were assessed by data collected from home visits with a response rate of 95.4%. The prevalence of any degree of UI was 98/1000 in both sexes and 34/1000 of the population was incontinent of urine on a daily basis. Although there was an increasing prevalence with age, there was no greater prevalence in women. Risk factors were age >75 years, poor general health as measured by activities of daily living, stroke, dementia, the absence of participation in social activities, and poor quality of life.

In another multihospital epidemiological study [41] to elucidate the prevalence and characteristics of UI in elderly inpatients throughout Japan, all patients were evaluated by medical doctors for the following parameters: age, sex, duration of hospitalization, activities of daily living, medical diagnosis, the presence or absence of UI, type of UI, and therapy for UI. The prevalence of UI in patients under 70, 70–79, 80–89, and over 90 years old was 59.3%, 67.7%, 79.8%, and 82.2%, respectively. Overall, 1142 patients (72.0%) suffered from UI. Cerebrovascular disease was the major cause of admission to hospital in patients with UI (37.0%). The most frequent type of UI was functional UI, which was seen in patients who were mentally and/or physically unable to go to the bathroom without aid (21.5%). Specifically, 38.1% of patients in geriatric hospitals were diagnosed as having functional UI, in contrast to only 3.9% of patients in nongeriatric units. In patients with dementia, 88.7% were incontinent, whereas in patients without dementia, the prevalence of UI was significantly lower at 51.5% ($p < 0.001$). Another predisposing factor for UI was urinary tract infection (UTI). The prevalence of UI in patients with and without UTI was 87.8% and 59.5%, respectively ($p < 0.001$). Almost all patients with poor activities of daily living (who were bedridden) suffered from UI (98.5%). On the other hand, UI was less frequent in patients who could walk (26.9%). Pad (42.8%) and indwelling bladder catheter (18.3%) were the major means of containment of incontinence, whereas behavioral therapy (4.9%) and surgery (0.5%) were less common.

Yoshida et al. [13] examined the prevalence and risk factors of UI and potential factors hindering individuals from seeking treatment for UI among a community-dwelling population aged over 40 years. Data were collected by mailing a 23-item UI questionnaire to a random sample of community-dwelling individuals aged 40–75 years ($n = 3500$) in seven towns of Shiga Prefecture, Japan. The overall response rate was 52.5%. Prevalence of UI for male and female respondents was 10.5% and 53.7%, respectively. The incidence of urge incontinence increased with age in the male group. In women, stress incontinence was prevalent at all ages and the incidence of urge incontinence increased over 70 years of age. UI was more likely as activities of daily living limitations and cystitis increased. Women with a history of hysterectomy or diabetes mellitus and men who had had a stroke were at increased risk for UI. Of those who reported UI, only 3% had ever consulted doctors or other health-care professionals concerning it, 25% recognized their condition as a disease, and 38% considered it curable by appropriate treatments. In addition, 63% regarded UI as an unavoidable consequence of aging, 63% considered their condition was embarrassing, and 54% were reluctant to seek treatment from a health professional.

Lee [42] assessed the impact of UI in older Chinese care home residents in Hong Kong by a cross-sectional study using face-to-face interviews with a questionnaire mainly composed of closed-ended questions. The study was conducted at two selected elderly homes and one elderly center. The sample was composed of 92 elderly home residents and 122 elderly center users. Fultz and Herzog's [18] modified operational definition of the severity of UI was used to measure respondents' levels of UI. Specht and Maas's [21] concept of social impact was used to assess respondents' social-life suffering. It was reported that prevalence of UI increased with adult age and that incontinence affected women more than men. About 86.1% of the incontinent respondents experienced negative social impact. There were no statistically significant differences between levels of incontinence and social impact on older respondents' employment, social, family, financial, and physical conditions. Also, there were no significant differences between levels of UI and the reported levels of social impact.

OPERATIONAL DEFINITION OF IMPACT OF UI ON SOCIAL LIFE

Specht and Maas's [21] concept of social impact was adopted with modifications. To measure the adverse impact on sufferers with UI, nine complaints were developed and grouped into the following five subscales: employment, social, family, economic, and physical well-being. To measure the level of suffering (a functional issue), an operational definition of social impact was developed using the following dichotomous (yes/no) criteria:

1. Limitation of job opportunities (employment)
    a. Reductions in employment opportunities
2. Negative impact on social life (social)
    a. Restrictions on opportunities for participation in social activities
    b. Restrictions on participation in outings
    c. Need for cumbersome precautions while going out
3. Negative impact on family life (family)
    a. Need for family help
4. Negative impact on finances (economic)
    a. Increase in daily expenditure
5. Negative impact on physical condition (physical well-being)
    a. Fear of odor
    b. Fear of leakage
    c. Affect on personal appearance

It is generally assumed that moderately to severely incontinent older people experience more impact on their social lives than mildly incontinent people. Contrary to these assumptions, this study found no statistically significant differences in social impact at different levels of UI. Also, there is no significant difference in terms of the impact of moderate to severe incontinence relative to mild incontinence in older sufferers. This is noteworthy as it appears that the level of UI is not a crucial factor in determining impact on older peoples' social lives. The implication is significant; negative impact on incontinent respondents' social lives is basically unique, universal, undeniable, and unavoidable. The social impact on the entirety is the same and should be treated as "actual and real."

Theoretically, the result has four possible explanations: adjustment, habituation, social comparisons, and impression management. Moderately to severely incontinent older people may adjust to the adverse impacts of UI as time goes by or through whatever means available to handle the symptoms. The practice of adjustment and the feeling of habituation will actually reduce the significance of social impact. Additionally, moderately to severely incontinent older people frequently rely on social comparisons in making their social-impact appraisals. They assume that the social impact will become increasingly serious for their peers, while theirs will remain stable. The function of adjustment, habituation, and social comparisons is to uphold the self-esteem and self-worth of those with UI. This behavior helps them build up a better self-image and a positive impression among peers.

People with moderate to severe incontinence suffer from adjustment, habituation, and social comparisons, and impression management may effectively reduce the social impact. Methodologically, measurement and sample problems are two possible reasons for the statistically insignificant differences between the levels of incontinence. First, the measures may not be sensitive enough to detect the difference. Second, the sample is too small to allow for significant and powerful testing of the impact of incontinence. More studies are needed to further explore the social impact between levels of UI.

In a Korean telephone survey of the community by Won-Hee Park and colleagues [43] to estimate the prevalence of UI in females between 30 and 75 years, 1300 were interviewed (86.9% response rate). Overall, UI was reported by 40.8%, and 22.9%, 3.1%, and 14.9% reported pure stress, urge, and mixed UI, respectively. The prevalence of stress, urge, and mixed UI generally did not increase with age. Urge and mixed UI had a greater impact than stress UI on daily tasks ($p < 0.001$), social life ($p < 0.001$), depression or anxiety due to UI ($p < 0.001$), worry about UI ($p < 0.001$), sex life ($p < 0.001$), wearing of protection due to UI ($p = 0.011$), and quality of life ($p < 0.001$). In subjects with pure stress UI, 28.3% reported impaired quality of life compared with 43.9% and 43.8% of subjects with urge and mixed UI. Among these, willingness to seek medical consultation for their problem was seen in 19.1% (stress), 20.0% (urge), and 25.8% (mixed) of urinary incontinent individuals (Tables 6.1 and 6.2). A study has also been performed to estimate the prevalence rate of UI in a representative sample of women aged 50–65 years, using multistage sampling in South Jordan (Karak, Taffileh, Aqaba) in the Middle East [44]. The study was to assess the relationship between UI (stress and urge) and the following variables: age and parity, diabetes mellitus, UTI, body mass index (BMI), medications (diuretics), menopause, history of hysterectomy, and poor mobility. A questionnaire, which was preliminarily tested in a pilot study, and face-to-face interviews were used as the instrument for data collection. Approximately one-third of respondents had UI; 23.1% had stress UI, 26.4% had urge UI, and 18.1% had the mixed type. Prevalence rate of UI was 56.3% for women suffering from UTI and 50% for those who use diuretics. Approximately 54% of women who needed help to move around inside their house complained of UI. High prevalence rates were also observed with parity of five to six (43.5%), menopause (39.7%), and obesity (39.3%) and in diabetic women (35%). High prevalence rates of stress incontinence were found in women suffering from UTI (37.5%); in women using diuretics (39.5%), if parity was 5–6 (34.8%); and in women with a past history of hysterectomy (28.6%). Stress UI was found to increase with an increase in the BMI. The associations between urge incontinence, BMI, UTI, use of diuretics, and ability to go around inside the house were all statistically significant.

A survey of 11 cities in 11 different countries by the Asia-Pacific Continence Advisory Board (APCAB) established an overall prevalence of 12.2% (range 4.6%–23.1%) among both sexes and all age groups in these communities [45]. A Singaporean physician reported prevalence rates of 5%–15% for UI among older people living in his community [10]. In addition, more than one in five older hospital patients suffered from UI, with prevalence among nursing home residents of about 50% [10]. The APCAB study was conducted in the Philippines, Singapore, Malaysia, Thailand, and Indonesia, which was later expanded to 11 countries to determine the magnitude of UI in the region. In Thailand, the prevalence was 17%; in Taiwan, 12%; and in the Philippines, 13%. China and Singapore were reported to have the lowest prevalence rate of only 4%.

The study aimed to establish the prevalence of UI, identify the demographic factors related to its occurrence, and ascertain the determinants for seeking help for this condition among the female population of Southeast Asia.

A 34-item multiple-choice-type questionnaire–based assessment was designed to determine the presence of UI, defined by the inappropriate leakage of urine, its associated symptoms and the resulting degree of bother, and the action taken to address the condition. This questionnaire was translated into the local dialects, was validated in each country, and was administered by medically trained personnel to randomly selected women consulting at outpatient clinics for nonurologic or nongynecologic problems. The survey was conducted in a total of 10 centers: two in the Philippines, one in Singapore, two in Malaysia, one in Indonesia, and four in Thailand.

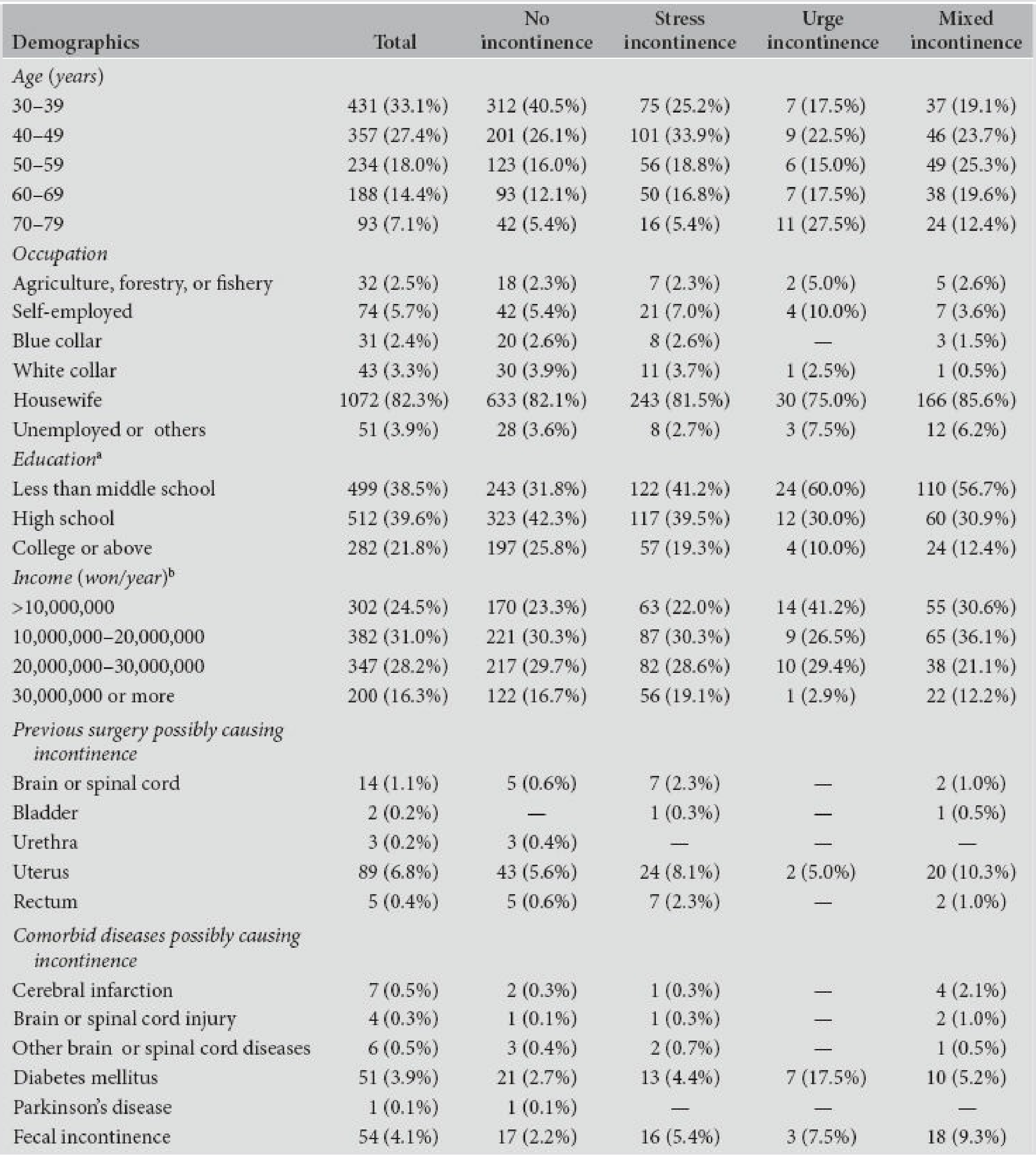
The first part of the questionnaire included questions on population demographics such as age, civil status, parity, educational attainment, occupation, monthly family income, and place of residence. The general voiding pattern was established by noting the normal daytime and nocturnal voiding frequencies. The main body of the questionnaire focused on establishing the presence of voiding dysfunction, particularly UI and overactive bladder through extensive inquiry on the different symptoms associated with these conditions.

Incontinence as a problem was assessed according to the degree of bother it caused the subject using a scoring system of 0–5 (0 as none, 5 as severe), as well as the need for leakage protection and whether the subject sought help for her condition. The relationship among the occurrence of UI and age, parity, number of vaginal deliveries, occupation, family income, type of toilet used, family history, and place of residence was also analyzed.

Study Population Demographics

Table 6.3 shows the distribution of the study population per country (total respondents 2422). While each age group was well represented (Table 6.4), the population studied was relatively young, with the majority aged below 60 years old and more than 50% younger than 40 years. Study population had 44% who were nulliparous. Among the parous respondents, the majority had had at least two deliveries (Table 6.5). Most of the women were doing office work (Table 6.6). There was a high literacy rate, with more than 85% of the population having had at least a secondary level of education (Table 6.7). The study population was evenly distributed among the income groups (Table 6.8), and at least 60% resided in the urban area (Table 6.9).

Table 6.1 Subject Demographics



Demographics	Total	No incontinence	Stress incontinence	Urge incontinence	Mixed incontinence
Age (years)					
30–39	431 (33.1%)	312 (40.5%)	75 (25.2%)	7 (17.5%)	37 (19.1%)
40–49	357 (27.4%)	201 (26.1%)	101 (33.9%)	9 (22.5%)	46 (23.7%)
50–59	234 (18.0%)	123 (16.0%)	56 (18.8%)	6 (15.0%)	49 (25.3%)
60–69	188 (14.4%)	93 (12.1%)	50 (16.8%)	7 (17.5%)	38 (19.6%)
70–79	93 (7.1%)	42 (5.4%)	16 (5.4%)	11 (27.5%)	24 (12.4%)
Occupation					
Agriculture, forestry, or fishery	32 (2.5%)	18 (2.3%)	7 (2.3%)	2 (5.0%)	5 (2.6%)
Self-employed	74 (5.7%)	42 (5.4%)	21 (7.0%)	4 (10.0%)	7 (3.6%)
Blue collar	31 (2.4%)	20 (2.6%)	8 (2.6%)	—	3 (1.5%)
White collar	43 (3.3%)	30 (3.9%)	11 (3.7%)	1 (2.5%)	1 (0.5%)
Housewife	1072 (82.3%)	633 (82.1%)	243 (81.5%)	30 (75.0%)	166 (85.6%)
Unemployed or others	51 (3.9%)	28 (3.6%)	8 (2.7%)	3 (7.5%)	12 (6.2%)
Education[a]					
Less than middle school	499 (38.5%)	243 (31.8%)	122 (41.2%)	24 (60.0%)	110 (56.7%)
High school	512 (39.6%)	323 (42.3%)	117 (39.5%)	12 (30.0%)	60 (30.9%)
College or above	282 (21.8%)	197 (25.8%)	57 (19.3%)	4 (10.0%)	24 (12.4%)
Income (won/year)[b]					
>10,000,000	302 (24.5%)	170 (23.3%)	63 (22.0%)	14 (41.2%)	55 (30.6%)
10,000,000–20,000,000	382 (31.0%)	221 (30.3%)	87 (30.3%)	9 (26.5%)	65 (36.1%)
20,000,000–30,000,000	347 (28.2%)	217 (29.7%)	82 (28.6%)	10 (29.4%)	38 (21.1%)
30,000,000 or more	200 (16.3%)	122 (16.7%)	56 (19.1%)	1 (2.9%)	22 (12.2%)
Previous surgery possibly causing incontinence					
Brain or spinal cord	14 (1.1%)	5 (0.6%)	7 (2.3%)	—	2 (1.0%)
Bladder	2 (0.2%)	—	1 (0.3%)	—	1 (0.5%)
Urethra	3 (0.2%)	3 (0.4%)	—	—	—
Uterus	89 (6.8%)	43 (5.6%)	24 (8.1%)	2 (5.0%)	20 (10.3%)
Rectum	5 (0.4%)	5 (0.6%)	7 (2.3%)	—	2 (1.0%)
Comorbid diseases possibly causing incontinence					
Cerebral infarction	7 (0.5%)	2 (0.3%)	1 (0.3%)	—	4 (2.1%)
Brain or spinal cord injury	4 (0.3%)	1 (0.1%)	1 (0.3%)	—	2 (1.0%)
Other brain or spinal cord diseases	6 (0.5%)	3 (0.4%)	2 (0.7%)	—	1 (0.5%)
Diabetes mellitus	51 (3.9%)	21 (2.7%)	13 (4.4%)	7 (17.5%)	10 (5.2%)
Parkinson's disease	1 (0.1%)	1 (0.1%)	—	—	—
Fecal incontinence	54 (4.1%)	17 (2.2%)	16 (5.4%)	3 (7.5%)	18 (9.3%)

Note: Data presented are numbers (%).

[a] Missing case, 10.

[b] Missing case, 72.

General Voiding Pattern

The voiding pattern of the study population was analyzed according to the frequency of urination (Table 6.10). The majority voided fewer than eight times during the day, with half of this population voiding between four and eight times. Almost all voided fewer than three times during the night, with nearly one-third not voiding at all at nighttime. Around 72% of the study population voided fewer than eight times per 24 hours.

Prevalence of UI

The prevalence of UI in the study population was 14.8% (359/2422). Nearly half of the incontinent individuals (47.9%) are presented with the mixed type. While less than 10% were presented with urge incontinence, 81 women (22.6%) had stress incontinence (Table 6.11).

Table 6.2 Prevalence and Frequency of Urinary Incontinence

	Stress incontinence	Urge incontinence	Mixed incontinence
Prevalence according to age cohort (years)			
30–39 (n = 431)	75 (25.2%)	7 (17.5%)	37 (19.1%)
40–49 (n = 357)	101 (33.9%)	9 (22.5%)	46 (23.7%)
50–59 (n = 234)	56 (18.8%)	6 (15.0%)	49 (25.3%)
60–69 (n = 188)	50 (16.8%)	7 (17.5%)	38 (19.6%)
70–79 (n = 93)	16 (5.4%)	11 (27.5%)	38 (19.6%)
Total (n = 1303)	298 (100.0%)	40 (100.0%)	194 (100.0%)
Frequency			
Many times a day	6 (2.0%)	2 (5.0%)	9 (4.6%)[a]/8 (4.1%)[b]
A few times a day	1 (0.3%)	2 (5.0%)	17 (8.8%)[a]/13 (6.7%)[b]
About once a day	8 (2.7%)	2 (5.0%)	11 (5.7%)[a]/16 (8.2%)[b]
2–3 times in a week	13 (4.4%)	4 (10.0%)	24 (12.4%)[a]/22 (11.3%)[b]
>1 in a week	270 (90.6%)	30 (75.0%)	133 (68.6%)[a]/135 (69.6%)[b]

*Note:*Data presented are numbers (%).

[a] Stress incontinence.

[b] Urge incontinence.

Liu et al. [46] assessed the prevalence of UI among Chinese women and its associated risk factors. Using standardized questionnaire, 5467 women with a median age of 46.8 years were randomly sampled from four communities in Shanghai. The study showed a prevalence rate of 23.3% with stress UI at 14.0%, urge UI at 3.0%, and mixed UI at 6.3% all increased with age.

Table 6.3 Frequency Distribution of Study Population according to Country

	n	**%**
Philippines	682	28.2
Singapore	228	9.4
Malaysia	351	14.5
Indonesia	257	10.6
Thailand	904	37.3
Total	2422	100.0

Table 6.4 Frequency Distribution of Study Population according to Age (in years)

	n	**%**
18–28	726	30.0
29–39	676	27.9
40–49	474	19.6
50–59	324	13.4
60–69	153	6.3
≥70	64	2.6
NI	5	0.2
Total	2422	100.0

*Abbreviation:*NI, not indicated.

UI risk factors were aging, lack of education, poor rural living environment, intense manual labor, the absence of physical exercise, hyperlipemia, diabetes, nocturia, consumption of greasy food, divorce, chronic pelvic pain, pelvic organ prolapse, frequent UTI, and vaginal delivery without episiotomy.

Lee et al. [47] interviewed 18.4 million Korean adult women in a national survey and showed significant UI in 4.2 million, an overall incidence was 22.8%. The prevalence was slightly lower than other Asian studies.

The survey demonstrated an increasing prevalence from 19 years (2.55%) to a peak prevalence of 37%–42% at ages 55–75 years. UI was 10 times more common in married women than unmarried women.

Table 6.5 Frequency Distribution of Survey Population according to Parity

	n	**%**
0	1059	43.7
1	273	11.3
2–4	786	32.5
5–8	260	10.7
>8	40	1.7
NI	4	0.2
Total	2422	100.0

*Abbreviation:*NI, not indicated.

Table 6.6 Frequency Distribution of Survey Population according to Occupation

	n	**%**
Manual labor	296	12.2
Office work	1105	45.6
Others	904	37.3
Unemployed	117	4.8
Total	2422	99.9

Table 6.7 Frequency Distribution of Survey Population according to Educational Attainment

	n	**%**
Never went to school	84	3.5
Primary school	293	12.1
Secondary school	582	24.0
Pre-university	380	15.7
University	652	26.9
Professional education	414	17.1
NI	17	0.7
Total	2422	100.0

*Abbreviation:*NI, not indicated.

Table 6.8 Frequency Distribution of Survey Population according to Monthly Income

	n	**%**
A	316	13.0
B	310	12.8
C	493	20.4
D	322	13.3
E	424	17.5
F	375	15.5

NI	182	7.5
Total	2422	100.0

*Abbreviation:*NI, not indicated.

Table 6.9 Frequency Distribution of Survey Population according to Place of Residence

	n	%
Urban	1473	60.8
Semiurban	676	27.9
Rural	230	9.5
NI	43	1.8
Total	2422	100.0

*Abbreviation:*NI, not indicated.

Stress UI was the most common type of involuntary urine loss experienced by Korean women. Of the incontinent women, 48.8% reported stress UI symptoms only; 7.7%, urge UI symptoms only; 41.6%, mixed UI symptoms; and 1.9%, other UI symptoms.

Lee et al. [48], in a Korean EPIC study, adapted on the basis of the European EPIC study, a unique and first population-based prevalence study of lower urinary tract symptom (LUTS), overactive bladder (OAB), and UI.

LUTS was seen overall in 61.4% of respondents (53.7% of men and 68.9% of women). Storage LUTS was more common in women (44.6% of men and 64.4% of women); however, men showed more incidence of voiding LUTS (28.5% of men and 25.9% of women) and postmicturition LUTS (15.9% of men and 13.9% of women).

Table 6.10 Frequency Distribution of Survey Population according to Voiding Frequency

	n	%
Daytime		
1	74	3.1
2–4	917	37.9
4–8	1217	50.2
>8	167	6.9
NI	47	1.9
Total	2422	100.0
Nighttime		
0	628	2509
1	1027	4204
2–3	667	27.5
>3	73	3.0
NI	27	1.1
Total	2422	99.9
24 hour frequency		
<8	1737	71.7
≥8	638	26.3
NI	47	1.9
Total	2422	99.9

*Abbreviation:*NI, not indicated.

Table 6.11 Frequency Distribution of Incontinent Population according to Type of Incontinence

Type	n	%
Stress	81	22.6
Urge	31	8.6
Mixed	172	47.9
Undetermined	75	20.9
Total	359	100.0

Incidence of OAB was similar in men and women at 12.2% (men 10.0% and women 14.3%), with a marginal increase over the age of 40 years.

UI was predominantly seen in 28.4% of women and 2.9% of men, with urge incontinence being the most prevalent in men and stress incontinence in women.

Bodhare et al. [49] conducted a cross-sectional study above the age of 35 years in two villages in rural Andhra Pradesh state in India showed a UI prevalence of 10%. The most prevalent type of incontinence was stress incontinence (57%) followed by urge (23%) and mixed incontinence (20%). Obstetrical factors, parity, age at first delivery, history of forceps delivery, and prolonged labor were factors affecting outcome of UI.

Singh et al. [50], in their single-center obstetrics and gynecology department cross-sectional study attending outpatient department, screened women for UI. The overall UI incidence was 21.87%, of which stress incontinence contributed 73.8%, followed by mixed 16.8% and urge incontinence 9.5%. The prevalence was low in women up to 30 years of age (7.5% in women less than 20 years and 11.6% in women between 21 and 30 years of age). In women above 30 years of age, the prevalence ranged from 27.8% to 42.8% with maximum prevalence in the age group of 61–70 years of age.

Prevalence of UI was higher in the vaginal delivery group (26.84%) compared to the nulliparous women (9.42%) and those with cesarean deliveries (8.59%). Postmenopausal women and women who have had hysterectomy showed higher incidence.

INCONTINENCE AS A PROBLEM

The majority of the population who experienced incontinence in this survey was not bothered or, if so, was only mildly bothered by their condition (Table 6.12). However, a major portion (157/359 or 43.7%) felt that protection from leakage was necessary. Of the 359 affected individuals, 150 (41.8%) sought help for their condition.

Factors Related to the Occurrence of UI

Age, parity, mode of delivery of childbirth, number of vaginal deliveries, occupation, family history, and family income were found to be significantly related to the occurrence of UI. The type of toilet used and the place of residence were not found to be related to the occurrence of the condition (Table 6.13).

Age

Increasing age was found to be significantly related to the occurrence of incontinence. By the age of 40 years, the risk for incontinence was found to be increased by 2.5 times (95% CI: 2.0–3.1). The odds progressively increased to 2.8 times and 3.4 times at ages 50 and 60 years, respectively.

Parity

The majority of the incontinent population was parous. There was a significant correlation between the increasing prevalence of incontinence and higher parity. A woman who had delivered at least once was found to be 2.1 times (95% CI: 1.6–2.7) at risk for incontinence compared to a nulliparous woman. With a parity of more than four, the odds increased to 2.5 times.

Table 6.12 Frequency Distribution of Incontinent Population according to Degree of Bother

Bother score	n	%
0—none	130	36.2
1—very mild	94	26.2

2—mild	54	15.0
3—moderate	23	6.4
4—severe	14	3.9
5—very severe	18	5.0
NI	26	7.2
Total	359	99.9

*Abbreviation:*NI, not indicated.

Mode of Delivery

There was a higher prevalence of incontinence among those who delivered vaginally, by forceps, or a combination of both; a woman who has given birth vaginally has twice the risk of UI than one who has delivered abdominally.

Number of Vaginal Deliveries

Taking into account vaginal deliveries (including forceps delivery), there was a significant relationship of increasing prevalence of incontinence with a higher number of deliveries. More than one vaginal delivery increased a woman's risk for incontinence to 2.0 times (95% CI: 1.6–2.6). The odds increased to 2.6 times when the number of deliveries reached five.

Occupation

The prevalence of incontinence was highest among those doing manual labor (see Table 6.6). This was found to be statistically significant, with a woman who has done manual labor at 1.6 times (95% CI: 1.3–2.1) the risk of having incontinence.

Family History

The family history of incontinence was significantly related to the occurrence of the condition. A woman with a positive family history was 2.4 times (95% CI: 1.9–3.0) at risk of having the condition as compared to one without.

Family Income

A higher prevalence of incontinence was found among those from the lower-income group, which was found to be statistically significant. A woman earning less than "E" had 1.7 times risk (95% CI: 1.3–2.2) of having incontinence.

Factors Associated with Seeking Help for UI

Of the incontinent population, 42% sought help for their condition, consulting either a specialist or a general practitioner (Table 6.14). Among the factors studied in relation to the likelihood of seeking help for UI, only age and degree of bother were noted to be significant (Table 6.15). Increasing age positively influenced the likelihood of seeking a consultation. A woman of at least 50 years of age is 2.4 times more likely to seek help for her condition compared to a younger woman. This likelihood increases to 2.5 times by age 60 years.

The incontinent female who is moderately bothered (score of at least 3) is 3.7 times (95% CI: 2.0–6.9) more likely to seek consultation for her condition compared to one who is less affected. A severe condition increases this likelihood to 5.1 times (95% CI: 2.5–10.4).

Discussion

Prevalence: Comparison with World Figures

The prevalence of UI in this Asian survey is comparable to the Western figures [51–54] and demonstrates the fact that while the condition may not present as a significant problem, UI is prevalent in the Southeast Asian population. Additionally, this puts into question the presumed fact that UI is more common in those with European ancestry than in those with Pacific ancestry. Thus, it is worthwhile investing time and effort to study the problem, its causes, and its management (Figures 6.1 and 6.2).

Table 6.13 Demographic Factors and Their Relation with the Occurrence of Urinary Incontinence

	Incontinence[a]	*p*-value			
Factor	Yes	No	Odds ratio	95% confidence interval	
Age (in years)					
18–28	58	661	<0.001	2.466 (<40 vs. ≥40)	1.959–3.105
29–39	82	587	2.766 (<50 vs. ≥50)	2.178–3.512	
40–49	76	397	3.391 (<60 vs. ≥60)	2.491–4.615	
50–59	69	248			
60–69	49	103			
>70	24	40			
Parity					
0	104	943	<0.001	3.391 (0 vs. ≥1)	1.648–2.685
1	38	232		(<5 vs. ≥5)	
2–4	133	646			
5–8	69	191			
>8	14	26			
Mode of delivery					
Vaginal only	197	813	<0.001	2.067 (vaginal/forceps vs. cesarean/none)	
Cesarean only	26	160			
Forceps only	3	18			
Combination	25	94			
None	104	945			
Number of vaginal deliveries					
0	131	1111	<0.001	2.025 (≤1 vs. >1)	1.613–2.541
1	34	183			
2–4	108	531			
5–8	69	181			
>8	13	24			
Occupation					
Manual labor	62	231	<0.001	1.645 (manual labor vs. office work/others)	1.284–2.108
Office work	139	958			
Others	152	752			
Monthly income					
A	30	286	<0.001	1.367 (<F vs. F)	1.021–1.831
				1.682 (<E vs. ≥E)	1.303–2.171
B	56	253			
C	82	406			
D	54	264			
E	43	377			
F	69	302			
Family history					
Yes	174	631	<0.001	2.411	1.924–3.021
No	104	1056			
Type of toilet used					
Sitting	239	1345	NS	NA	NA
Squatting	109	595			
Both	9	86			
Place of residence					
Urban	210	1249	NS	NA	NA
Semiurban	107	566			
Rural	35	194			

Abbreviations: NA, not applicable; NS, not significant.

[a] Counts may not total to 2422 because category “not available” was not included in the analysis.

Table 6.14 Frequency Distribution of Incontinent Females Who Sought Help according to Person Consulted

Person consulted	*n*	%

Herbalist/traditional medical practitioner	19	12.7
General practitioner	34	22.7
Primary health-care center	17	11.3
Specialist	37	24.7
Nurse	16	10.7
Others	9	6.0
TMP + GP	5	3.3
TMP + GP + SP	3	2.0
GP + SP	3	2.0
TMP + PHCC	6	4.0
NI	1	0.7
Total	150	100.1

*Abbreviations:*GP, general practitioner; NI, not indicated; SP, specialist; TMP, traditional medical practitioner; PHCC, primary health-care center.

Types of Incontinence: Comparison with World Figures

The proportion of females with stress incontinence in relation to the other types appears to be relatively low compared to previous studies citing numbers as high as 50%. This may be due to the fact that the population surveyed is relatively young while stress incontinence is more associated with advancing age. Thus, closer attention to the problem of mixed incontinence may be necessary, being the more prevalent type among Asian females [55–57].

It must be recognized, however, that the classification of incontinence used in many of these surveys is based mainly on symptoms alone and not on any objective parameter. This is a limitation inherent in the study design, as previous studies have noted that symptoms alone do not accurately classify incontinence. Therefore, further studies must be done to verify the discrepancy in the distribution of the different types of incontinence among Asian females compared to their Western counterparts.

The factors found to be related to the occurrence of incontinence were not unexpected. Older age, higher parity, higher number of vaginal deliveries, the increased physical strain associated with manual labor, and the use of a sitting toilet have all been cited and accepted as contributing to the weakness of the pelvic floor leading to incontinence [58]. Aging has been associated with the loss of striated muscle in the area of the urethra leading to impaired continence. The change in the hormonal milieu brought about by aging also affects the ability of the urethral submucosal layer to provide the watertight closure of the female urethra. Childbearing, childbirth [59], and physical straining have been found to cause hypermobility, innervation injuries [60], and connective tissue changes [61] to the pelvic floor leading to loss of support.

Family History, Family Income, and the Occurrence of Incontinence

The significant relation between a positive family history of UI and its occurrence may be indicative of a possible hereditary component to the disease. A congenital predisposition to UI has been proposed, citing a common collagen makeup of the pelvic floor found among the affected group. However, a more likely explanation is the tendency of the members of one family to be exposed to the same type of work and physical stresses that predispose an individual to UI.

It is difficult to explain the reason behind the relationship between family income and the occurrence of incontinence. This factor may be related to parity, with those belonging in the lower-income bracket having a higher parity. In addition, the lower-income group tends to do more manual labor. Thus, it may be necessary to test the interdependence of these factors to see the true relationship between income and UI.

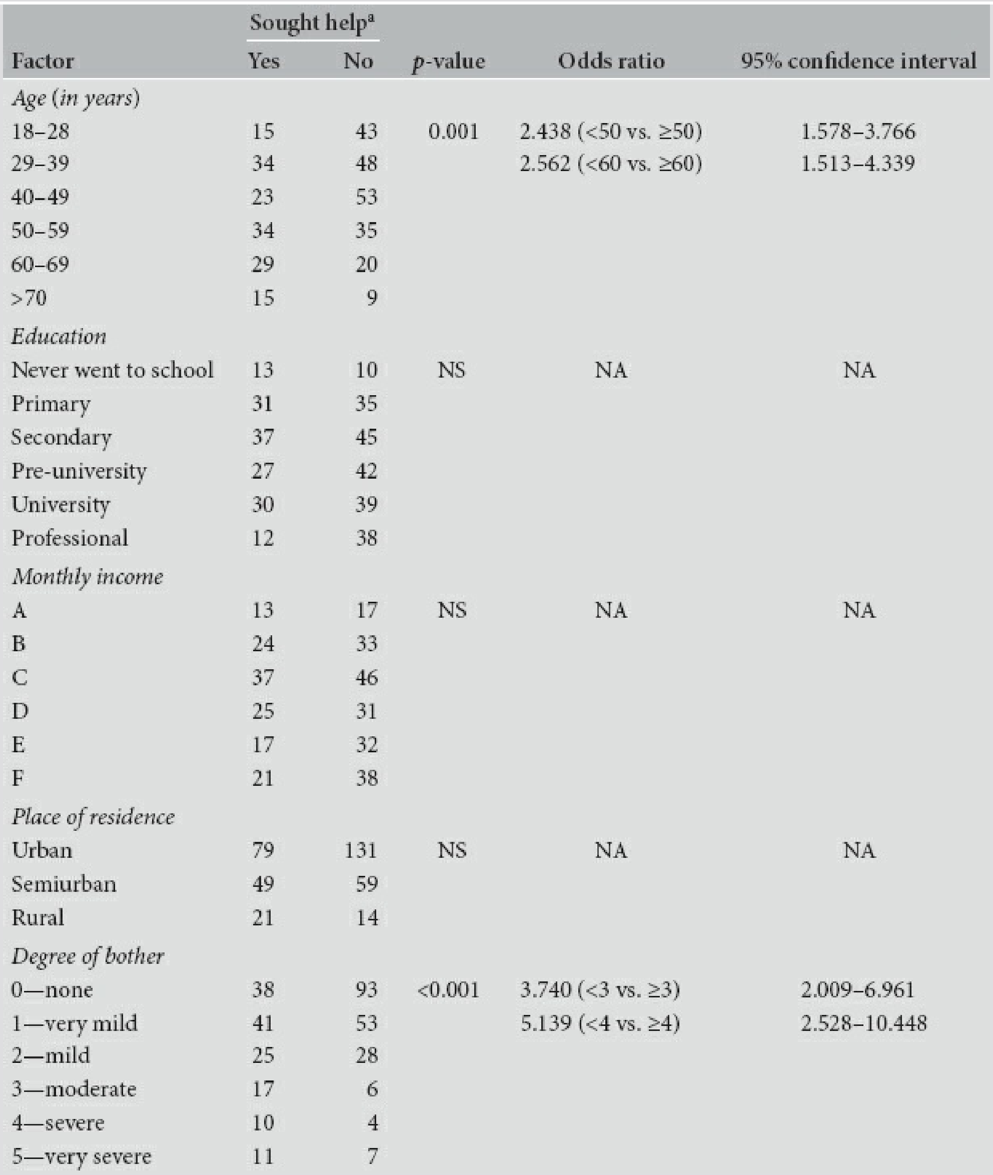
Factors Related to Seeking Help: Possible Explanations

The proportion of the incontinent population seeking help in the APCAB study is higher than most study investigators expected since this condition has been regarded as a rare clinical entity among Asians, though the same is not true for studies in other countries [62]. While this observation is an interesting finding, this high figure may be due to the fact that this survey is institution-based and the population surveyed may be those who are motivated to seek a medical consultation for any disease condition. Therefore, a community-based survey must be undertaken in order to verify this finding.

It is interesting to note that almost one-fifth of those seeking help do so by seeing a traditional medical practitioner. This underscores with high regard that the Asian patient still gives to traditional medical science despite decades of Western medicine with its advances. Further studies must be conducted to determine why this is so. This is important in the creation of efficient and effective programs that aim to encourage the affected population to find the solution to their problem.

It is apparent that demographic data are inadequate to fully explain the occurrence of UI and why an affected individual seeks help for the condition. A more objective assessment and a clinical study of the disease must be undertaken to completely understand its pathophysiology. In addition, a deeper and more exhaustive analysis of the attitude of the population toward the disease and the reasons for seeking consult is warranted. Knowledge gained from this will be valuable in future programs and campaigns to increase awareness of UI and to encourage the affected population and the caregivers to address the problem and pursue its solution.

Table 6.15 Demographic Factors and Their Relation with Seeking Help



	Sought help[a]				
Factor	Yes	No	*p*-value	Odds ratio	95% confidence interval
Age (in years)					
18–28	15	43	0.001	2.438 (<50 vs. ≥50)	1.578–3.766
29–39	34	48		2.562 (<60 vs. ≥60)	1.513–4.339
40–49	23	53			
50–59	34	35			
60–69	29	20			
>70	15	9			
Education					
Never went to school	13	10	NS	NA	NA
Primary	31	35			
Secondary	37	45			
Pre-university	27	42			
University	30	39			
Professional	12	38			
Monthly income					
A	13	17	NS	NA	NA
B	24	33			
C	37	46			
D	25	31			
E	17	32			
F	21	38			
Place of residence					
Urban	79	131	NS	NA	NA
Semiurban	49	59			
Rural	21	14			
Degree of bother					
0—none	38	93	<0.001	3.740 (<3 vs. ≥3)	2.009–6.961
1—very mild	41	53		5.139 (<4 vs. ≥4)	2.528–10.448
2—mild	25	28			
3—moderate	17	6			
4—severe	10	4			
5—very severe	11	7			

*Abbreviations:*NA, not applicable; NS, not significant.

[a] Counts may not total 359 because category “not available” was not included in the analysis.

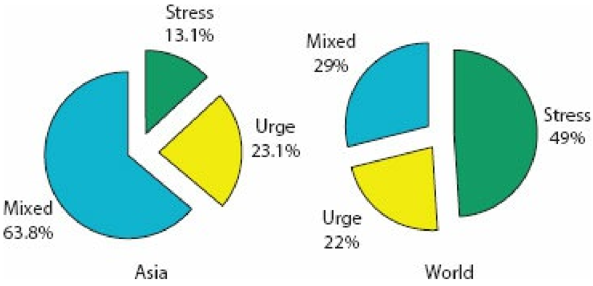


Figure 6.1 Types of urinary incontinence in the world and in Asia. (From Choo MS et al., *Int Urogynecol J Pelvic Floor Dysfunct*, 18, 1309, 2007.)

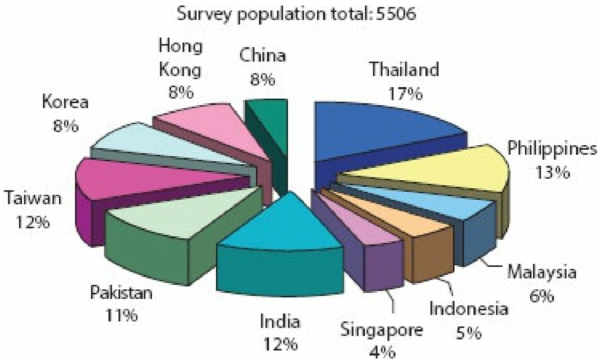


Figure 6.2 Prevalence of urinary incontinence in Asia.

The prevalence of UI among Southeast Asian females appears comparable to worldwide figures. As such, it is a significant and common problem requiring attention. The incontinent female in Southeast Asia is most likely to be older, be of higher parity, and have delivered vaginally, does manual labor, earns less, has a positive family history for the disorder, uses a squatting toilet, and resides in a rural area. A significant portion of the incontinent population has been noted to seek help. This is most likely composed of the older age group and those who suffer from the condition to a greater degree.

CONCLUSION

The occurrence of UI can be described in terms of prevalence (the number of individuals who have incontinence at a point in time), incidence (the number of individuals who newly develop incontinence in a period of time), and the natural history (whether incontinence improves, stays the same, or worsens over time) [63]. Each of these measures varies with factors such as whether the individual is living in the community or in a nursing home and the individual’s sex, age, and racial or ethnic group. Severity of incontinence also varies in its frequency and amount. In addition, incontinence has many different causes.

Prevalence of UI in women living in the community increases with age, from 19% at an age younger than 45 years to 29% in age 80 years and older; the rate levels off from age 50 to age 70 years, after which prevalence again increases.

Information comparing prevalence in racial or ethnic groups suggests that UI is prevalent in all ethnic groups, with some suggestion of higher rates among white women.

With the exception of prevalence of UI, most estimates of the incidence and prevalence of incontinence in adults are based on relatively small numbers of studies. Because these studies used varying definitions of incontinence and different methods of population sampling, the preceding statistics should be considered to be fairly crude estimates.

Although it is impossible to compare surveys between different time periods, countries, or even authors from the same continent or country, the numbers reported seem higher than actually seen in clinical practice, which could be due to many different factors that cause differences in various prevalence rates, which may be due to technical or cultural differences or due to management strategies offered. Hampel [64], in a meta-analysis, reviewed a series of publications for prevalence rates of incontinence throughout the world, which reported stress incontinence as the most prevalent type of all incontinence.

We must have a uniform standardized survey questionnaire [65] that is as applicable in all over the world in developed and developing countries. Without standardizing the questionnaires, we will continue to have reports that may not be meaningful for all interested parties, and it will be impossible to compare the outcomes of different studies. In determining the severity of incontinence, the frequency of UI is important, but equally important is the volume loss. A vast majority of women suffering from stress incontinence with small volume loss will usually cope with their problem and not necessarily seek medical care, whereas an individual who experiences an episode of one big volume loss will be urgently seeking help (Tables 6.14 and 6.15). It is therefore imperative that when obtaining history and performing a survey, volume loss in addition to frequency would be part of the information. Recording this information would make it possible to measure the severity on the basis of a combination of these parameters.

The type of urine loss is also of utmost importance [66]. We all know that there are different types and that each has its own unique signs and symptoms and unique methods of management. Urge type and mixed stress and urge type of incontinence appear to be the most common forms of UI in elderly men and women. If we are to understand UI better, we have to know which type we are dealing with. The correlates of UI are well known.

Finally, conventional epidemiologic [67] studies must incorporate issues relevant to all individuals suffering from incontinence, including quality of life (social and emotional well-being), financial burden, and effects on work and home.

Although UI is common among community-dwelling individuals over 40 years of age, the majority of affected individuals remained untreated due to the lack of knowledge and/or a negative perception of UI [68]. Thus, community education on UI may be needed to increase the number of UI patients who receive treatment.

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7 Epidemiology of Female Pelvic Floor Dysfunction in Africa

Stephen Jeffery and Peter de Jong

INTRODUCTION

The impact of pelvic floor dysfunction and urinary incontinence in particular, on the lives of African women, is very different from the experience on any other continent. Stress and urgency urinary incontinence, pelvic organ, and fecal incontinence no doubt affect the quality of life of African women, but by far the heaviest burden Africa carries is the prevailing problem of obstetric vesicovaginal fistulas, and the profound suffering this causes.

Africa has unique problems and challenges. Life expectancy is below 60 years in a large proportion of countries on the continent compared to the world median of 74 years [1]. The total population of Africa is estimated at 1.1 billion [2]. Despite being rich in natural resources, Africa remains the world's poorest continent due to a combination of corrupt governments, human rights violations, high levels of illiteracy, and frequent military conflicts. This clearly impacts on the quality and availability of medical services on the continent.

Obstetric fistulas overshadow all other issues related to pelvic floor dysfunction and are responsible for a huge burden of disease. A major factor affecting the treatment of women with incontinence in Africa is the poor quality of health care. Many women do not have access to even the most basic medical services, not to mention expensive anticholinergic drugs, incontinence pads, and mid-urethral tapes. Access to specialist services is even more confined and usually limited to the large cities. This translates to reduced access to the necessary skills and resources to investigate and treat women with pelvic floor dysfunction.

There are limited data on the epidemiology of pelvic floor dysfunction on the continent. In a literature review on urogynecology research in Africa, Maki et al. [3] looked at the extent and origin of published papers on this subject. The top four countries publishing papers were Nigeria (87 papers), Egypt (71 papers), South Africa (54 papers), and Ethiopia (42 papers). These countries accounted for more than two-thirds of the total number of publications in the 54 African countries. Overall, the number of papers on anal incontinence, prolapse, and sexual function was low. Fistula is appropriately a major focus of incontinence research in Africa. Maki et al. [3] found 200 papers on this subject, but more than half of these originated in Nigeria and Ethiopia. Maki et al. also report that of published papers on nonfistula urinary incontinence, more than a third originated in Guinea. The Central African Republic produced the only paper on patients' perceptions of prolapse, while South Africa produced the only paper in Africa on complications of vaginal mesh. The majority of the published research on sexual dysfunction was on postmenopausal women or in women following genital cutting. Maki's paper highlights the fact that very little is known regarding pelvic floor dysfunction for large areas of the continent.

It is important to appreciate that there are significant hurdles associated with obtaining useful epidemiological data in Africa. One of the problems is the broad range of languages spoken on the continent. UNESCO [4] estimates that close to 2000 languages are spoken, making the collection of robust data difficult. This is compounded by the unavailability of suitable questionnaires. Another issue is a lack of appropriate funding to perform good, representative epidemiological studies. The field of urogynecology and pelvic floor dysfunction is in its infancy on the continent, and until the region develops a sizeable cohort of clinicians with an interest in this specialty, good epidemiological data will not be available.

The available published prevalence data vary extensively between studies. For example, Ojengbede et al. [5] reported a prevalence of incontinence of only 2.8% in a cohort of 5000 women compared to a figure of 70.8% reported by Walker and Gunasekera [6]. Similarly, the extent of bothersome pelvic organ prolapse in Africa remains unknown. Of the few studies, the range is between 3.4% and 56.4% [6–8].

Most doctors underestimate the impact of pelvic organ prolapse, stress, and urgency incontinence in

African women because the number of women seeking care for pelvic floor disorders is significantly lower than those in well-resourced settings. The limited number of prevalence studies, however, suggests that the proportion of women suffering with these problems is comparable to other regions. The reasons for these women failing to seek help have not been properly determined. It may be that women lack the financial resources for a problem that only has an impact on her quality of life. Another possibility is the perception that nothing can be done about the problem and this may be reinforced by the relative lack of training in managing female pelvic floor dysfunction in large parts of Africa. Women on the continent also play an important socioeconomic role in their respective communities and may not prioritize seeking help for quality of life issues such as incontinence or pelvic organ prolapse. It is also important to note that in many parts of Africa, women are not empowered regarding their health and their reproductive health in particular.

Fistula-Related Incontinence

Obstetric fistulas are overwhelmingly the most important problem in female pelvic floor dysfunction in Africa. They are a devastating condition that leave women profoundly stigmatized and isolated from their communities. When one considers the pathophysiological mechanism responsible for the development of an obstetric fistula, the patient experience in the evolution of a fistula is horrifying. Prolonged, neglected obstructed labor will result in the fetal head being wedged into the maternal pelvis, leading to increasing tissue necrosis. Fetal death then occurs and macerates results in softening and eventual passage of the soft, macerated body [9]. If the woman survives this ordeal, the ensuing maternal injuries are often extensive. Many urogynecologists working in well-developed settings will be astounded by the extent of bladder and urethral injuries incurred by many of these women. This often includes either partial or total necrosis of the urethra, total avulsion of the urethra from the bladder, and extensive defects of the bladder itself. In addition to vesicovaginal fistula, many women have severe vaginal scarring and the cervix is often destroyed. They are often amenorrheic due to uterine damage and pituitary necrosis. A study in Nigeria found that 32% of women with fistula also had significant skeletal injuries, including symphyseal separation with gait abnormalities, marginal fractures, bone spurs, and complete obliteration of the symphysis [10].

The United Nations Population Fund in 2003 launched a global campaign to end fistula [11]. Accurate figures of the prevalence of fistula are not available. A recent systematic review by Adler et al. [12] has reported the overall prevalence in sub-Saharan Africa for fistula to be 1.60 per 1000 women of reproductive age. This was calculated from data extrapolated from two studies that included 28,128 participants.

One of the largest studies was a prospective population study of 19,342 women in west Africa [13], and this reported a prevalence for fistulas of 10.3 per 100,000 urban and 123.9 for rural dwelling women. Extrapolating from these data, the authors estimate a prevalence of 33,451 new obstetric fistulas per year for sub-Saharan Africa. Another cross-sectional study [14], this time reporting on data captured in Ethiopia, found a prevalence of 2.2 per 1000 women of reproductive age. They also found that at least 1.5/1000 of women remained untreated. The 2005 Malawi Demographic and Health Survey [15] collected national prevalence data on fistula through a proxy measure of symptoms. After interviewing 11,698 women, a crude rate of 1,557 per 100,000 live births and a lifetime prevalence of 4.7% was calculated.

Sobering demographic data on fistula emerged from a sample of women treated at the renowned Addis Ababa Fistula Hospital between 1983 and 1988 [16]. The mean age was 22 years, 42% were younger than 20 years of age, 52% had been deserted by their husbands, and 21% lived by begging. Furthermore, 30% had delivered without assistance and the average labor had lasted 3.9 days. Kelly and Kwast [17] also reported on a sample of 309 women attending in the Hamlin Bahir Dar Fistula Centre in Ethiopia and found that 82% had travelled at least 700 km for treatment, walking an average of 12 hours, and spending an average of 34 hours on a bus, before arriving at the treatment center.

Wall and colleagues [18] analyzed 899 obstetric fistula patients from Jos, Nigeria, and found that women with fistulas tended to have been married early (often before menarche), to be short (nearly 80% were less than 150cm tall) and small (mean weight less than 44 kg), to be impoverished and poorly educated, and to live in rural areas. Kelly [16] report that more than 50% of women with fistulas had been rejected by their husbands.

Much concern has focused on the impact of genital cutting practices, commonly referred to as “female circumcision” or “female genital mutilation” (FGM) [19] and its relationship to fistulas. About 2 million African girls per year undergo female genital cutting. It is most prevalent in Somalia, Ethiopia, Sierra Leone, Sudan, and Djibouti. Urinary incontinence may occur if there is direct injury to the bladder or urethra. It may also obstruct the vaginal outlet and hence make fistulas more common following delivery. The literature reporting on the role of FGM in the development of fistula and incontinence is thus unclear. Peterman and Johnson [20] could not find a significant relationship in their Demographic and Health Surveys study in Malawi, Rwanda, Uganda, and Ethiopia. Dirie and Lindmark [21] interviewed 290 Somali women between the ages of 18 and 34 who had undergone FGM. The mean age of the cohort was 22 years. Eighty-eight percent of women had undergone excision and infundibulation is 88%, 6.5% clitoridectomy, and 5.5% excision of the clitoral prepuce. Thirteen percent of the women experienced late complications including pain at micturition, dribble incontinence, and poor urine flow.

Various traditional African remedies are also associated with the development of fistulas. The Northern Nigerian practice of “gishri cutting” involves making a series of vaginal incisions with a glass, a blade, or a knife. Between 2% and 13% of women undergoing this gishri procedure will get a fistula [18]. Herbal remedies for various gynecological conditions, which involve the insertion of caustic chemicals vaginally, are also often used by traditional Africa healers [22]. The ensuing vaginal fibrosis and stenosis will occasionally lead to fistula formation.

Fistulas caused by sexual abuse and rape are a particularly troubling phenomenon [23]. Peterman and Johnson [20] used the recent Demographic and Health Surveys in Malawi, Rwanda, Uganda, and Ethiopia to determine the relationship between sexual violence, female genital cutting, and incontinence. Sexual violence was a significant determinant of incontinence in Rwanda and Malawi but not in Uganda. They suggest that elimination of sexual violence will result in up to a 40% reduction of the burden of incontinence. In situations of conflict, refugees and displaced women and girls often have been sexually assaulted. In wartime conditions, sexual violence is a commonly used tactic to intimidate and control. Aid workers have estimated that in war-affected areas, one woman in three is a rape victim, and the majority of new nonobstetric fistula cases are caused by sexual violence.

Fistula reconstructive surgery is complex and usually requires a high level of experience and skill. Most gynecologists, urologists, and general surgeons will not be able to offer this service without extensive training, and therefore, access to surgery varies extensively in sub-Saharan countries. Most women are dependent on the goodwill of itinerant surgeons who offer their services at little or no cost. In 2004, Browning [24] calculated that it will take 400 years to catch up on the backlog of candidates waiting for surgery and a concerted effort to train local physicians in the management of fistula is therefore required. The support of the international community is also mandatory, and this includes increasing involvement from the large organizations involved in continence care, including the International Urogynecological Association and the International Continence Society.

It is important to note that a significant proportion of women remain incontinent following repair of vesicovaginal fistula [24–26]. A group of 150 Ethiopian women was studied using urodynamics by Goh et al. [27], to determine the reasons for ongoing incontinence after repair. In their cohort, 49% had stress and 43% had mixed incontinence. They concluded that the reduced success rates following surgery for fistula may be due to the lack of attention to the other reasons for urinary symptoms and markedly impaired urethral function. This study highlights the importance of increased engagement between the clinicians involved in fistula repair and those with a urogynecology interest.

The main focus of fistula programs in Africa should be on their prevention. An obvious strategy would be to emphasize the establishment of a large number of rural obstetrics facilities on the continent. As far back as 1998, Waaldjik [28] reported that 75,000 new obstetrics hospitals would need to be built to address this problem. Millennium Development Goal (MDG) 5A [29] is to improve maternal health by 2015. Unfortunately sub-Saharan Africa has fallen far below the required reduction in maternal mortality. The aim of having an increase in the number of women delivering with a skilled birth attendant has also not been achieved. MDG 5A also required a significant reduction in teenage pregnancy and increase in access to contraception. It is unfortunate that large parts of Africa will not even come close to achieving the goals of MDG 5A by 2015. A concerted effort at multiple levels will have to be made in the future if obstetric fistulas are to be eradicated on the continent.

Nonfistulous Incontinence

Stress urinary incontinence, overactive bladder, and mixed urinary incontinence have been overshadowed by the profound problem of fistula-related incontinence. However, African doctors will not be able to ignore this problem for much longer. Irwin et al. [30] have predicted a 30.8% increase in the number of women with urinary incontinence in Africa. This increase is primarily attributed to the substantial growth (29.3%) that is predicted within the general population between 2008 and 2018.

One of the challenges in acquiring data in Africa has been the unavailability of validated incontinence questionnaires in the local languages. Fortunately, this is changing and clinicians are now making an attempt to address this need. Juul et al. recently validated the Kings Health Questionnaire in Xhosa and Afrikaans, 2 of the 11 official languages of South Africa [31]. El-Azab and Mascha [32] have made a valuable contribution by validating the UDI-6 and IIQ-7 in Arabic, which is spoken by 178 million Africans living in the north and the horn of the continent. The Arabic IIQ-7 was modified to suit the Egyptian culture. Of note is that they reported a prevalence of 54% for urinary incontinence using the UDI-6. The prevalence of urge, stress, and mixed incontinence were 15%, 15%, and 25%, respectively [33]. An important aspect of quality of life emphasized by this study was that 90% of the subjects stated that the main issue was the inability to pray, due to the presence of urinary soiling. Out of the 1000 Moroccan women older than 18 years sampled by Mikou et al. [34], 271 (27%) reported incontinence in the previous month, with 49% complaining of stress urinary incontinence.

Ojengbede et al. [5] performed one of Africa's largest epidemiological studies on nonfistulous incontinence in Nigeria. In this community survey of 5001 women, the proportion of women who had ever experienced urine leakage was 7.2%, whereas only 2.8% experienced leakage at the time of the survey. The types reported included stress (2.3%), urge (1%), and mixed (0.6%) incontinence. This is significantly lower than the prevalence for all types of incontinence reported in other studies both in Africa and in other parts of the world [35]. The low prevalence of incontinence in Ojenbede's study is most likely due to the fact that 70% of the women were under the age of 50 years. This study also highlights the challenges of epidemiological research in Africa. The authors made use of an interviewer-administered questionnaire, and the authors have suggested that women may have underreported their symptoms due to embarrassment. The questionnaire was also not an internationally recognized and standardized instrument. Okonkwo et al. [36] in another paper, also from Nigeria, reported much higher incontinence rates in 3963 women presenting, with symptoms other than pelvic floor dysfunction, to a gynecology clinic The results revealed that 773 (19.5%) respondents had stress incontinence, while 864 (21.8%) had urge incontinence. An even higher percentage of women had urinary incontinence in another West African study, this time from Ghana [37]. In 200 randomly selected women attending for ultrasound, 62% had at least one symptom of incontinence. A "paper towel" test was used to objectively detect stress urinary incontinence, and 42% had a positive test with 80% of these having at least one symptom of incontinence.

Table 7.1 Results of an Incontinence Survey in South Africa

	Black	**Colored**	**White**
Numbers	411	390	406
Age	41	42	47
Parity	2.9	2.5	1.9
Stress urinary incontinence	9.0	8.2	10.3
Urge incontinence	15.3	12.8	9.9
Urinary urgency	23.4	25.0	15.3
Bothered by symptoms	13.9	12.6	10.6
Has had treatment	9.8	10	11.6

Source: Adapted from Rienhardt G et al., *Int J Urogynecol*, 14, S23, 2003.

There have been a number of studies in South Africa. Bailey et al. [38] evaluated 109 women working in a hospital setting and reported a prevalence of 25% for incontinence, but only 11% of these described it as severe. Another community-based study in South Africa [39] reported a prevalence of 35.4%, with a quarter of these women having sought help for the condition. This study also reported on pelvic floor exercises. Thirty-five percent of the total cohort had some knowledge of pelvic floor exercises with the majority of these women getting this information from the media.

In another South African study, Rienhardt and coworkers [40] interviewed 1207 women in a primary care setting using a questionnaire based on the Leicester MRC incontinence study survey (Table 7.1). This study showed little difference in the incidence of stress urinary incontinence across different age groups and race.

The clinical observation that black women have less stress incontinence than their white counterparts has long been suspected, perhaps on the basis of differences in the quality of connective tissue [41]. This impression has been strengthened recently by work by Laborda et al. [42] and Thiem et al. [43] who demonstrated the presence of an elevated elastin content in the tissue of black women. This issue needs to be clarified by further studies.

The management of incontinence in Africa remains a major challenge. The standard treatment options for incontinence that are available to women in well-resourced settings are not accessible in most parts of Africa. A mid-urethral sling, for example, costs approximately $500, which is often a lot more than the average household income for a middle-class African family. When training doctors working in low-resource settings, it is essential for them to be familiar with cost-effective strategies. Options such as the fascial pubovaginal sling and Burch colposuspension will remain standard treatment options in this region for women with stress incontinence.

PELVIC ORGAN PROLAPSE

For most parts of Africa, there are even fewer epidemiological data on pelvic organ prolapse. In their review on a urogynecology research in Africa, Maki et al. [3] found only 21 papers in PubMed on prolapse from the continent. With the high parity associated with African women, one would expect large numbers of African women to be suffering with this problem. One of the best studies on the epidemiology of pelvic organ prolapse in Africa was the community-based reproductive health survey conducted in Gambia by Scherf et al. [7] In this paper, authors used questionnaires to assess 1067 women for pelvic organ prolapse symptoms. These women were also examined to determine the presence or absence of prolapse. Of note is that the mean parity in this cohort was 6.7. Fourteen percent of the patients had moderate or severe prolapse, warranting surgical intervention. The proportion of these women who actually reported symptoms in the questionnaire, which was administered via a fieldworker, was only 16%. The authors felt that the most likely explanation for the underreporting of symptoms is that women do not interpret what they feel as abnormal, perhaps assuming that a certain amount of discomfort or even pain does not indicate a problem. Zurayk et al. [44] have found that women in developing societies are socialized to endure pain and discomfort particularly if it is related to a problem of the reproductive organs. Walraven et al. [45], in their reproductive morbidity study found that women tend to underreport their symptoms, unless they were related to a genital ulcer or infertility. The issue of underreporting of pelvic floor symptoms and the delay in seeking medical care requires further investigation in Africa.

Another Ghanaian community-based [45] study of 200 women reported a prevalence for pelvic organ prolapse of 12%, with 80% of these women reporting significant symptoms. Only one-third of women with symptoms had sought medical care. The main reason for not having treatment was cost. A hospital-based study of 143 women in Ethiopia [46] found that the patient’s occupation was a significant risk factor for prolapse. They report that 68% of women were employed as rural women farmers and that their day-to-day tasks included assisting in the farmland, marketing, wood and water collection, carrying their babies on their backs, and grinding corn. Many of these women were even expected to perform these tasks during pregnancy and puerperium that may have a detrimental effect on pelvic organ support structures.

Very little data are available on the procedures that are being offered to women with pelvic organ prolapse. However, the data that are available [46,47] would suggest that most surgeons are opting for a native tissue vaginal surgery approach to address the prolapse. Most often this involves a vaginal hysterectomy and colporrhaphy.

FUTURE CONSIDERATIONS

In the next 90 years, the population on the African continent is projected to grow fourfold [48]. This will be associated with significant challenges for a region that has traditionally faced significant poverty and unemployment. The continent has, however, demonstrated encouraging signs of development with economic growth exceeding 4% in 2012 and 2013 [49], despite a global economic recession. Large parts of Africa are rich in natural resources, and there are numerous indicators suggesting rapid growth in the proportion of people with a sizeable disposable income. We can only hope that this will have a significant impact on the obstetric services and reduce the number of fistula on the continent. Economic growth and an improvement in the status of women will also increase the demand for medical services that enhance quality of life. The international urogynecology community therefore has a responsibility to increase training opportunities in the management of women with nonfistula incontinence and pelvic organ prolapse.

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8

Tackling the Stigma of Incontinence

Diane K. Newman

INTRODUCTION

It is estimated that a quarter of a billion people worldwide suffer from urinary incontinence (UI) of varying degrees with the burden of this condition greater in developing countries (Asia, South America, Africa), making it a global health problem. The prevalence of fecal incontinence (FI) is near 10% in the general population [1]. Brown and colleagues [2] reported that one-fifth of mature U.S. women suffer from bothersome leakage of stool in the absence of acute diarrhea illness at least once a year. Despite the considerable impact of UI and FI (referred to as “incontinence”) on quality of life (QoL), many people never seek help for either UI or FI and are thus uncounted [3–6]. There has been extensive research documenting the success of various forms of conservative treatment, but reality is that less than 50% of persons with UI seek help [7,8], and even less inform a health-care provider that they have FI. Many more, especially in less developed countries, do not have help available [8,9]. The psychological consequences of incontinence are well documented, and barriers to seeking help have been frequently identified in the literature. Barriers include embarrassment, social stigma, and the mistaken belief that incontinence is either inevitable, untreatable, or a normal part of aging [10]. Public awareness and community-based continence promotion programs are ways to destigmatize UI and to promote understanding about this widespread condition [8]. This chapter will discuss the stigmatization of UI and FI and provide examples of what is currently being done worldwide to increase awareness and understanding.

THE BASIS OF STIGMA

The word stigma has been defined in different ways including “as a mark of disgrace or reproach” and as “a moral or physical blemish that serves to identify a disease or condition.”

These are negative attributes as they discredit an individual, reduce the person from a whole and usual person to a tainted, discounted one. Gartley’s [11] definition of stigma is the “recognition of difference based on some distinguishing characteristic or ‘mark’ and a consequence of devaluation for the person.” Garcia and colleagues [12] note that persons who are stigmatized are discredited thus reducing the person to a tainted human being. Stigmatization is characterized by chronic social and physical avoidance of a person(s) by other people. The key feature associated with stigma is that often, the stigmatized person and society represent extreme positions of the condition. These definitions and attributes of stigmatization are closely aligned with incontinence. Gartley [13] notes that stigma in health care is a subset of stigmatization in society and is costly for all. Heinz [14] notes that stigma associated with UI signifies something lost or abnormal.

There are several types of stigma (see Table 8.1), and each addresses an aspect of incontinence behavior. Oaten and colleagues [15] proposes that many forms of stigmatization reflect the activation of this disease-avoidance system, which is prone to respond to visible signs and labels that connote disease, irrespective of their accuracy. Joachim and Acorn [16] developed a framework that would explain how people respond to stigmas. They found that the visibility or invisibility of the condition was crucial. If it could be kept invisible (e.g., urine or stool leakage), individuals had options about whether/when to disclose information about their condition. When it was more visible, they had to focus on whether the condition could be hidden. When it could not be concealed, more stigma was likely.

STIGMA AND ITS ASSOCIATION WITH INCONTINENCE

Being stigmatized because of a chronic disabling illness means being responded to differently by the general public [17]. Three strategies are used to manage stigma: avoid hurtful situations, pass as normal, and appropriate a philosophy to help cope with the stigma (Figure 8.1).

The stigma, level of shame, and embarrassment attached to incontinence is higher than that for depression and cancer [18]. This is not surprising as bladder and bowel continence is an adjustment to the social norm, especially in Western cultures, which have developed acceptable rules and behavior for bladder and bowel emptying [19–21]. UI has frequently been linked with incompetence because control and self-restraint is important to notions of adulthood in Western society. Many feel humiliated with their condition and uncomfortable discussing UI with health-care providers [8]. Yuan et al. [22] found that many patients considered UI as shame and their own fault and were unwilling to talk about incontinence with their families, friends, or doctors.

Our society places a significant emphasis on sanitation and personal hygiene [23]. Discussions of personal hygiene and/or elimination are not part of social conversations, especially in Western cultures. During toilet training, children are inoculated with all the cultural norms and expectations concerning elimination of urine and stool [24]. If incontinence occurs in adulthood, persons revive those childhood beliefs and begin to internalize their condition causing a decrease in self-esteem and feelings of shame and of not being "normal" [10]. These barriers are shared by the public as well as by many health-care providers and may contribute to the burden of caregiving [25].

Table 8.1 Types of Stigma

Type	Definition	Behavior related to incontinence
Felt or perceived stigma	Internalize negative perceptions regarding oneself	• Denial of the problem. • Embarrassment resulting in lack of disclosure to family members, friends, or providers. • Feels "dirty," contaminated. • Discomfort with disclosing symptoms. • Concerned about odor.
Self-stigma	Harsh or unjustified beliefs about oneself	• Belief that they are the only person with the problem. • Self-isolation. • Avoids intimacy, feels sexually undesirable. • Mistaken beliefs such as "art of being a women," "part of growing old."
Enacted stigma	Discrimination that takes place at an institution or from a group	• Disgust expressed by others because of odor, frequent trips to the bathroom, etc. • Long-term care staff avoid or ignore UI complaints. • Fear of institutionalization. • Media subtle messages to "keep UI in the closet" or comparisons to "plumbing" that can be fixed.

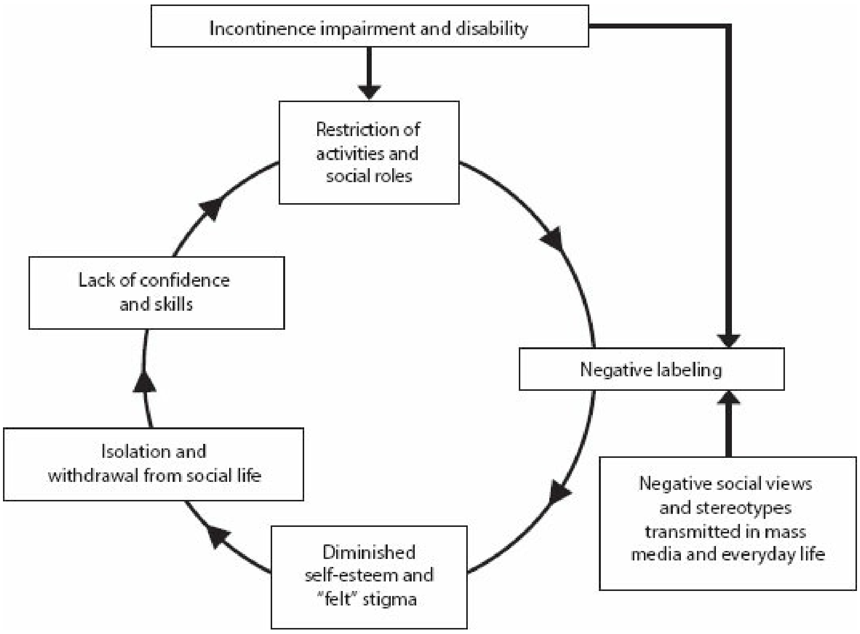
Incontinence impairment and disability
Restriction of activities and social roles
Negative labeling
Negative social views and stereotypes transmitted in mass media and everyday life
Diminished self-esteem and "felt" stigma
Isolation and withdrawal from social life
Lack of confidence and skills

Figure 8.1 Cycle of incontinence stigma: negative feedback between incontinence stigmatization, self-esteem, and participation in social activities.

Avoidance of incontinence is a strategy many use and is a worldwide coping measure. Seshan and Muliira [5] conducted a study by going door to door in Coimbatore, South India, to interview women about the presence of UI and attitudes on the condition. Of the 598 participants recruited in the study, a total of 202 (33.8%) reported that they had UI and 396 (66%) denied having UI. The attitudes of these women about UI were negative whether they experienced the problem or not. More than 80% of all respondents stated they agreed with the following statements:

- Accidental loss of urine is a common problem that every woman faces.
- Women should not go for social events if they have UI.
- There is no treatment available for UI.
- UI cannot be prevented or cured.

The embarrassment associated with UI was evident as 65% of women who reported UI had not revealed their problem to anyone, professional or not. There is no question that the stigma of UI prevents help-seeking in women [26]. Persons with incontinence experience insensitive language and loss of freedom and endure questions of a sensitive nature.

The experience of UI generally included the subthemes of fear, stigmatization, and shame. Siddiqui and colleagues [27] systematically reviewed perceptions regarding UI in women of different racial and ethnic backgrounds. Dominant themes fell into two categories, UI management and UI experience, and were similar across racial/ethnic groups. Women reported a preference for discussing UI with other women, even if this was not a physician. Nonwhite women expressed self-blame and perceived UI as a negative outcome from childbirth or prior sexual experiences. Latina women maintained more secrecy around this issue, even among family members. Figure 8.2 depicts the themes among these women.

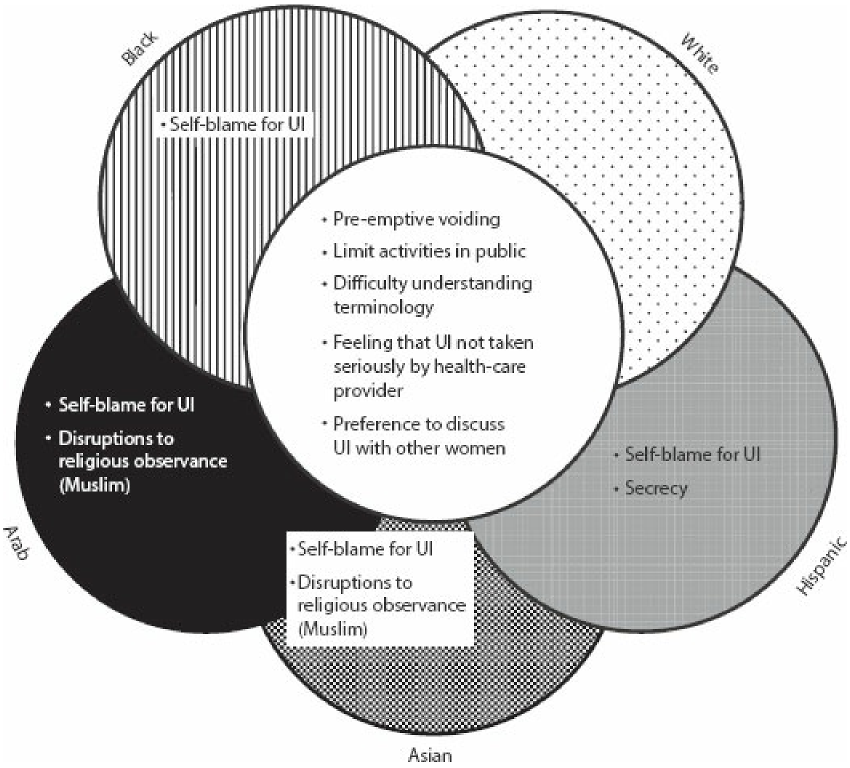
Black
• Self-blame for UI
White
• Pre-emptive voiding
• Limit activities in public
• Difficulty understanding terminology
• Feeling that UI not taken seriously by health-care provider
• Preference to discuss UI with other women
• Self-blame for UI
• Disruptions to religious observance (Muslim)
Arab
• Self-blame for UI
• Secrecy
Hispanic
• Self-blame for UI
• Disruptions to religious observance (Muslim)
Asian

Figure 8.2 Similarities and differences in perceptions about urinary incontinence on different ethnic groups.

Similar perceptions are reported by persons who experience fecal or anal incontinence. Olsson and Berterö [28] conducted a qualitative interpretative study based on interviews conducted with five women living with FI. The analysis resulted in four different themes: self-affirmation, guilt and shame, limitations in life, and personal approach. They found that living with FI had a lot in common with living with a stoma, including associated taboo, guilt and shame, and a persistent need for control.

Ignorance and lack of tolerance by and of others is common, leading frequently to anger and withdrawal. Whether the condition is visible or apparent to others (e.g., disfigurement) or concealed (e.g., colostomy or incontinence) does not change the way the person with the condition feels or reacts. The stigma associated with incontinence is similar to the stigma in other conditions and is associated with public ignorance and lack of awareness. The shame, embarrassment, and stigma associated with these conditions pose significant barriers to seeking professional treatment, resulting in many persons who suffer from these conditions living in silence [12,29]. The traditional medical model of care is very much focused at "treatment" but does not empower the sufferer to actually develop strategies to cope with what is often a lifelong condition. The topic of stigma associated with both UI and FI have received scant attention in the research literature despite its associational.

SOCIAL "TABOO" SURROUNDING THE LACK OF BLADDER AND BOWEL CONTROL

Bladder and bowel problems are ignored, they are taboos, subjects not talked about because the truth is too unpleasant for people to acknowledge [30]. Society also ignores the presence of a taboo by refusing to acknowledge or address it; the taboo is stigmatized [31]. It is possible to understand the long-standing stigma surrounding unexpected loss of urine and feces by considering the potential health consequence of incontinence on society [9]. Epidemiological and clinical studies of individuals with incontinence indicate that the condition has a considerable impact on overall QoL and well-being. The inability to control urine or feces is one of the most unpleasant and distressing symptoms a person can experience, causing stigmatization and denial of the condition [12]. Emotional well-being is impaired, probably as a result of social isolation and feelings of stigmatization produced by the incontinence. Society does not know how to respond to persons with incontinence, so avoidance is the norm. This public stigma affects treatment-seeking attitudes through internationalization of messages [32].

STIGMA AND ITS EFFECT ON CARE-SEEKING

A common phenomenon seen in conditions that have greater stigma (and often are less life-threatening) is that they tend to take a much longer time to be reported to a health-care provider (e.g., physician) and even longer to family, friends, and others. Urologic and gastrointestinal symptoms are associated with feelings of stigma, making it challenging for individuals to talk with doctors about their condition [33,34]. To avoid embarrassment, persons with incontinence turn to "self-management" rather than "seeking help" from a doctor or nurse. Unfortunately, factors that promote care-seeking behavior for incontinence issues remain less researched and are complex and multifactorial [8]. With chronic problems like urinary and FI, it is important to understand what triggers the patient to consult a health-care provider [35]. Older adults may be keen to seek help if they are concerned that a health issue such as how incontinence impacts on their ability to remain independent and living in the community [21]. In certain parts of the world, the gender of the person with incontinence may be a factor in help-seeking behavior and the gender of the health-care provider may be a barrier. A known barrier is terminology for incontinence as how patients relate their condition may not match health-care professional's medical assessment. In an Internet-based survey of mature women who reported FI, they preferred the term "accidental bowel leakage" (n = 667, 71.1%) as opposed to "bowel incontinence" (n = 211, 22.5%) and FI (n = 60, 6.4%) [2].

Barriers to seeking help for continence issues that have been frequently identified in the literature include embarrassment, social stigma, and the mistaken belief that incontinence is inevitable, untreatable, and/or a normal part of aging. The authors of a Swedish study suspected that lack of knowledge, worries about different procedures, and negative expectations may be important factors in reducing the desire to seek treatment among even those most severely affected [36]. Embarrassment and fear of humiliation have been identified as the major factors influencing reluctance to seek help among women with long-term UI [37]. Among women affected by UI in the UAE, reasons for not seeking help included embarrassment (38.2%), choice of self-treatment because of low expectations from medical care (38.2%), and assuming that UI is normal (23.3%) [38]. Among women with gynecological cancers who experience concomitant LUT, failure to seek help for the latter symptoms has been attributed to a perception that the LUTS were not serious enough symptoms to warrant attention and lack of awareness of treatment options [39].

The Boston Area Community Health population-based random epidemiological survey of urologic symptoms (n = 5503) indicated that the stigma of UI also includes other lower urinary tract symptoms (LUTS) [34]. Overactive bladder (OAB) symptoms of urgency and frequency were linked to social interruption, loss of socially expected control of the body, not understanding the nature of the bladder problem, and the need to mix private behavior and public space. The stigma of OAB and UI was correlated to whether the problem was perceptible (i.e., odor or observation of trips to the bathroom or soiled clothes) or concealed. Men reported feeling stigmatized for being seen making frequent trips to the bathroom and feared being viewed as impotent. Women feared being stigmatized based on having an unclean body and a compromised social identity. Like others, Hispanic individuals wanted to keep urinary symptoms a secret from others.

Patel et al. [40] found that many patients had a significant emotional component to their experience of FI and that knowledge about the terms used to describe the condition was often limited.

INCONTINENCE, ATTITUDES, AND BELIEFS

The way people react to a person with incontinence is influenced by many factors. The further the person is connected from the sufferer, the more negative attitudes become. As the condition becomes more severe, the more obvious it becomes to others, and often, therefore, the more the person is likely to be stigmatized [12,21]. In addition, attitudes and reactions of both the person with incontinence and those in society who interact with that person may vary according to the age of the person. At the extreme is the newborn child, where incontinence is regarded as a norm, through to childhood bedwetting, all the way to a frail old person in a nursing home. Depending on the age, sex, and social situation of the person, the reaction may well be different.

It is important to understand how attitudes and stigma changed for these conditions. An important component is breaking the cycle of public and personal ignorance through education and public awareness programs [8,29]. For this to be successful, there needs to be a partnership between health-care professionals, governments, and industry groups with a vested interest to work together to break the cycle of ignorance and negative attitude. Central to this is the availability of funds, either in allocated dollars or “in kind” (e.g., access to advertisements), which represents an ongoing funding source. A group of experts [9] conducted a systematic review of existing evidence, collated qualitative data, and used expert consensus to develop an internationally applicable service specification for continence care around the world. This service can be tackled locally and internationally in order to raise awareness of incontinence, bring a greater opportunity to incontinence management, and improve the plight of hundreds of millions of people around the world.

The good news about stigma is that individuals and society as a whole continues to change its views on what is or is not a stigmatizing condition. One reason is technology as consumers now have immediate access to information about incontinence via the Internet and social media (e.g., YouTube). In light of the reluctance of those affected by stigmatized illnesses such as incontinence to seek treatment or to ask health-care professionals for information, the Internet may prove to be a useful tool for patient education, public health outreach, and improving QoL in those with incontinence [41]. In a national survey of Internet users in the United States, Berger and colleagues [42] found a trend among people with a stigmatized illness such as UI to more likely report that using the Internet increased their health-care utilization and communication with a health-care provider.

ROLE OF NATIONAL ORGANIZATIONS

As previously mentioned, the stigma associated with incontinence is similar to other conditions and is associated with public ignorance and lack of awareness. An important component is breaking the cycle of public and personal ignorance through education and public awareness programs. As the stigma associated with incontinence is similar to other conditions and is associated with public ignorance and lack of awareness, educating the public will increase their awareness of the condition. Therefore, it is important to understand how attitudes and stigma have changed for these conditions. There have been some advances in breaking the cycle of public and personal ignorance through education and public awareness programs [43]. Patient advocacy organizations for UI have been formed worldwide to promote awareness (www.icsoffice.org).

Continence promotion involves informing and educating the public that incontinence is not inevitable or shameful, but is treatable or at least manageable [8]. The International Continence Society, a professional organization, has supported the work of organizations that promote incontinence awareness and education, and promotion. Although the ratio between affected patient populations and continence national organization funding has not been formally studied, anecdotal information suggests that continence promotion is among the most difficult of medical problems for which to obtain funding. In view of all these challenges, the proliferation of new national continence organizations, especially in Asia and South America, is a validation of both the need for continence promotion and the dedication of those who have recognized and are addressing this need.

SUMMARY

In order to improve health care for those men and women with incontinence, the social stigma must be removed, public education about resources and treatment must be increased, and health-care professionals need to be trained in incontinence management. The good news is that there is a growing international awareness about the need to "destigmatize" incontinence by promoting awareness through partnerships of health-care professionals, governments, and industry. This process must continue in order for incontinence to be removed from the list of conditions associated with stigma so that people can and will seek help.

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9

Natural History and Prevention of Urinary Incontinence and Urogenital Prolapse

C. K. Madhu, R. Trochez, and Robert M. Freeman

INTRODUCTION

There are few studies that have prospectively evaluated the natural history of urinary incontinence (UI), pelvic organ prolapse (POP), and fecal incontinence (FI) in women who have not undergone treatment. Epidemiological studies are described in Chapters 2 through 7. A hypothesis for the natural history is presented with possible implications for preventative strategies.

The chapter is organized under the following headings:

1. Natural History Urinary Incontinence
2. Natural History of Pelvic Organ Prolapse
3. Natural History of Fecal Incontinence
4. Risk Groups and Preventative Measures
5. Prevention of Urinary Incontinence and Prolapse following Gynecological Surgery

NATURAL HISTORY OF UI

Hypothesis for the Genesis of SUI

The processes during pregnancy and childbirth and factors like age, body mass index (BMI), chronic cough, and genetic factors seem to have an effect on prevalent UI and POP [1]. During pregnancy the endopelvic fascial attachments of the bladder neck and distal sphincter are weakened possibly due to hormonal influences [2]. Progesterone reduces urethral closure pressures and produces connective changes [3,4] that probably contribute to the high incidence of any antenatal incontinence. In most cases, however, incontinence *improves* after delivery [5]. Why stress urinary incontinence (SUI) should persist postpartum in some women is unclear, but vaginal delivery is implicated. If the endopelvic fascial attachments and sphincter function are not damaged at delivery, then the changes seen antenatally are likely to revert to the *nonpregnant* state with the return of urethral function and continence. However, if these structures are damaged or are inherently weak in the *nonpregnant* state, then recovery might not arise. Support for this hypothesis comes from studies suggesting the presence of a constitutional factor, e.g., weak connective tissue/fascia in women with SUI [6,7]. For example, there is a known association between connective tissue disorders and UI and POP, e.g., in Marfans and Ehlers–Danlos syndromes [8]. Also, in women with POP, an association with joint hypermobility has been demonstrated suggesting a possible underlying connective tissue weakness [9]. Should such individuals suffer pelvic floor trauma at delivery, then recovery might not be complete resulting in postpartum SUI. This, along with further deliveries, aging, menopause, and muscle weakness, seems to increase the risk of long-term incontinence [10]. Further support for the hypothesis comes from the growing volume of evidence suggesting that *antenatal SUI* and, in particular, incontinence *before* a first pregnancy are high risk factors for the development of incontinence in later years [11–13].

Natural History of UI

The association between SUI and parity is well known, and, based on the available evidence, the following hypothesis regarding the genesis and natural history can be made (Figure 9.1).

A recently published large prospective longitudinal study with 16 years follow-up of over a thousand women found considerable rates of both incidence and remission of UI, overactive bladder (OAB), and other lower urinary tract symptoms (LUTS) [14]. They reported cumulative incidences of UI and urgency/OAB of 21% and 20%, respectively, with corresponding regressions of 34% and 43%, respectively. However, regression was more frequent in women with mild symptoms, suggesting that clinically relevant UI infrequently improves spontaneously. A systematic review of longitudinal studies of OAB and UI suggests that there is a dynamic progression of symptom severity in OAB, with 28% of women progressing from OAB dry to wet over 16 years, and that symptoms persist over a long period of time [15]. In a study of women reassessed 6 years after childbirth [13], there was a rate of new-onset incontinence of approximately 30% in women who had been continent at 3 months postpartum. However, in 27% who were *incontinent* at 3 months, there was spontaneous remission at 6 years. Of particular interest were those women who were incontinent *prior* to pregnancy; there was a markedly increased risk for leakage at 6 years. These interesting findings suggest that there are women at risk of incontinence, while in others there is spontaneous remission. Identification of such individuals might help in prevention of SUI (and POP) if they can be identified at an early stage (see section “Childbirth”).

Based on data from a systematic review, during the first 3 months postpartum, the pooled prevalence of any postpartum incontinence is 33%, with longitudinal studies showing small changes in prevalence in the first year after childbirth [5]. A study at 3 months postpartum showed nearly one-third of women (29%) had new-onset UI [16]. The same authors showed that at 6 years following the index childbirth, the prevalence of persistent UI was 24% [17]. Another study followed 526 women following childbirth and showed that a prevalence of UI was 11.3% at 6 weeks postpartum and this did not change at 1-year follow-up [18]. In another study (from Australia) at 4–18 months following the women’s first childbirth, 44% of them reported UI and 25% had persistent UI, and majority of these women were symptomatic during pregnancy [19].

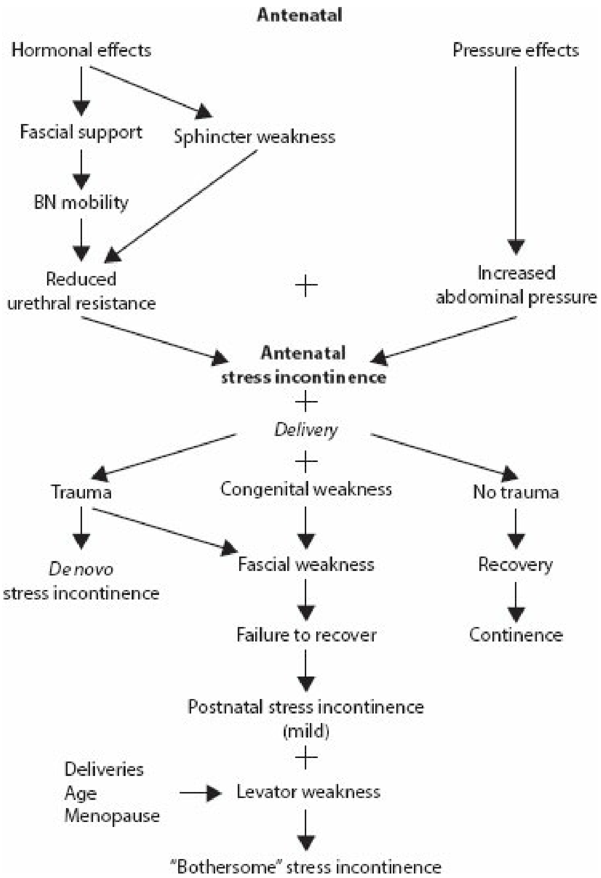

Figure 9.1 Hypothesis for the genesis and natural history of stress urinary incontinence. (Reproduced from Maclean AB and Cardozo L eds., *Incontinence in Women*, RCOG Press, London, U.K., 2002. With permission of the Royal College of Obstetricians and Gynaecologists.)

Remission of UI

UI can be considered as a dynamic condition. A 5-year longitudinal study of women less than 65 years with a baseline prevalence rate of UI of 23.6% (27.5% at 5 years) showed a mean annual incidence rate of incontinence of 2.9% and a mean annual remission rate of 5.9% [20]. A 4-year longitudinal study of women aged less than 50 years showed a mean annual incidence and remission rates of UI of 4% [21]. Another longitudinal study over 6.5 years showed a mean annual remission rate of 2.9%, and more than half of women in this study with a mild form of UI at baseline had full remission [22]. A larger 2-year study of 64,650 women aged 36–55 years showed complete remission in 13.9% of women with incontinence at baseline [23]. A 2-year study of noninstitutionalized women over 60 years showed a 1-year remission rate of 12% [24].

A study followed 2025 women aged over 65 years for 6 years (baseline prevalence of urgency incontinence was 36.3%, and of stress incontinence it was 40.3%) [25]. This study showed for urgency incontinence, the 3-year incidence and remission rates between the third and sixth years were 28.5% and 22.1%, respectively [25]. For stress incontinence, the 3-year incidence and remission rates between years 3 and 6 were 28.6% and 25.1%, respectively [25].

A longitudinal Swedish population-based study of over 100 women from 1991 to 2007 showed incidence and remission rates of 21% and 34%, respectively [14].

NATURAL HISTORY OF POP

There is limited knowledge on the natural history of POP. The reported incidence for cystocele is around 9 per 100 woman-years, 6 per 100 woman-years for rectocele, and 1.5 per 100 woman-years for uterine prolapse [26].

A 4-year observational study [27] in postmenopausal women showed an overall 1- and 3-year prolapse incidence of 26% and 40%, respectively. This study [27] also showed a 1- and 3-year resolution risk of 21% and 19%, respectively. The study also showed that over 3 years, the maximum vaginal descent increased by at least 2 cm in 11% of the women and decreased by at least 2 cm in 2.7%, with obesity and grand multiparty increasing the risk of vaginal descent progression [27].

The ProLong study, which was a longitudinal study of women (most women were asymptomatic for symptoms of POP) following childbirth, showed a 24% objective POP rate (20% of the study group) at 12 years following the index birth [13]. The SWEPOP (Swedish Pregnancy, Obesity and Pelvic Floor) study showed a 12.8% prevalence of symptomatic POP at 20 years following one childbirth [28].

As with SUI, alterations in pelvic organ support leading to prolapse might occur before delivery. Previously published prevalence studies, which might have been helpful in identifying the natural history of POP, have been hampered by selection bias (e.g., hospital-based populations in developed countries). For example, in such groups, 30%–50% of women seen for other gynecological problems have signs of POP [29,30], but most will be asymptomatic. In older age groups (>70 years), many are symptomatic and approximately 11% will undergo surgery, but there are few data on the numbers treated conservatively, e.g., with pessaries [31].

The natural history of untreated POP has been assessed in menopausal women as part of the estrogen, progestin trial of the Women's Health Initiative (University of California) [26]. Annual pelvic examinations for POP were performed on 412 women (mean 5.7 years) using a (nonvalidated) classification system. At baseline 31.8% had POP. The annual incidences of new-onset POP were 9, 5, and 7 per 100 woman-years for anterior vaginal wall prolapse, posterior vaginal wall prolapse, and uterine prolapse, respectively. Of interest were the rates of progression and regression. For *progression*, the rates were 9.5, 13.5, and 1.9 per 100 woman-years, respectively. Corresponding figures for *spontaneous regression*, especially Grade 1 POP, were 23.5, 22, and 48, suggesting that spontaneous regression is common. Only 3 women (0.7%) required surgery. These findings have been supported by a recent study [32] of 64 women with POP who chose no treatment (observation only) and were followed up with sequential POP-Q examinations (median follow-up 16 months; range 6–91 months). The majority (78%) demonstrated no change in the leading edge of the prolapse between the first and the last visit, following which 63% still continued observation [32]. These data suggest that the clinical sign of POP is common and that spontaneous regression occurs in many cases. The symptom of vaginal bulge is specific to prolapse, and the leading edge at or beyond the hymenal remnants helps define symptomatic POP [33,34]. Treatment might be unnecessary unless the symptoms are bothersome.

In developing countries, untreated POP might be more prevalent. For example, in rural Gambia an epidemiological study showed a prevalence of 46%. Only 8 of 152 with "severe POP" (i.e., subjective and objective) accepted the offer of treatment [35]. There are no data on the outcome for these untreated women. If severe and left untreated, POP can sometimes result in obstructed voiding and recurrent urinary infection. This could progress to obstruction of the upper tracts and renal failure. In a small case series of women with untreated severe POP (i.e., beyond the introitus), all had evidence of bilateral upper tract dilatation, and three had obstructive renal failure. Treatment of POP resolved the renal failure in all but one patient [24]. These findings highlight the need for prevention of upper tract changes by early treatment of advanced POP. Trauma to the cervix and vaginal skin might increase the risk of neoplasia in women with severe POP. However, there are few prospective studies to assess the risk.

NATURAL HISTORY OF FECAL INCONTINENCE

The prevalence of FI at 3-months postpartum was 9.6% in one study [36]. The authors from the same study group showed a 3.6% prevalence of persistent fecal incontinence at 6 years following childbirth (90% of these women were asymptomatic before their first birth) [37]. At 12 years follow-up, 43% of women who complained of FI at 3 months complained of persistent FI (overall prevalence rate of FI was 6%) [38]. There are few data on the prevalence of anal incontinence, which includes flatus incontinence, but it is likely to be much higher than FI alone.

RISK GROUPS AND PREVENTATIVE MEASURES

Ideally, the aim of healthcare is prevention rather than cure. Prevention can be classified as *primary* (interventions in asymptomatic individuals to reduce known risk factors for the development of a disease) or *secondary* (to detect symptoms at an early stage and to intervene to stop further development or to improve the prognosis of the condition). To stop recurrence of an illness or preventing it becoming chronic is *tertiary* prevention. In urogynecology, there is a paucity of large prospective trials to assess the impact of prevention on UI and POP.

There are known predisposing factors such as age, obesity, family history, parity/vaginal childbirth, and surgery. Identification of individuals at risk might help with implementing preventative measures.

Risk Groups

Age

POP is a common condition in older women, and advancing age has a strong correlation with the prevalence prolapse [39,40]. With advancing age, a progressive and age-dependent decrease of the density of striated muscle cells can be observed in the rhabdosphincter (due to apoptosis), which may contribute to UI [41]. Although the prevalence of incontinence is increased in the elderly, the two do not necessarily have a cause-and-effect relationship; other pathological processes associated with aging might be responsible. Resnick has created the mnemonic “DIAPPERS” to describe these: *D*elirium, *I*nfection, *A*trophic change, *P*harmacological, *P*sychological, *E*xcess urine output, *R*estricted mobility, and *S*tool impaction [42]. There is a known association between constipation and POP [43], and attention to regular bowel habit, avoiding straining, a high-fiber diet and, if necessary, laxatives might have a positive effect on prevention. Likewise, management of other risk factors such as chronic cough, smoking, and adjusting medication that has an adverse effect on the bladder could help incontinence (e.g., diuretics, calcium channel antagonists [that can cause polyuria], nonsteroidal anti-inflammatory drugs [that can lead to fluid retention], ACE inhibitors [leading to chronic cough], and sedatives) [44]. Regular toileting, easy access to toilets, restricting fluids (especially caffeine), and prevention of urinary tract infection, e.g., with cranberry juice or vitamin C, might also be effective in the prevention of incontinence in the elderly [44].

Menopause and Hormone Replacement Therapy

There is a definite aging process in the lower urinary tract, resulting in atrophic change and poor urethral function. Hormone replacement therapy (HRT) should in theory prevent LUTS. A recent Cochrane review concluded that local estrogen treatment for incontinence may improve or cure it; however, systemic hormone replacement therapy (HRT), using conjugated equine estrogen, might make incontinence worse [45]. There is limited evidence from randomized controlled trials (RCTs) regarding the use of estrogens for the prevention and management of POP [46].

Urgency

Urgency is a distressing symptom for the older patient with restricted mobility, causing panic and anxiety on the sensation of bladder fullness. There is a strong association between mobility impairment and urgency urinary incontinence (UUI), which is proportional to the severity of UUI [47]. Often, patients void more frequently to prevent urgency incontinence, which can have the opposite effect, by reducing bladder capacity and worsening the symptoms.

Strategies such as explanation, bladder retraining, pelvic floor exercises, easy access to toilets, and the use of bedside commodes might prevent urgency developing into UUI and could also prevent falls. There is evidence that patients with urgency incontinence (more than once a week) are at increased risk of falls and bone fracture than in those without [48]. These might be preventable.

Obesity

Obesity is common in women with UI and POP. When defined as "more than 20% above average weight for height and age," obesity has been shown to be more common in patients with urinary stress incontinence (USI) and detrusor overactivity (DO) than in the asymptomatic population [49]. Increasing BMI is associated with progression of POP for all three compartments, but weight loss was not associated a significant regression of POP, suggesting an irreversible damage to the pelvic floor with obesity [50]. Obesity is also a risk factor for vaginal vault prolapse after hysterectomy [51]. In pregnancy, an increased BMI has been shown to be an important risk factor for persistent UI postpartum [52,53]. Obesity is strongly associated with UI and the odds of UI increases by 1.6 for every 5-unit rise in BMI [54]. In theory weight loss should be preventative. However, studies are often hampered by the failure of subjects to lose weight. One study in morbidly obese women undergoing surgically induced weight loss showed subjective and urodynamic improvement in incontinence 1 year after surgery [55]. In a larger case series of women (BMI > 30) with UI undergoing weight loss, reduced incontinence loss and improved quality of life have been demonstrated in women losing more than 5% body weight [56]. A randomized trial in 338 overweight and obese women found that a mean weight loss of 8% in the intervention group (vs. 1.6% in controls) led to a significant decrease in weekly episodes of incontinence (47% vs. 28%) [57]. A recent systematic review and meta-analysis of studies on weight loss in UI including 2352 women showed that nonsurgical weight loss can improve UI and should be considered part of the standard practice in the management of UI in overweight women [58].

Familial and Genetic Factors

Identification of risk groups is important and family history might be relevant. It has been shown that daughters of women with UI are more likely to develop incontinence themselves [7,59]. A genetic predisposition to abnormal extracellular matrix remodeling, influenced by reproductive hormones, trauma, mechanical stress, and aging could alter normal tissue architecture and mechanical properties leading to SUI and POP [60]. Studies also suggest increased collagenolysis due to genetic polymorphisms playing a key role in extracellular protein turnover, resulting in decreased collagen and development of POP and SUI [61]. A linkage to chromosome 9 has also been demonstrated in families with POP and SUI [62]. A large twin registry study from Sweden concluded that genetic effects do contribute to the occurrence of SUI and POP, but there was a substantial effect of environmental factors providing some hope for preventative strategies [63]. A small study in four pairs of postmenopausal identical twins with different parity status, i.e., nulliparous/parous for each set of twins, found identical continence status in all four pairs, and a difference greater than one stage on the Pelvic Organ Prolapse Quantification (POPQ) assessment in only one set of twins [64], which seems to support a genetic predisposition for both UI and POP rather than parity. Racial differences have also been demonstrated, with white Caucasian women having an increased risk of SUI [65,66] and POP [39] compared to African American women. Also childhood symptoms, e.g., nocturnal enuresis and OAB might predispose to incontinence in adulthood [67]. Identifying and treating these children, e.g., by pelvic floor muscle training (PFMT), might help to prevent symptoms in adulthood.

Childbirth

Vaginal birth probably has an important role in the pathogenesis of pelvic floor dysfunction. However, not all women develop pelvic floor problems following vaginal birth, suggesting that identifying "at-risk" groups might provide an opportunity for prevention [68]. Primigravidae with excessive bladder-neck mobility antenatally (a possible marker for weak pelvic floor collagen) appear to be at higher risk of postpartum stress incontinence [69], itself a risk factor for long-term incontinence [10]. Antenatal and prepregnancy incontinence [11,13] family history of incontinence in pregnancy, obesity [53], and persistent postnatal incontinence [70] also appear to be important risk factors. Age at childbirth, BMI, and maternal height are also known risk factors that increase the risk of UI following childbirth [28]. Levator ani muscle injuries that occur in 13%–36% of women who have a vaginal delivery is associated with the development of pelvic floor dysfunction including SUI, POP, and obstetric anal sphincter injuries (OASIS) [71,72]. Prolonged second-stage labor is also associated with increased likelihood of postpartum incontinence in women who had a spontaneous vaginal birth (adj OR = 1.9) or operative vaginal birth (adj OR = 1.7) [73]. This might be related to pudendal nerve injury [74]. Such nerve damage is seen in patients with USI [75], and it has therefore been assumed that vaginal delivery alone is responsible for subsequent USI and POP. However, this assumption might not be correct; pregnancy itself might also be responsible [76]. For example, nulliparous women with USI appear to have weak pelvic floor collagen [6], and vaginal delivery in these women might increase the risk of SUI and POP if/when they become pregnant.

BMI and maternal height are other risk factors with POP. Symptomatic POP have been shown to increase by 3% for every unit increase in current BMI. Short stature women, e.g., height ≤ 160 cm who deliver a baby ≥4000 g, have been shown to have a doubled prevalence of symptomatic POP 20 years following one vaginal childbirth [28].

Identifying women at risk before or early in a first pregnancy might enable preventative measures to be introduced.

Prevention

Cesarean Section

Identification of risk groups might help with prevention, but what this intervention should be is a matter of debate. While elective cesarean section might prevent neuromuscular damage and postpartum SUI [77], this latter finding is not consistent with incidences of SUI of up to 16% in women delivering exclusively by cesarean section being reported [78,79]. However, a 12-year longitudinal study showed that such women were less likely to have UI than those who only had spontaneous vaginal births (OR = 0.46), but not if they had a combination of cesarean and spontaneous vaginal births (OR = 1.14) [80].

Patients delivered exclusively by cesarean section have a significantly reduced risk of objectively demonstrable POP, 12 years after delivery [13] and symptomatic POP by 20 years after childbirth [28]. After two decades after one vaginal childbirth, there is a 67% increased risk of UI and UI > 10 years increased by 275% compared to cesarean section [81]. This study indicates that 8–9 cesarean sections are need to prevent one case of UI [81]. The numbers needed to treat (NNT) in women who are of short stature with a baby >4 kg is 4 for SUI and 6 for POP (Gyhagen M, personal communication).

A review also concluded that short-term occurrence of any degree of postpartum SUI is reduced with cesarean section; severe symptoms are equivalent by mode of birth [82]. A prospective study showed a significantly increased risk of surgery for SUI and POP 26 years after vaginal childbirths compared to cesarean deliveries [83]. Results from these studies provide evidence for patient counseling and careful planning of mode of delivery to prevent pelvic floor dysfunction. Various models for scoring risk factors have been proposed and are being validated to provide estimates of postpartum pelvic floor pathologies to facilitate decision making and prevention of pelvic floor trauma [84,85].

PFMT

PFMT might be a less invasive form of prevention. For example, in primigravidae with antenatal bladder-neck mobility [69], antenatal PFMT has shown a reduced incidence of postpartum SUI compared with untreated controls [52]. Similar results have been seen in “unselected” primigravidae [86,87]. Postpartum PFMT also seems to be preventative both in the short [88,89] and medium term [90]. A Cochrane review with 22 studies involving over 8000 patients found evidence that PFMT can prevent UI in pregnancy (relative risk [RR] 0.71, 95% confidence interval [CI]: 0.54–0.95) and postpartum (RR 0.60, 95% CI: 0.35–1.03). It seemed that the more intensive the program, the greater the treatment effect [86]. However, the level of intervention, i.e., the PFMT regime, varied greatly in the studies, and it remains unclear whether PFMT should be targeted to women at risk, i.e., primiparous women and women with large babies and forceps deliveries, or should be a population-based intervention. Recent RCTs however failed to show any benefit of postpartum PFMT on POP [91] or UI [92].

Longer-term studies with 6 and 8 years follow-up [93,94] and one review [95] have shown that the initial beneficial effect does not persist, probably due to poor compliance. However, the incontinence in those women was not severe enough to require surgery. As PFMT antenatally and postnatally can be preventative in the short and medium term, Cesarean section might not be necessary except possibly for those women with severe incontinence before and/or during the first pregnancy [10,12] or in those with early-stage symptomatic prolapse.

Can Changing the Management of Labor Help in Prevention of SUI?

This is unlikely as the exact role of obstetric factors in the genesis of postpartum SUI is unclear. For example, there is conflicting evidence regarding prolonged second stage of labor, birth weight, epidural, episiotomy, and mode of delivery. A Cochrane review has shown an increased association of maternal perineal trauma with forceps delivery [96]. The review also suggested a significantly more third- or fourth-degree tears (with or without episiotomy), vaginal trauma, and flatus incontinence with forceps [96]. A study has suggested that the incidence and severity of SUI 1 year after forceps delivery was greater than that after spontaneous or vacuum/ventouse delivery [97]. Forceps and vacuum extraction have different benefits and risks, and the choice of instrument should be based on clinical circumstances and the level of skill of the operator (RCOG Green-top Guidance no. 26, 2011).

Episiotomy

In a Cochrane review, restrictive episiotomy compared with routine use, resulted in less severe perineal trauma, less suturing (RR = 0.71), and fewer healing complications, but with more anterior perineal trauma. There was no difference in UI or several pain measures [98]. However, as with all studies assessing episiotomy, the technique and angle are poorly described (see later).

It would appear that prevention by changing obstetric practice is not possible with the current state of knowledge. However, it might be worthwhile considering earlier delivery (by cesarean section) in short stature primigravidae who have obstructed labor before full dilatation to prevent pelvic floor injury [28]. This might be preferable to prolonged augmentation of labor and the risk of instrumental delivery (see OASIS in the following text).

Prevention of OASIS and FI

OASIS is the most important risk factor for anal incontinence that affects young women [99]. Nearly one-third of primiparous women (29.2%) have occult OASIS following vaginal childbirth (high with assisted vaginal delivery, ventouse less traumatic than forceps) [100]. An ultrasound study reported OASIS in 27.9% of women after their first childbirth, which was not recognized clinically after delivery [101]. Despite repair, 30%–50% of affected women suffer from anal incontinence [102–104], and 40% will opt for a future elective cesarean section to avoid worsening of symptoms from a further vaginal birth [105,106].

A recent study [107] of data from the English Hospital Episodes Statistics (HES) involving over 1 million women who delivered vaginally between the years 2000 and 2012 found that the rate of reported third- or fourth-degree perineal tears tripled from 1.8% to 5.9% during the study period. The rate of episiotomy varied between 30% and 36%. An increasing proportion of ventouse deliveries (from 67.8% to 78.6%) and noninstrumental deliveries (from 15.1% to 19.1%) were assisted by an episiotomy. A higher risk of third- or fourth-degree perineal tears was associated with a maternal age above 25 years; instrumental delivery (forceps and ventouse), especially without episiotomy; Asian ethnicity; a more affluent socioeconomic status; higher birth weight; and shoulder dystocia. The authors concluded that changes in risk factors were unlikely explanations for the observed increase and that this was likely due to better training and recognition. Episiotomy is associated with the lowest risk of OASIS (see the following text).

Detection of OASIS

In women with recognized OASIS/third-degree tears, 85% of them have been shown to have residual sphincter damage despite repair at delivery, with 50% being symptomatic [108]. Many remain unrecognized with one-third of women having an undetected OASI after their first delivery [109]. It is important that obstetricians and midwives are adequately trained in the identification and treatment of OASI as this might help in prevention of FI. Appropriate methods of defect repair are also important. For example, the "overlap repair" for complete tears seems to be associated with a lower incidence of fecal urgency and deterioration of anal incontinence symptoms compared with "end-to-end" repair [110]. Training is therefore recommended. Identification and repair of OASIS might be important in the prevention of long-term FI. This is ongoing via excellent courses run throughout the world (Sultan A and Thakar R, personal communication).

Obstetric Management

Episiotomy might prevent OASIS. For example, fewer third- and fourth-degree tears have been seen following mediolateral episiotomy [111,112], whereas the risk is increased by midline episiotomy [113]. The latter should probably be abandoned due to the high risk of OASIS. HES data in England have shown that episiotomy is associated with the lowest rate of OASIS [107]. A recently published study has confirmed this finding and shown that the prevalence of FI was lower after vaginal delivery with an episiotomy and similar to that after cesarean section [114].

One possible reason for the discrepancy in the literature is that many episiotomies are performed at different angles, closer to the midline resulting in an increased risk of OASIS. Standard obstetrics textbooks state that a mediolateral episiotomy should be performed at an angle of at least 40°, with most suggesting an angle of between 45° and 60°. However, two studies found that most doctors and midwives perform mediolateral episiotomies at a much lesser angulation [115,116]. These findings were confirmed by another study [117], which in addition demonstrated that the risk of OASI decreased significantly from 9.7% in women who had episiotomies at less than 25%–0.05% in women whose episiotomies exceeded 45°. The authors estimated a 50% relative risk reduction of OASIS for every 6° away from the midline that an episiotomy was performed. Instruments to accurately cut a 45°–60° episiotomy are now available [118].

The management of the perineum in the second stage of labor seems to be an important factor in the incidence of OASIS. There is some evidence that the lack of perineal protection ("hands off/poised") has become increasingly prevalent [119] and that this may play a role in the rising incidence of OASIS [107]. Studies have shown a lower OASIS rate with use of active perineal support along with episiotomy [102,120]. A recent Cochrane review, however, showed no differences in the OASIS rates with or without perineal support, but showed reduced perineal trauma with warm compresses on the perineum [121]. However, description of the methods of perineal support was poor and OASIS was not the primary outcome in the studies reviewed by Cochrane.

A recent Cochrane review also failed to demonstrate any benefit of cesarean section in the prevention of anal incontinence and recommended that preservation of anal continence should not be used as a criterion for choosing elective primary cesarean delivery [122]. However, a recently published large cohort study has shown an increased prevalence of FI in primiparous women at 20 years after one vaginal birth compared to cesarean section [114].

Forceps and Ventouse in OASIS

Use of the ventouse rather than forceps might help in prevention. While it has been claimed that both are risk factors for OASIS [123], other data suggest that ventouse is associated with fewer OASIS compared with forceps [124]. In an RCT of ventouse versus forceps delivery, there was a significant reduction in the incidence of third- and fourth-degree tears in the ventouse group [125].

HES data show that forceps without episiotomy has the highest rate of OASIS [107]. However, it might not be the particular instrument that is important, but the indications for the assisted delivery (e.g., prolonged labor), large baby [67], occipitoposterior position [126], short maternal stature [28] are known risk factors for pelvic floor trauma and OASI. These factors are out with the obstetrician's control. Nonetheless, awareness might help in the prevention, e.g., by performing an elective 45° episiotomy or if there are other obstetric indications, e.g., obstructed labor in a woman at risk and delivery by cesarean section.

Subsequent Deliveries in the Prevention of OASIS

Two prospective studies have shown that in primiparous women with persistent FI, the risk of deterioration appears to increase after the second vaginal delivery [103,127]. For these women, secondary prevention might be achieved by elective cesarean section. Large retrospective studies using an anatomical rather than a physiological outcome, i.e., recurrence of OASIS instead of anal incontinence, have also shown that there is a threefold to sevenfold increased risk of recurrent OASIS with subsequent deliveries [128–130]. However, these findings have not been replicated by other equally large retrospective studies [131,132]. Further prospective long-term studies are required before elective cesarean section can be recommended for prevention in asymptomatic women.

PFMT in the Prevention of OASIS

For women without FI, PFMT might be preventative. For example, in one study treating women with persistent SUI 3 months after delivery, lower rates of FI were seen compared with controls [70]. It is recommended that women with OASI receive supervised PFMT as a form of secondary prevention. However, as with SUI, a randomized trial showed that the significant improvement in FI compared to controls at 1 year (4% vs. 11%) did not persist at 6 years (12% vs. 13%) irrespective of subsequent deliveries [93].

These research findings have focused the attention of obstetricians and midwives to the potential risk of anal sphincter injury and the possible association with long-term FI. This should result in improved awareness, training, and prevention.

Other nonobstetric modifiable risk factors for FI including obesity, SUI, and associated medical conditions such as irritable bowel syndrome have been identified [133,134]. Addressing these might also help in prevention.

PREVENTION OF INCONTINENCE AND PROLAPSE FOLLOWING GYNECOLOGICAL SURGERY

Hysterectomy and Incontinence

Urinary tract fistulae are (fortunately) rare, but are not always preventable. A rate of 0.5%–3% of lower urinary tract injury has been reported at hysterectomy. Many of these are due to congenital abnormalities and distortion of structures caused by disease [135]. Preoperative intravenous urography, intraoperative cystoscopy, and the use of ureteric catheters in potentially difficult cases might help prevent trauma to the urinary tract. An increased risk of UI after hysterectomy has also been reported. In a systematic review, women over the age of 60 years who had undergone hysterectomy had a higher odds ratio compared with women less than 60 years [136]. Overall, the estimates suggest a 60% increased risk of developing incontinence after hysterectomy. How this can be prevented is unclear, but with a reduction in the number of hysterectomies for menorrhagia, by the use of progesterone-containing intrauterine devices and endometrial ablation, posthysterectomy incontinence might become less prevalent. Consideration might be given to concomitant continence surgery as secondary prevention for women with preexisting urodynamic stress incontinence, requiring hysterectomy. This has been shown to improve the chances of continence at 1 year postoperatively [137]. However, there is no evidence that this is indicated for primary prevention. For “occult SUI,” see the following text.

It has been suggested that subtotal hysterectomy might reduce the incidence of UI [138], as the cervix might act as a posterior support for the sphincter mechanism. It is also thought that division of the cardinal ligaments can result in denervation [139]. However, RCTs have failed to show any benefit of subtotal over total hysterectomy with regard to the onset of UI [140–142]. On the basis of current evidence, UI does not seem to be adversely affected in the short term following hysterectomy. However, there is an association with incontinence in the long term [136]; therefore, preventative measures need to be investigated. A systematic review of 9 trials with 1553 participants has not shown improved outcomes for sexual, urinary, or bowel function with subtotal hysterectomy compared to total abdominal hysterectomy either in the short term of long term [143].

Hysterectomy and POP

The risk of vaginal vault/apical prolapse and enterocele following hysterectomy has been reported as 3.6/1000 person-years. The risk increases from 1% (at 3 years) to 5% (at 15 years) [31]. After colposuspension, the incidence of new-onset enterocele has a reported incidence of 18%–30% [144,145]. Possible causes of postsurgical POP include reduced and weakened collagen [9,146]. failure to support the vault at hysterectomy or "anteversion" of the anterior vaginal wall following colposuspension. Similarly "retroversion" of the vaginal vault at sacrospinous ligament fixation can result in a high incidence of cystocele (see Chapter 100, "Laparoscopic Sacrocolpopexy"). Prevention will depend on the surgical procedure, the technique, and the strength of the supporting structures.

It is generally accepted that apical support is the key to preventing recurrence of vault prolapse following hysterectomy [147,148].

For example, laparoscopic and robot-assisted sacrocervicopexy with supracervical hysterectomy and sacrohysteropexy have been reported to have good success rates, but these findings need to be confirmed by randomized controlled studies [149].

Prevention of Urgency Urinary Incontinence after Surgery for Urodynamic Stress Incontinence

Midurethral Tapes

There are few data on whether midurethral slings, e.g., tension-free vaginal tape (TVT), have a better effect in the prevention of de novo urgency symptoms/DO than colposuspension. In a large RCT comparing the two procedures, the incidence of new-onset urgency and urgency incontinence was less than 2% for TVT and less than 5% for colposuspension at 5 years [150], although this might be an underestimate given the high incidence (over 90%) of preoperative OAB symptoms in both groups in this study. In a follow-up of patients 7 years after TVT, 22.5% had "urge symptoms." In a further 6.3%, this was "de novo" [151], similar to the 9.1% incidence reported by other authors [152]. In those with preoperative OAB symptoms, 57% resolved after surgery [152]. From these case series, it would appear that the incidence of urgency incontinence and OAB after TVT is similar to that reported after colposuspension. Likewise, the rate of de novo urgency and urgency incontinence after transobturator tape (TOT) seems to be comparable to that of TVT [153,154] and Burch colposuspension [155].

Colposuspension

Following colposuspension (an operation done less frequently since the introduction of midurethral tapes but nonetheless still undertaken), OAB (± DO) with urgency incontinence can arise in 15%–18.5% of cases [145,156]. Overelevation of the bladder neck (>2.6 cm on MRI) with obstruction has been implicated [157], but no reliable intraoperative method has been found to reproduce the 2.6 cm measurement of elevation; it can only be done subjectively. It is recommended that excessive elevation be avoided by whatever surgical technique.

Preoperative SUI or UUI is the most important predictor of SUI and UUI postoperatively [158]. However, new-onset incontinence is a particularly worrying complication following surgery for POP. It has been shown that 7%–22% of patients can develop incontinence following POP surgery [159]. It is generally acknowledged that the incidence of "occult" stress incontinence (i.e., that seen preoperatively following a pessary or POP reduction test) exceeds that actually seen after the procedure [160]. Incidence ranges from 23% [161] to 83% [162].

The pessary test can be used preoperatively in patients with POP to identify those with potential occult SUI postoperatively [163]. Five prospective studies have investigated several prophylactic anti-incontinence procedures at the time of POP surgery, including Pereyra needle suspension [164], Kelly plication [165], Stamey procedure [166], pubovaginal sling [167], and needle suspension vs. endopelvic fascial plication [159]. The latter was a small randomized trial that failed to confirm that a concomitant anti-incontinence procedure is preventative. None of these studies have a nonintervention arm ("no anti-incontinence procedure"), which makes difficult to determine and compare the risk of postoperative incontinence with those not having an anti-incontinence procedure.

The potential role of prophylactic midurethral sling (TVT) has been evaluated in two controlled case series, which report conflicting results. One small retrospective trial involving 19 patients [168] reported no difference between the groups, while another prospective trial [169] reported significant reduction in the incidence of postoperative incontinence in the women undergoing prophylactic TVT.

The most rigorous study into the prevention of potential/occult incontinence, the Colpopexy and Urinary Reduction Efforts (CARE) study [170], randomized 322 women undergoing sacrocolpopexy into concomitant Burch colposuspension and no intervention. They demonstrated a significant reduction in postoperative stress incontinence at 3 months, which seems to be maintained at 2 years [171]. The pessary test and preoperative urodynamics were not very helpful in predicting outcome. A prediction model with a level III evidence has also been proposed to predict the risk of de novo SUI in women undergoing POP surgery [172]. A recent systematic review has concluded that combined anti-incontinence surgery and POP surgery reduces the risk of postoperative stress incontinence, but short-term voiding difficulties and adverse events were more frequent [173]. A review suggested that women undergoing prolapse surgery may have benefited from having continence surgery performed concomitantly, especially if they had SUI (RR 7.4, 95% CI: 4.0–14) or if they were continent and had occult SUI demonstrated preoperatively (RR 3.5, 95% CI: 1.9–6.6) [174]. A recent RCT has however questioned the policy of routine sling insertion at the time of surgery for POP [175].

Since these results cannot be extrapolated to other anti-incontinence procedures/POP operations, further research is required.

In the meantime, it is advisable to warn patients of the potential risk of incontinence and the possible need for treatment in the future.

However, there is not enough evidence to counsel patients on prophylactic surgery at present. Minimally invasive midurethral slings might allow for secondary surgery as an “interval” procedure in those who do develop “occult” SUI.

Recurrence of Stress Incontinence after Vault Suspension: Prevention

A rare but potentially distressing scenario is recurrence of stress incontinence (SUI) following vault prolapse surgery in patients who have had a previously successful colposuspension. While there are fewer of these procedures being performed since the introduction of midurethral tapes, nonetheless about 30% of patients can develop symptomatic prolapse requiring surgery with the potential risk of recurrence of SUI. The exact prevalence is unknown. However, a case study highlighted this risk and suggested methods of prevention [176]. For example, measuring that vault elevation (in cms from the hymen) preoperatively that will not result in demonstrable SUI and reproducing it at sacrocolpopexy might prevent this complication. Also, performing sacrospinous fixation under spinal anesthesia allows the patient to perform a cough stress test, thus enabling alterations in the placement of the sutures to prevent incontinence [176]. These reports highlight the need for “vigilance” and to be aware of the possible risk of rendering a patient incontinent again despite previously successful incontinence surgery.

Prevention of Failed Surgery for Incontinence and Prolapse

SUI Surgery

The usually quoted success rates for USI surgery are 80%–90% [145].

However, these rates might be less depending on the definition of success/cure. Using patient-reported outcomes only and satisfaction, the success rates are often less than those quoted earlier [177]. Reasons for poor outcome include previous incontinence surgery and intrinsic sphincter deficiency (ISD). For example, a 54% failure rate has been reported in patients with ISD [178] although this is not a consistent finding [179]. Other predictors of treatment failure 2 years after surgery for USI including urgency incontinence, more advanced prolapse, and postmenopausal status (not on HRT) have been reported [180]. These are difficult to modify but might need to be considered when counseling women on the operative prognosis.

Studies are required to compare the various surgical procedures for ISD, such as slings, colposuspension, injectables, and midurethral tapes so that failure can be prevented. A recent randomized trial comparing the efficacy of TVT vs. TOT in women with ISD found that a significantly higher proportion or women in the TOT group had urodynamic stress incontinence at 6 months follow-up (45% vs. 21%) and that more women in the TOT group required repeat sling surgery [181]. It therefore seems that TVT might be a more appropriate operation for this group of patients.

The surgical “gold standard” for USI due to bladder-neck “hypermobility” has been the Burch colposuspension [182]. although the midurethral tapes (e.g., TVT) have comparable short- and medium-term outcomes [150,151]. The longest follow-up data for TVT suggest that at 17 years about 90% of women are still cured or significantly improved [183]. Prevention of failed surgery might be achieved by avoiding procedures with a poor success rate (e.g., anterior repair) or those that have not been fully evaluated or failed to show benefit over colposuspension or TVT. Attention to the aforementioned should lead to a reduced failure rates with surgery. The old adages are still apt: "the first operation must be the best one" and we should "choose the right operation for the right patient and the right patient for the right operation." The latter will depend on factors such as obesity, age, previous surgery, concomitant prolapse, and DO. In addition patient expectations and goals should be assessed preoperatively and whether they achieved after surgery [184].

Pelvic Organ Prolapse Surgery

Cystocele/anterior repair has long been known to have a high anatomical failure rate [185] with incidences as high as 40% being quoted [186]. The reasons for failure are unclear and might be related to surgical technique, patient selection, poor tissue collagen, etc. It is also possible that the anatomical defects associated with cystocele have not been corrected. For example, it is known that in many cases the anatomical defect is a detachment of the paravaginal fascia from the arcus tendineus fascia pelvis/"white line." It is unlikely that an anterior repair, which is a midline fascial plication, will correct this defect; paravaginal repair might be more appropriate. However, it's been shown with MRI scanning that 50% of paravaginal defects can be corrected with traditional anterior repair [187]. While success rates of 76%–97% have been quoted [188], a RCT is required to determine if paravaginal repair produces a better outcome than anterior repair in cases of paravaginal defect.

Based on 56 RCTs, a recent Cochrane review showed that for surgical management of upper vaginal prolapse (uterine or vault), abdominal sacral colpopexy had superior outcomes (reduced recurrent vault prolapse) compared to a variety of vaginal procedures including sacrospinous colpopexy, uterosacral colpopexy, and transvaginal mesh, but was associated with a longer operating time, longer time to return to activities of daily living, and increased cost of the abdominal approach [174]. The Cochrane review also evaluated 21 trials and compared a variety of surgical procedures for anterior compartment prolapse (cystocele) and showed that standard anterior repair was associated with more anterior compartment prolapse on examination and the use of mesh or graft inlays at the time of repair reduced the risk of recurrent anterior wall prolapse on examination [174]. Anterior vaginal polypropylene mesh also reduced awareness of prolapse; however, these benefits must be weighted against increased operating time, blood loss, rate of apical or posterior compartment prolapse, de novo SUI, and reoperation rate for mesh exposures associated with the use of polypropylene mesh [174]. This Cochrane review also showed that posterior vaginal wall repair may be better than transanal repair in the management of rectocele in terms of recurrence of prolapse and there was paucity of evidence to support use of grafts at the time of posterior vaginal repair [174].

Several surgical techniques have been tried to prevent recurrent POP, mainly aimed at reinforcing apical support (see section "Hysterectomy and POP").

The use of vaginal grafts/meshes to prevent recurrence of prolapse was introduced despite a lack of supporting evidence on long-term efficacy and safety. There are numerous studies investigating a wide variety of vaginal meshes for either anterior, posterior, or upper compartment prolapse (or combinations of them). However, in 2008 the U.S. Food and Drug Administration issued a warning with regard to the safety and lack of evidence of efficacy of vaginal meshes when compared to native tissue repairs, which they updated in 2011, stating that serious complications associated with surgical mesh for transvaginal repair of POP are not rare. Furthermore, it is not clear that transvaginal POP repair with mesh is more effective than traditional nonmesh repair in all patients with POP, and it may expose patients to *greater risk* [189]. Since then several meshes have been removed from the market in view of complications and litigation. The use of transvaginal mesh for POP remains highly controversial and further large, well-conducted RCTs are required. The results of one such study in the United Kingdom (*PRO*lapse *S*urgery: *P*ragmatic *E*valuation and randomised *C*ontrolled *T*rials [PROSPECT]) are awaited.

Prevention of Detrusor Overactivity

As the etiology and natural history of DO are unclear, prevention is difficult. There are few studies assessing long-term outcomes. Those that exist suggest that OAB is a chronic condition that persists urodynamically and symptomatically [190]. For prevention of postoperative urge incontinence, accurate diagnosis by urodynamic studies might help avoid unnecessary surgery in patients who have DO and not USI. It is possible that DO might have its origins in childhood (see section "Familial and Genetic Factors"). For example, patients with persistent primary nocturnal enuresis have a high incidence of DO

[191]. In an attempt to prevent symptoms in their children, some mothers with OAB often “toilet” the children more frequently [192,193]. This might be counterproductive as frequent voiding might develop into urgency and urge incontinence. Although none of the studies cited here are large or the findings conclusive, nonetheless they highlight the need for further investigation in this area. Should symptoms in childhood be relevant to the etiology of DO, then education of parents regarding toileting and bladder drill might be preventative. Psychological factors have been implicated in the etiology of DO [194,195]. Identification together with appropriate psychotherapy has shown encouraging results [195]. This might also prove valuable in prevention. Anecdotal evidence suggests that a high fluid intake is associated with symptoms of frequency and urgency. Restricting bladder stimulants (e.g., caffeine and alcohol) should be considered. Finally, the “integral theory” suggests that bladder-neck opening (due to a weak anterior vaginal wall) might lead to the development of DO [196]. PFMT might therefore have a role in prevention. However, long-term studies are needed to test this hypothesis. Further research is needed into the etiology of DO, which might be multifactorial. In the meantime, prevention can only be speculative.

CONCLUSIONS

The natural history of incontinence and POP requires more study, but there is evidence that spontaneous remission occurs. Effective prevention will only be achieved by long-term prospective studies of appropriate interventions in “at-risk” groups.

Some of the preventions are as follows:

- Treatment of coexisting factors, such as obesity, chronic cough, or constipation, might help in the primary and secondary prevention.
- Studies of interventions in children with symptoms and asymptomatic individuals with a strong family history of incontinence and/or POP.
- Further research is required to assess the preventative effects of hormone replacement in menopausal women.
- Long-term follow-up of patients with incontinence as a result of pregnancy and vaginal delivery is required before elective cesarean section can be recommended for prevention. PFMT seems to have a beneficial effect in “at-risk” groups at least in the short term. However, methods to improve compliance are required if the effect is to be maintained.
- Attention to the potential risk of incontinence following hysterectomy or POP surgery is suggested. For a patient to be rendered incontinent, following unrelated surgery is distressing; measures to identify the risk and prevent this outcome should be considered.
- Further research is required to identify the reasons for poor treatment outcomes.

With attention to the aforementioned and the natural history, appropriate preventative measures should be found to protect women from incontinence and POP.

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10 Medical Error and Patient Safety in Surgery

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INTRODUCTION

By nature of the human condition, surgery-related errors and adverse events are inevitable. Consequences from these events directly and indirectly affect patients and their families and surgeons and their colleagues throughout the world wherever such events happen to occur. The exact number of surgical procedures performed worldwide is not known. Information about inpatient procedures is more readily available, but the quality and scope varies by location. Weiser et al. [1] analyzed a variety of data obtained from the World Health Organization (WHO) member states and found only 29% of the member states collected information on surgical volume, and none had reliable data about inpatient death rates or adverse events. Given these limitations, they estimated that a minimum of 234.2 million major surgical procedures are performed annually, most occurring in countries with high health expenditures per capita. Their definition of major surgery included any intervention taking place in a hospital operating room (OR) involving incision, excision, manipulation or suturing of tissue requiring profound sedation, and regional or general anesthesia for pain control. Based on a 0.5% perioperative mortality rate and a 3% perioperative adverse event rate, they estimated that 1 million surgery-related deaths and 7 million major complications occur as a result of such procedures. Furthermore, data available from developed countries indicated that about half of surgical adverse events were deemed to have been preventable.

Information is uneven and less readily available regarding outpatient surgery procedures performed worldwide. Global analysis as of February 2014 reported that the site of surgery has shifted over the past few decades from the inpatient to outpatient settings [2]. Outpatient surgical procedures in the United States has definitely increased, comprising about one-third of all surgical procedures in 2000 to more than half by the end of 2010 [3]. This trend is expected to continue albeit on a slower trajectory due to continued growth in the aging population and the proportion with high medical case complexity necessitating an inpatient surgery venue. Healthy patients deemed at low risk for adverse events are typically selected for outpatient procedures. However, more complex patients may be selected for outpatient surgery as less invasive techniques become available and economic factors, including changes in cost and reimbursement for health-care services, drive provision of services away from hospital inpatient settings.

Similarly, the precise number of female urology and urogynecology inpatient operative procedures performed worldwide is not known. Where data are available, the rates of specific female urology and urogynecology surgical procedures appear to be on the rise. For example, Oliphant et al. [4] analyzed the National Hospital Discharge Survey (NHDS) database and determined that age-adjusted rates for inpatient stress urinary incontinence (SUI) procedures performed in the United States between 1979 and 2004 more than doubled from 0.64 to 1.60 per 1000 woman. They projected that both the overall and age-adjusted rates would continue to increase over time since about 20% of the U.S. population is expected to be 65 years or older by 2030, most of whom will be women [5]. The exact number of female urology and urogynecology outpatient surgical procedures that are performed worldwide is also not known but appears to be growing. In the United States, Boyles and colleagues [6] found that female urinary incontinence procedures performed in the outpatient setting doubled between 1994 and 1996. Furthermore, Jonsson, Funk, Levin, and Wu [7] reported a 27% increase in the overall rate of SUI surgical procedures between 2000 and 2009, the highest rate being for sling procedures. They also reported that 67% of all SUI procedures were performed in the outpatient setting during this specific 10-year period.

Patient safety is a serious international public health-care issue [8]. Interest has been growing over the past decade to better define the role of surgical care among other global health priorities and its role in addressing the global burden of disease [9]. Given the volume of surgery estimated to take place worldwide and the shift in the site of surgery from inpatient to outpatient settings, it would behoove surgeons of all specialties to understand how multiple factors can contribute to error such as factors related to cognition, fund of knowledge, clinical judgment, diagnostic problem-solving, and decision-making; technical skills, communication, and teamwork; supervision and documentation; administrative; and clinical systems and environment. It is imperative that surgeons of all specialties develop and master techniques for mitigating or preventing errors, resulting in adverse surgical events and patient harm across the continuum of surgical care. Fortunately, multiple efforts are underway worldwide to make healthcare safer for patients and clinicians [8,10,11]. This chapter will provide an overview of medical errors and adverse events and address multiple efforts aimed at preventing their occurrence or mitigating their effects in the surgical setting. Specific clinical approaches for improving quality and safety of patient care such as prophylaxis for infection and deep venous thrombosis and the prevention of retained objects and safe introduction of new technology will be covered elsewhere.

PATIENT SAFETY AND MEDICAL ERRORS

Patient safety, the prevention of harm to patients, is regarded by the Institute of Medicine (IOM) as inseparable from quality of care [12]. Safety is the first domain of quality. All patients expect and deserve safe care. Their care should be free from hazards that increase the likelihood of adverse events or harm. The call to action in 2000 by the IOM to improve patient safety and decrease medical error was driven in large part by findings from two signature studies in the United States. These researchers reviewed medical records of hospitalized patients to estimate the rate of adverse events and negligence occurring in the states of New York, Colorado, and Utah. In New York, adverse events were found to have occurred in 3.7% of hospitalizations, and 27.6% of the adverse events were due to negligence [13]. In both Colorado and Utah, adverse events were found to have occurred in 2.9% of hospitalizations, and more than 25% of these cases were due to negligence [14]. The landmark study involving Colorado and Utah showed that operative adverse events accounted for 44.9% of all adverse events identified and 16.9% of these were due to negligence. Poor surgical technique accounted for 29.9% of surgical adverse events, 23.6% of which were due to negligence. Bleeding, infections, and deep venous thrombosis were the next most common surgical adverse events identified. Overall, surgical technique–related complications, infection, and bleeding accounted for about half of all surgical adverse events. The rates of adverse events identified in these studies extrapolated to the population of all patients hospitalized in the United States during 1997 placed medical errors among the eighth leading cause of death [15], exceeding causes due to car accidents, breast cancer, or AIDS. A more recent analysis in 2013 by James [16] examined information from four separate studies published during 2008–2011 about preventable adverse events in hospitalized patients. Each of these studies employed the Global Trigger Tool [17] as the core method used by trained health-care professionals to extract data from medical records and determine if an adverse event may have harmed a patient. He concluded that a lower limit of 210,000 deaths per year of hospitalized patients was associated with preventable harm, and the true number may be upwards of 400,000 deaths per year. He noted that nonlethal but serious harm was 10- to 20-fold more common than lethal preventable adverse events. Based on James' analysis and preliminary data on deaths in the United States for 2011 [18], deaths due to preventable adverse events would more likely be the third leading cause of death in 2011 compared to the eighth leading cause of death in the United States in 1997.

Around the world, the year 2000 was pivotal in the call to action to improve safety of patient care and decrease medical errors. The National Health Service (NHS) of the United Kingdom in 2000 reported on the occurrence of health-care-related adverse events and their impact on patients and their families, clinicians, and NHS organizations [19]. In their landmark report, *An Organisation with a Memory,* they stated that preventable errors are the result of human error whether intentional or not. They also highlighted the relationship between human factors and medical errors. The launch of patient safety initiatives in Australia occurred around this same time. Lessons learned from the Australian incident monitoring study of the 1980s [20,21] did much to inform their efforts to improve patient safety in their country. Similar awareness and patient safety initiatives began in New Zealand around 2001 [22]. Canada released a multifaceted action plan to improve patient safety, *Building a Safer System*, in 2002 [23]. The WHO passed a resolution in early 2002 urging countries to pay the greatest possible attention to patient safety and establish evidence-based systems to improve safety and quality healthcare worldwide [11]. Successful efforts in such endeavors led to the formation of the World Health Alliance for Patient Safety in 2004, and the Global Patient Safety Challenge to *Safe Surgery Saves Lives*—improving the safety of surgery around the globe [24].

Fundamental to the global call to action to improve patient safety is the understanding that "to err is human" [25]. James Reason asserted in 1990 that errors are inevitable and an acceptable price to pay in coping with difficult, complex tasks [25]. In his landmark book, *Human Error*, he described a framework for human error, highlighting the relationship between various aspects of human cognition and error. His framework differentiated three error types—"skills-based slips and lapses, rule-based mistakes and knowledge-based mistakes" [26]. He stressed that understanding the differences between these error types helps to identify suitable means by which to intervene and address them. To that end, James Reason promoted two main approaches by which to deal with the problem of human error: the person approach and the systems approach [27]. The person approach embodies the long-standing tradition of targeting and blaming individuals for errors. The systems approach accepts the fallibility of human nature and expects errors. The systems approach scrutinizes how and why defenses fail and designs ways to trap or minimize the effect of errors via measures that address the person, the team, the workplace, and the institution as a whole. This concept embodies a "just culture," a concept that resonated with the IOM as evidenced by their strong advocacy for such approach to human error, not assigning blame, and building safer health-care systems that reliably trap error and mitigate their effects [28]. The health-care industry is highly complex, and some 24-hour-a-day services are more vulnerable to error than others such as intensive care settings, the operating theater, emergency departments, and labor and delivery units. High reliability organizations (HROs) are known to exemplify the systems approach to human error [29].

HIGH RELIABILITY ORGANIZATIONS

An HRO is one that operates in hazardous conditions 24 hours a day under the pressure of time but with fewer than expected accidents, "less than their fair share of adverse events" [30]. Examples of such organizations include naval aircraft carriers, nuclear power plants, offshore oil platforms, and air traffic control systems. Around the world, more and more hospital emergency units, operating theaters, and perinatal units are striving to transform themselves into HROs. All HROs strive to manage the unexpected with determined mindfulness. Weick and Sutcliffe assert that "good management of the unexpected is mindful management of the unexpected" [31]. HROs are characterized by a shared commitment to safety throughout the organization and distinguish themselves by their "collective preoccupation with the possibility of failure" [32]. Preoccupation with failure involves anticipating and recognizing where failure can occur and taking measures to prevent it. Standardizing procedures where possible and taking stock of where and when adverse events and near misses may occur facilitate error prevention or mitigating their effect. Establishing effective systems for reporting errors and adverse events further optimizes the ability to track them and opportunities to learn from them. HROs are not error-free but are resilient when error occurs. One way HROs manifest a preoccupation with failure is by training their personnel and teams intensively through drills and simulations.

CULTURE OF SAFETY

HROs manifest a positive culture of safety. An organization's culture of safety is the product of individual and group values, skills, and behaviors that shape an organization's commitment to and proficiency of their own safety programs [33]. A simple way to think about culture is "the way we do things around here and why we do them" [34]. Edgar Schein [35] advocated analyzing organizational culture at three levels to better understand shared basic assumptions and the processes by which they came to be. He asserted that the knowledge gained could then be used to facilitate organizational culture change as needed. The first level is comprised of observable behaviors that are evident in the workplace; the second level consists of the beliefs and values espoused by members within the organization; and the third level, perhaps the most important, consists of the basic underlying assumptions that may be taken for granted, are largely subconscious, and are not verbalized. According to Schein, these underlying assumptions may best inform why things unfold within an organization the way they do. For example, moving from a culture of shame and blame to one that is nonpunitive yet preserves accountability can provoke high anxiety for members in the organization and present challenging obstacles and consumption of valuable resources, especially the element of time. The IOM acknowledged that one of healthcare’s biggest challenges in providing reliably safe, high-quality care was changing from a culture of shame and blame to one that is fair and just [12].

Establishing a safe and just culture is not an easy task and cannot be mandated [34]. Moving toward a culture of safety takes time, and incremental steps are needed to facilitate and solidify the change if it is to be longlasting. Transparency, professional responsibility, mutual accountability, and nonnegotiable mutual respect are among the key elements of a systems approach to error management [36–38]. Individual health-care providers are responsible for ethical practice, clinical competency, and mindfulness in the provision of safe patient care.

HUMAN FACTORS AND THE DEMANDS OF CLINICAL PRACTICE THAT WEAKEN DEFENSES

Humans are integral to the provision health-care services and therefore to the safety and quality of care they provide. Not all human errors result in adverse events, events that unexpectedly result in death, injury, extended hospital stay, or disability. However, most adverse events are preventable. Understanding how and why errors and adverse events occur provides a road map by which to obviate them. The study of human fallibility and the science behind why errors happen and how to mitigate and prevent their occurrence are encompassed by the field of human factors. Much has been written about human factors and their contribution to errors in the military and aviation and nuclear industry [39–41]. Human factors involve the interactions among humans and elements in their systems and the application of theory, principles, data, and methods designed to prevent error and optimize human and system performance. Calland et al. [42] articulated in 2002 the virtues of taking a systems approach to surgical safety. This sentiment was echoed in 2004 by Vincent et al. [43] They argued for a wider assessment of factors that may be relevant to surgical outcomes and the development of an “operation profile,” a characterization of all the salient features of a surgery including equipment design and use, communication and team coordination, and factors affecting individual performance and the working environment (see Table 10.1).

According to Catchpole [44], tremendous progress has been made over the past decade in the degree to which health-care providers have become aware of the role and value human factors can play in achieving better and safer human-centered health-care systems.

The limitations of being human in combination with certain features of clinical practice within which health-care providers work often create challenges for delivering safe, high-quality care. Veltman [45] highlighted several clinical practice–related issues and inherent demands that weaken defenses to error and contribute to perinatal harm. These practice-related issues and demands, expanded from those of Veltman, are applicable to the field of surgery regardless of the specialty and locus of surgery-related activities, whether inpatient, outpatient, or office based (see Tables 10.2 and 10.3).

The following human factors’ focus areas were identified by Russ et al. [46] as being applicable to healthcare: aging, cognition, cognitive engineering and decision-making, communication, human performance modeling, industrial and macroergonomics, perception and performance, product design, safety, training, and usability–user experience when interacting with a product or system. They stress that the science of human factors does not promise instant solutions for improving healthcare. However, the partnership of human factors professionals with health-care professionals can generate relevant and long-term solutions designed to systematically address clinical practice–related issues and strengthen clinicians’ defenses to error, thereby facilitating patient safety and quality of healthcare. Shouhed et al. [47] further underscored the importance of building collaborations between human factors experts and surgeons to better understand the complexity of factors leading to surgical errors and use valid, real-world data to develop evidence-based interventions that detect and prevent errors before patient harm occurs.

Table 10.1 Operation Profile

Item	Features
Patient factors	Principal complaint Comorbidities Other relevant clinical information
Surgical team	Personnel

	Experience of previous work together Familiarity with procedure Fatigue, sleep loss, stress, etc.
Process and procedures	Adequacy of notes and management plan Consent and preparation Anesthetic procedures
Operative events	Blood loss Major and minor complications Error compensation and recovery
Flow of information following patient	Adequacy of notes and consent Specific intraoperative communication Handover
Technical skills	Ratings of good general surgical practice Ratings of operation-specific steps Identification of specific technical errors
Team performance and leadership	Leadership Team coordination Willingness to seek advice and help Responsiveness and flexibility
Decision-making and situation awareness	Patient limitations Operation limitations Surgeon’s limitations Team limitations
Operative environment	Availability and adequacy of equipment Availability of notes, records, etc. Noise and lighting Distractions
Interruptions	Phone calls, messages, events external to operating room

Source: Modified from Vincent C et al., *Ann Surg*, 239, 475, 2004.

SOURCES OF ERROR IN SURGERY

In their classic study published in 2006, Rogers and colleagues [48] retrospectively analyzed malpractice claims from four liability insurers that contained allegations of surgical error and had closed between 1986 and 2004. Of 444 surgical claims reviewed, 258 (58%) were confirmed as being due to surgical error. The majority (76%) were elective procedures involving the gastrointestinal tract (29%), spinal and nonspinal orthopedic procedures (24%), hysterectomies (7%), and the genitourinary tract (5%). Most injuries (75%) had occurred during the intraoperative period. The severity of the injury was deemed significant (temporary major, permanent minor, and permanent significant injury) in 55% and major (permanent major and permanent grave injury) in 10% and resulted in death in 23%. Most (54%) surgical injury–related cases were due to errors in operative technique, in which most (83%) involved more than one clinician. Surgical injury–related cases were analyzed for factors contributing to the occurrence of the error. These contributing factors included cognitive errors involving judgment (66%) or failure of memory or vigilance (63%), lack of technical competence or knowledge (41%), or communication breakdowns (24%) such as inadequate handoffs, unclear lines of responsibility, or conflict among personnel. Patient factors such as excess weight, difficult or unusual anatomy, and behavioral issues also contributed to the occurrence of surgical error. Other system factors contributing to surgical error included lack of supervision (18%), failed technology (15%), and excessive workload/inadequate staffing, fatigue, interruptions/distractions, and issues related to lighting or setup. Three contributing factors were the median number found per case. Overall, 82% of cases involved system factors, human factors that are not cognitive related. Although data were limited to closed malpractice claims and overrepresented academic medical centers, their analysis characterized how human factors contribute to the occurrence of surgical error and can help to identify strategies by which to reduce patient harm.

Table 10.2 Practice-Related Issues Contributing to Patient Harm

Issue	**Example**

Regional variation in surgical practice	Deficient or inadequate guidelines, policies, or procedures Lack of adherence to guidelines, policies, or procedures
Variation in operative expertise	Surgical experience and technical skill
Uncertainty in clinical care	Presentation Diagnosis Risk assessment Management Adherence to treatment Response to treatment
Resource limitations	Staff Space Equipment Time
Wishful thinking	"Fallacy of the low-risk patient"—continuing to perceive and manage a patient as low risk when their clinical circumstances have become high risk

Source: Modified from Veltman L, *Obstet Gynecol*, 10(5), 1146, 2007.

Table 10.3 Inherent Demands That Weaken Defenses to Error

Demands of clinical practice
Presence demanded in more than one place at the same time
Critical decision-making under stress
High clinical volume, largely normal patients
Increasing growth in elderly population with comorbidities
Off-site monitoring of high-risk clinical situations
Frequent handoffs and inadequate sign-out
Protocols inadequate for referrals, consultations, or patient transfers
Frequent interruptions and distractions
Fatigue, stress, etc.
Hierarchical systems
Poor teamwork and communication
Yielding to patient pressures regarding clinical practice
Overconfidence (hubris)

Source: Modified from Veltman L, *Obstet Gynecol*, 10(5), 1146, 2007.

The need for patient safety initiatives to be implemented in the outpatient setting was stressed by Bishop et al. [49]. These investigators reviewed paid malpractice claims data contained in the U.S. National Practitioners Data Bank from 2005 through 2009, involving adverse events in the inpatient and outpatient setting. They found that the number of claims overall significantly decreased ($p < 0.001$) in both settings, but the rate of decline was greater ($p < 0.001$) for the inpatient compared to the outpatient setting. Of claims paid in 2009, they found that surgical adverse events were most common (34%), followed by diagnosis-related adverse events (21.1%) and treatment/medication related (20.3%). Whereas in the outpatient setting, diagnosis-related adverse events were most common (45.9%), followed by treatment/medication related (29.5%) and surgical related (14.4%). However, major injury was the most common outcome in the inpatient (37.8%) and outpatient (36.1%) setting, and death was the second most common outcome in the inpatient (36.1%) and the outpatient (30.6%) setting. Bishop et al. raised concerns about the growing shift in surgical care and procedures from inpatient to outpatient settings and the potential for increased risk of surgical adverse events in outpatient surgical centers or physician offices where safety measures were less stringent compared to hospitals.

SURGICAL ERROR IN FEMALE UROLOGY AND UROGYNECOLOGY

Data regarding sources of error, adverse events, and their preventability in female urology and urogynecology procedures are limited. In 2002, Brown and colleagues [50] used 1997 NHDS and 1997

National Census databases to estimate the prevalence, morbidity, and mortality of pelvic organ prolapse surgery. They found that pelvic organ prolapse surgery was common, 22.7 per 10,000 women in the United States and 21% of these also had an incontinence procedure. Mortality occurred in 3 per 10,000 surgeries. Notably, 15.5% of all pelvic organ prolapse surgeries were complicated by infection (5.4%), bleeding (5.4%), and surgical injury (4.2%).

Waetjen and colleagues in 2003 [51] reviewed the 1998 NHDS and 1998 National Census databases to estimate prevalence, morbidity, and mortality rates for SUI inpatient surgeries in the United States. Adjusting for population growth, they found a 45% increase in the frequency of such surgeries between 1988 and 1998. Retropubic suspension was the most common procedure performed (46%), followed by anterior repair (27%) and other SUI procedures (14%). Mortality from stress incontinence surgery was low at 1 per 10,000 surgeries. However, 18.3% had 1 or more complications of which nearly half were due to infection (44%), surgical injury (24%), bleeding (16%). This analysis was limited to incontinence surgery requiring hospital admission, not accounting for those performed in the outpatient or office-based setting and their associated injuries or adverse events.

Gilmour and Baskett [52] in 2005 found a low rate of urinary tract injury (3 per 1000 surgeries) at a benign gynecological surgery in Canada. However, such injury was associated with a high risk (91-fold) of litigation. Gilmour et al. [53] noted in 2006 that the most common major surgery in gynecology worldwide is the hysterectomy. They found a low rate of urinary tract injury (bladder or ureter), ranging from less than 1 per 1000 (subtotal hysterectomy with or without bilateral salpingo-oophorectomy) to 13 per 1000 surgeries (laparoscopic hysterectomy with or without bilateral salpingo-oophorectomy). A Cochrane review of surgical approach to hysterectomy by Nieboer et al. [54] also noted a higher rate of urinary tract injuries with laparoscopic compared to an abdominal approach. In France, David-Montefiore et al. [55] conducted a prospective, observational, multicenter study of women undergoing hysterectomy for benign disease between June and December 2004. Of 634 procedures performed, they found perioperative complications occurred in 5.8% of the laparoscopic approaches, 8.2% of vaginal approaches, and 18% of abdominal approaches. However, they found no differences in rates of intraoperative complications regardless of the surgical approach. Intraoperative complications included injury to the intestinal tract (~0.8%), urinary tract (~2%), and bleeding (~1%), whereas postoperative complications where more likely due to infection (~1%–2%) and bleeding (~2%).

Most recently, Edozien [56] examined malpractice claims related to gynecology filed between 2001 and 2011 in the UK NHS Litigation Authority. Gynecology accounted for 4% of open claims as of March 31, 2011, compared to obstetrics (20%) and surgery (8%). Most of the 3757 gynecology-related claims revolved around events that occurred in the OR. Causes of claims in gynecology entailed wrong diagnosis (20%), intraoperative problems such as damage to adjacent organs (17%), inappropriate treatment (14%), failure/delay in treatment (9%), failure/delay in diagnosis such as missed ectopic pregnancy or cancers of the reproductive tract (8%), failure to obtain valid consent (5%), failure to recognize complication (4%), operator error (3%), failed sterilization (2%), and failure to perform operation (2%). Of note, injuries involved the bladder in 30%; additional/unnecessary operations, such as reoperation for retained foreign object or unplanned removal of one or both ovaries, occurred in 17%; unnecessary pain occurred in 11%; and bowel damage or dysfunction occurred in 5%.

The extent to which these complications and incidents were due to human error and were deemed preventable was not specifically assessed in any of these studies. However, operative skills and technique accounted for most surgical adverse events that led to injury, bleeding, and infection. Edozien’s analysis highlights the critical role of human error in surgical adverse events and further substantiates the intraoperative period as being a priority area for patient safety interventions.

METHODS FOR MITIGATING ERROR AND MANAGING THEIR EFFECTS

Over the past two decades, multiple methods have been developed within health-care communities around the world to promote safer patient care and reduce errors or mitigate their effects. Some approaches target clinical systems and environments, while others target individuals and teams. The following section will address a variety of ways to tighten up our defenses against clinical practice–related issues and demands and facilitate safer surgical care.

Importance of Teamwork and Communication

Successfully managing routine clinical and crisis situations requires expert knowledge, technical skills, sound decision-making, and optimal teamwork behaviors [57]. Teamwork is an essential component of HROs [58]. The culture of healthcare, including medical education and residency training programs, has traditionally emphasized individual attainment of a high level of medical knowledge and procedural skills and abilities, with little emphasis on effective teamwork behaviors and systems approach to problem-solving. Formal instruction and practice of optimal teamwork behaviors for multidisciplinary teams confronting routine and crisis situations was nil to absent in most health profession training programs until about 1990s. The aviation industry was among the first to confront the reality of human error's contribution to accidents and the need for various skilled professionals to learn to work together better and communicate more effectively [59]. Salas et al. [60], the aviation team training professionals, advised that the way to turn a team of experts into an expert team is by (1) fostering shared mental models of the task and team member roles, (2) training team members on teamwork skills (situation awareness, communication, team leadership, adaptability, and compensatory behavior), (3) providing team members with guided practice on skills needed in naturalistic conditions, (4) developing simulations that allow teams to experience different course of actions, (5) linking cue patterns to response strategies with respect to task and other team members, (6) training team members on each other's roles and building realistic expectations about task requirements, and (7) training team leaders to maintain shared situational awareness by providing periodic updates to team members. Team training and cockpit resource management were central components of the aviation industry's efforts to groom expert aviators into expert aviation teams in the early 1980s. Cockpit resource management, now known as "crew" resource management (CRM), focuses on acquisition of timely information and optimizing skills in leadership, teamwork behavior, problem-solving, and situation awareness [61]. Aviation CRM has evolved to include error management in its CRM curriculum, EMCRM, techniques for enhancing error recognition, management, and recovery. In 1989, Howard et al. [62] were instrumental in adapting aviation CRM to anesthesia, known as anesthesia crisis resource management (ACRM), to evoke change and improve teamwork and communication among anesthesiologists. This body of work paved the way for dissemination of ACRM to anesthesia leadership across the United States and around the world [63–66]. Helmreich and associates furthered this transformation by integrating principles of organizational behavior and culture [67,68]. Helmreich [67] played a crucial role in promoting teamwork and communication in the field of surgery, and Shortell et al. [69] were similarly key among health-care professionals working in intensive care unit (ICU) settings.

Around this same time, the U.S. Department of Defense (DoD) adapted their Army aviation CRM and introduced such training to healthcare upon realizing their aviation CRM program had produced a 20% improvement in mission performance and a 40% reduction in safety-related task errors [68,70]. This intervention was further bolstered by findings of a review conducted by Risser et al. [71] of closed malpractice claims from a total of eight military and civilian hospital emergency departments. They found that 43% of these claims involved issues related to poor teamwork and communication. As a result, the DoD sponsored the development of the MedTeams project and an Emergency Team Coordination Course, a teamwork curriculum specifically designed for emergency medicine clinicians [72].

Similar findings of inadequate teamwork and communication were appreciated in about 60% of the DoD's obstetrical closed claims—unpublished data. Likewise, an internal review of obstetrical closed claims involving Harvard-affiliated hospitals revealed that 43% had elements of poor teamwork and communication [73]. These two findings led to the expansion of the MedTeams project to include systematic teamwork and communication training for labor and delivery clinicians in civilian and military hospitals [74].

Surgical teamwork failures have been identified via a number of methods, such as voluntary reports of adverse events, malpractice claims, and during real-time observations. The Joint Commission [75] reported that communication failures were the leading root cause in 66% of sentinel events reported to them between 1995 and 2004, the leading root cause for medication errors, delays in treatment, and wrong-site surgery, and the second leading root cause for operative and postoperative events. As previously mentioned, Rogers and colleagues [48] were able to identify communication breakdowns in 24% of surgical malpractice claims they reviewed. Lingard et al. [76] in 2002 explored the nature of communication in the OR. Of 35 surgeries and 128 hours of OR interactions, patterns of conversations were observed as subtle, complex, and socially motivated. Conversations revolved around the following themes of time, safety, sterility, resources, roles, and situation. Tension surfaced regularly and one to four higher tension events arose per procedure. These events had an observable effect on members of the team, including surgical trainees who responded either by withdrawing from the conversation or by mimicking their senior surgeon. Both of these responses by trainees had negative implications for effective teamwork. Lingard et al. [77] subsequently used trained observers to study communication failures in the OR during 2003. Of 48 surgical procedures and 90 hours of observations, they identified communication failures in about 30% of team exchanges. Such failures included poor timing, incomplete or inaccurate information exchanged, issues not resolved, or key individuals excluded. About one-third of these failures were seen to visibly affect system processes and jeopardize patient safety, such as tension amidst the team, inefficiency and delays, work-arounds and wasted resources, patient inconvenience, and procedural errors. Such research by Lingard and colleagues highlights critical aspects of team communication and opportunities for interprofessional training to improve it. They deemed a curriculum to address interprofessional communication across systems and processes to be worthwhile. Tension among and between surgical teams and the occurrence of higher tension events are inevitable in the OR. How these moments are managed by members of surgical team, across the hierarchies within and between the disciplines, can directly and indirectly affect the safety of patient care and surgical outcomes.

Greenberg et al. [78] conducted an in-depth analysis of 60 closed malpractice claims with communication breakdowns resulting in patient harm, a subset of the 444 closed malpractice claims previously described by Rogers et al. [48] Communication breakdowns were about evenly divided between the preoperative (38%), intraoperative (30%), and postoperative (32%) periods. Verbal communication breakdowns occurred between 1 transmitter and 1 receiver, more commonly involving the attending surgeon. Factors associated with these breakdowns included hierarchy and power differentials and ambiguity about roles and responsibilities. Handoffs and transfer of care were problematic. Failures in resident-to-attending communication concerned notification of critical information, while attending-to-attending communication failures were related to inadequate handoffs. About 14% of cases involved intraoperative surgical sponge or instrument miscounts. These investigators proposed a series of triggers for notifying the responsible attending about clinical changes or staff concerns about a patient during the preoperative and postoperative periods. They estimated 26%–44% of communication breakdowns would have been prevented if these triggers had been used. They postulated that the use of standardized handoffs and protocols for transferring patients would have prevented 11%–35% of problematic occurrences. The combination of triggers and standardized transfers or handoffs could potentially prevent half or more of communication breakdowns. Implementation of read-back protocols, closed-loop communication techniques could further augment communication of critical patient information. They advocated for instituting structured communication techniques such as standardized team briefings, time-outs or surgical pauses to improve surgical safety, and exploring technological solutions to mitigate or prevent instrument or sponge miscounts.

SURGICAL TEAM TRAINING INTERVENTIONS

Having documented that deficiencies in teamwork contribute to the occurrence of adverse events in surgical patients, two classic studies illustrate the impact of interventions aimed at improving communication and teamwork within surgical teams. Haynes et al. [79] evaluated implementation of the WHO surgical safety checklist, a structured communication tool designed to improve communication and consistency of surgical care before administering anesthesia, immediately prior to skin incision and before the patient leaves the OR. The checklist was used in eight economically and clinically diverse hospitals located across the globe. Significant reductions were seen in death rates (1.5%–0.8%, $p = 0.003$) and intraoperative complications (11%–7%, $p < 0.001$). All sites had reductions in major postoperative complications. Although the reductions were greater in some sites than in others, the checklist program was deemed useful for improving surgical safety in a wide variety of clinical and economic settings worldwide.

McCulloch et al. [80] conducted a single institution (teaching hospital) before and after study of team skills training. They observed a series of laparoscopic cholecystectomy and carotid endarterectomy procedures before and after implementing a 9 hour aviation CRM-based teamwork training curriculum. On-site teamwork coaching was provided about twice a week for 3 months. They also evaluated Safety Attitude Questionnaires (SAQs) pre- and post-team training intervention. Formal team training led to significantly improved SAQ teamwork climate scores (*p* = 0.007), improved teamwork performance (*p* = 0.021) and reductions in technical errors (1.73–0.98 per operation, *p* = 0.009), and a 40% reduction in nonoperative procedural errors. Although these authors acknowledged the limitations in generalizing their results beyond their academic setting, their findings were consistent with the results obtained by Morey et al. [81] in their structured team training intervention for emergency department staff. Morey et al. in 2002 published findings of their prospective, quasi-experimental, multicenter trial of a systematic team training program intervention in the emergency room setting. They reported a significant improvement in team behaviors (*p* = 0.012) and significant reduction in observed errors (30.9%–4.4%, *p* = 0.039) in those departments participating in team training compared to controls. Significant improvement were also seen in staff attitudes toward teamwork (*p* = 0.047) and assessment of institutional support (*p* = 0.04).

SIMULATION-BASED TRAINING OF SURGICAL TEAMS

Simulation-based training and practice offers a viable means by which to promote safe practice and sharpen procedural and teamwork skills across the spectrum of inpatient and outpatient settings [82]. Formal training and deliberate practice of teamwork and procedural skills in simulated OR settings can obviate relying on the traditional apprentice approach. Human patient simulation is the medical simulation version of the simulator cockpit, employing an experiential learning model well suited to adult learners. Kolb and Fry [83] positioned four elements of experiential learning in a cycle: concrete experience, observation and reflection, formation of abstract concepts, and testing in new situations. Learners can enter at any point but most enter by means of a specific concrete experience in the context of a particular situation. Gaba incorporated this approach into his ACRM curriculum, allowing systematic presentation of a wide variety of routine and uncommon but critical events in a simulated medical setting [57]. Although there is no gold standard team training curriculum in healthcare, the IOM encourages team training programs such as CRM and simulation for personnel who work in critical care areas [84]. Medical simulation provides a vehicle by which clinicians can experience an event and reflect and learn in an atmosphere of safety, free of patient harm.

As per Gaba, medical simulation, practice, and drills never pose a risk to live patients [57].

Aggarwal and colleagues [85] further asserted in 2004 that practicing team skills enables surgical teams to function in a safer, more efficient manner when crises occur in real life. This was nicely illustrated in a study by Weaver et al. [86] who evaluated whether or not teamwork training improves performance in the OR. They compared a control group with an intervention group that was exposed to a medical team training curriculum, Team Strategies and Tools to Enhance Performance and Patient Safety, the next generation of MedTeams that was developed by the DoD in collaboration with the Agency for Healthcare Research Quality. The 4 hour curriculum included case-based interactive sessions and low-fidelity simulation for practice. Trainee reactions, learning, and behaviors were assessed, and team performance in the OR was observed, identifying the degree to which team training skills were enacted. They reported positive results in the intervention group compared to the control group in the quality of presurgical procedure briefings, use of high-quality teamwork behaviors during procedures, and perceptions of safety culture and teamwork attitudes.

Vincent et al. [87] strongly advocated for including team training as part of a broad-based systems approach to surgical quality and safety. They also strongly supported research aimed at optimizing the surgical environment, equipment design, and understanding subtleties of decision-making in the complex OR environment. Such broad-based efforts would include direct observations, including visual–audio recordings, assessment of surgical team performance, and the routine use of fully operating theater simulation targeting all members of the surgical team. Implementing such a system may be the most important intervention to enable surgical teams to achieve high performance and better outcomes for patients. To that end, Moorthy et al. [88] assessed technical and teamwork skills of two surgical teams managing a bleeding crisis during a simulated vascular procedure in a simulated OR. The event was videotaped and used to provide feedback in the immediate postscenario debriefing. Technical ability in controlling the bleeding was assessed with a global rating scale. Teamwork or “nontechnical” skills were assessed using a NOTECHS skills rating scale that was originally developed for aviation and adapted for use in healthcare. Additional metrics included evaluation of communication within the team, amount of time to complete specific tasks, and a surrogate outcome measure of the total (simulated) blood lost—amount captured in the canister and weight of blood-soaked sponges.

Participants also completed a questionnaire about their perception of the simulation experience. The investigators found that the simulated scenario was well received and deemed as realistic by the participants. Significant differences were seen between junior and senior trainees in managing the bleeding crisis, with seniors demonstrating quicker times for recognizing the crisis and instituting appropriate interventions. Junior trainees were more likely to blindly use and apply clamps to stop the bleeding and experience greater blood loss, and they were less likely to realize their limitations and call for help. There was utility in the variations found between and within groups, potentially for identifying and setting performance standards and guiding which trainees may need further assistance in skills acquisition and crisis management. NOTECH scores for teamwork did not differ significantly between the groups. The investigators postulated that the wide variability of scores within the groups may be related to the lack of focus on developing effective team skills in surgical training. The construct and content validity of the NOTECHS rating scale has since been evaluated and deemed a reliable instrument for assessing teamwork in the OR [89,90], and its use has expanded beyond the OR to trauma bays and surgical wards [91–93].

The current state of team training and its effectiveness in acute care settings was recently explored by Weaver et al. [94] They compiled a database of reviews having examined the effectiveness and implementation of team training and published between January 2000 and December 2012 and also included 26 additional primary studies about team training effectiveness on clinical processes or patient outcomes published between January 2011 and December 2012. Overall, they found moderate- to high-quality evidence indicating that team training, whether simulation or didactic based, has a positive impact on team processes and improved clinical process and patient outcomes in acute health-care settings, including critical care units, labor and delivery, surgery, and emergency care. They highlighted the study by Riley et al. [95], demonstrating significantly greater reductions in patient harm achieved by the simulation group compared to the didactic and control group. They also stressed that the greatest impact on patient outcomes was found in those studies [96–98] that had implemented team training as an intervention bundled with formal evaluation of readiness for such training and the use of interdisciplinary learning activities and tools that support transfer and daily use of teamwork skills. In particular, Neily et al. [96] reported an 18% reduction in annual surgical mortality, and Young-Xu et al. [98] reported a 15% decrease in hospitals in the Veterans Health System that had implemented a medical team training program compared to a 10% decrease in those that had not.

SURGICAL SIMULATORS FOR TECHNICAL SKILLS TRAINING

A variety of devices, ranging from simple to complex objects, cadavers, or animal models to elaborate virtual reality (VR) devices, have been developed for training and practice of surgical maneuvers and procedures involving the abdomen and pelvis [99]. These include knot-tying or suture placement trainers, pelvic exam training devices such as the Pelvic ExamSim™ (METI®, Sarasota, FL) that has internal sensors and software that feeds information back to the learner about their performance [100], and life-size human patient mannequins for simulating surgical scenarios in a simulated or real OR environment [101,102]. It is still not clear how much physical realism is needed for skills training and assessment of open laparotomy procedures involving major abdominal and pelvic organs, such as hysterectomy, vesicovaginal fistula repair, or vaginal vault suspensions. Video-simulation, VR, computer screen–based, or haptic systems may offer greater opportunities to enhance the realism and may be used in combination with human patient mannequin simulators [82,103]. The surgical robot system is revolutionizing surgical practice across a variety of specialties, including urology [104] and gynecology [105]. VR-assisted robotic surgery simulators are undergoing validation [106] and full simulations are being developed [107]. The total immersion in VR–haptic surgical environment, the “surgical holodeck,” remains an area rich for research and development [108–110].

The paradigm of surgical education and training continues to shift from the traditional “see one, do one, teach one” approach to that of “learn and practice on a simulator first.” Simulators are steadily being integrated into the surgical curriculum for training [111–113], assessment [114–116], credentialing [117–120], and reentry to clinical practice [121,122].

The integration of VR technology with endoscopic training devices was proposed by Satava in 1993 [123], and VR has since become integral to a broad range of surgical simulators. Box trainers and VR laparoscopic simulators have been shown to facilitate skills acquisition and training across the spectrum of novice to expert. Such training has translated into improved proficiency in the OR. Scott et al. [124] in 2000 evaluated global performance during laparoscopic cholecystectomy and found significantly higher scores among surgical residents who trained with box trainers than those who had not. Fichera and colleagues [125] in 2005 also noted statistically significant improvements in suture technique and coordination of trainees using the LTS 2000 laparoscopic box trainer. Seymour et al. [126] conducted a randomized, double-blind controlled trial evaluating VR simulator–based training and found improved performance of skills in the OR in those with such training. Similar findings were obtained by Gallagher et al. [127] and Grantcharov et al. [128] Laparoscopic skills have reportedly improved for novices who trained with either box or VR simulators. [129] Grantcharov et al. [130] conducted a randomized clinical trial of surgical residents using VR simulators. Surgical skills of residents who trained with the laparoscopic simulator directly translated into better performance in the OR. Even third year medical students rotating through gynecology and general surgery achieved proficiency whether they trained with laparoscopic box or VR simulators [131]. However, students training with laparoscopic VR simulators reached proficiency sooner than those who had not used them.

Aggarwal et al. [132] demonstrated that non-VR simulators can differentiate novice from expert. They evaluated the performance of novice and experienced gynecologists in a series of laparoscopic tasks needed for managing ectopic pregnancy. Novices significantly improved their surgical performance and experienced gynecologists demonstrated little change over time. Aggarwal and Darzi [133] showed that skills acquired using a VR simulator had high transferability to the porcine model, with every hour of training reduced by 2.3 hours, which is the time needed to gain proficiency. Demonstrating transferability to surgical procedures involving real patients and evaluating cost-effectiveness of such training will be an area of future research. Both Geoffrion [134] and Goff [135] showed simulation-based surgical skills training improved the technical performance of gynecology residents and such skills were translated well to the OR. They each underscored the need for standardizing simulator-based curriculum to consistently train and assess surgical care in clinical practice.

Kahol et al. [136] evaluated the potential role of surgical warm-ups, the preprocedure short-term practice sessions with a simulator, to exercise a surgeon’s psychomotor and cognitive skills. Kahol et al. conducted a series of experiments involving 46 surgeons that comprised of novice to senior gynecology and general surgery residents and attending trauma surgeons. The first experiment evaluated the impact of the warm-up on surgical proficiency and its relationship with experience, fatigue, and cognitive and psychomotor skills. The second evaluated whether basic skills warm-up improved performance of complex tasks. They found that regardless of the level of expertise, all surgeons benefitted from the surgical warm-ups as a 25%–45% range in reduction of error was noted. The time required to complete a task was substantially diminished. Warm-ups diminished cognitive errors ($p < 0.0004$) and improved performance in all parameters being studied in the fatigued individual. Even though performance improved in the fatigued individual, it did not return to baseline performance levels characteristic of the rested state. These findings suggest that the preoperative warm-ups may become a new surgical standard, assuring optimal care of the patient during surgery.

At that time, Satava predicted surgical simulation would steadily evolve and mature from its relatively infant to assume the breadth and scope of its use in the fields of aviation and the military [137,138]. In view of continued growth in the use of robotics in almost every surgical subspecialty and the evolution of robotic platforms, the continued use of simulation and telementoring to enhance surgical performance is thereby assured [139]. Indeed, preoperative simulation warm-up exercises on a VR robotic simulator have since been shown to significantly improve robotic surgery performance and reduce errors among surgeons, including general surgeons, urologists, and gynecologists, from experienced to novice [140].

Brewin et al. [141] recently reviewed simulation-based training from a urology perspective. They agreed that such training provides opportunities for surgeons to train without harming patients. They found good evidence that use of part task trainers shortens the learning curve, especially for newer trainees. They highlighted studies by Lee et al. [142] and Gettman et al. [143] whose findings supported the need for nontechnical skills training, and such training was possible in a high-fidelity simulated OR. Evidence they gathered in their review further bolstered the argument for formally incorporating simulation-based training of technical and nontechnical skills into a urology training curriculum.

CHECKLISTS

The use of checklists in surgical care has virtually exploded since the launch of the Universal Protocol in 2004 [144], a protocol aimed at preventing wrong-site-, wrong-patient-, wrong-procedure-related surgery, combined with the introduction of the WHO surgical safety checklist in 2008 [79]. Studies by Lingard et al. [145] and de Vries et al. [146] laid fundamental groundwork toward incorporating the use of checklists to improve communication among team members in the OR and facilitate safer care of the surgical patient. Lingard's team of researchers were particularly concerned with the impact of communication breakdowns in the OR, having previously identified communication failures in about 30% of procedurally relevant team exchanges of information [147], about a third of which jeopardized patient safety. They subsequently developed a checklist prototype and piloted its use in 18 vascular surgical procedures performed in Canada. Three researchers observed its use in real time, noting patterns of use. Their data indicated that a preoperative checklist could foster OR team communication about key information before a surgical procedure and facilitate team cohesion. Thereafter, Lingard and colleagues [148] conducted a 13-month prospective study to evaluate whether use of a checklist in preoperative briefings improved interprofessional team communication in the OR. Using a pre-/postintervention study design and trained observers, a total of 172 surgical procedures were observed. They found that the mean number of communication failures per procedure significantly decreased from 3.95 preintervention to 1.31 postintervention ($p < 0.001$). The checklist briefings revealed knowledge gaps, promoted learning, and triggered actions among members of the team. The investigators also appreciated the impact of a traditional silo approach of nurses, surgeons, and anesthesiologists working independently; staff shortages, educational demands, and economic pressures had on surgical workflow; and the potential for jeopardizing patient safety.

The surgical patient safety system ("SURPASS") checklist, developed by de Vries et al. [146] in the Netherlands, is a checklist whose design was based on a synthesis of human factors' literature and review of literature on surgical errors and adverse events. Items contained in their tool were validated with real-time observations in the OR and then introduced it into practice. All health-care providers involved with the patient along the surgical pathway were taught how to use the tool and complete their sections. SURPASS is comprised of five sections addressing the preoperative ward, OR, recovery room or ICU, postoperative ward, and time of discharge, thus serving as the first tool covering the entire admission to discharge pathway. The use of SURPASS was well received overall. However, some users did not complete the tool due to lack of consequences and some users strongly advocated for creating an electronic version and have it integrated with their hospital information system. The SURPASS checklist has since been shown to improve compliance with timing the administration of antibiotic prophylaxis [149] and was associated with a decrease in total number of complications from 27.3/100 patients prior to using the checklist to 16.7/100 patients after its implementation [150]. The latter study also showed in-hospital mortality, which decreased from 1.5% to 0.8% after implementation of the checklist, and no changes in outcome were found in the control hospitals who had not been exposed to SURPASS.

Bouchard et al. [151] conducted a systematic review of implementation of surgical safety checklists in 2012. Of about 5000 thousand articles published on this topic between 1995 and April 2011, they identified 22 for inclusion. Either the Universal Protocol, the WHO checklist, or a new protocol, based on either or both, was used in 17 studies, and 4 studies involved the use of SURPASS. At the time of their review, the Universal Protocol had been implemented in 2257 hospitals in the United States, WHO checklist had been implemented in 3000 hospitals among 25 countries, and SURPASS had been implemented in 16 hospitals in the Netherlands. Bouchard et al. found use of the checklist was associated with a relative risk for mortality of 0.57 and a relative risk of 0.63 for any complication. Overall compliance with using the tools ranged from 12% to 100% (mean 75%) and a range of 70%–100% (mean 91%) for the time-out. They deemed surgical safety checklists to be effective in decreasing mortality and morbidity, specifically the WHO and SURPASS checklists. High compliance was associated with involvement of multidisciplinary surgical staff in the process of development. Critical factors for successful implementation included explaining to staff why and how the checklist would be used, coupled with real-time coaching, feedback, audits, ongoing education and training, and support of hospital administrators and leaders.

Treadwell et al. [152] conducted an in-depth analysis of the impact and implementation of the Universal Protocol, SURPASS, and WHO surgical safety checklist. They reviewed 33 studies published between 2000 and 2012 and found checklists had been widely adopted worldwide and in diverse contexts, especially the WHO checklists. Checklists were associated with improved health outcomes such as decreased surgical complications and surgical site infections, increased detection of potential safety hazards, and improved communication among members of the operative team about relevant and important information about the patient. They confirmed that successful implementation of checklists involved factors such as administrative and leadership support, training staff on their use, adapting the checklist to incorporate staff feedback and avoid duplicate efforts in data collection. Barriers to effective implementation included confusion about practical use, managing workflow efficiently and the beliefs and attitudes of staff, especially surgeons, toward checklists. A concept central to all three checklists is that they are tools by which to encourage team-based interactions among multidisciplinary OR staff. The surgical safety checklist provides an opportunity for every team member to speak up and offer up information of concern, allowing everyone involved to be on the same page and situationally aware of what to expect. The extent to which such teamwork contributes to the impact of the checklist and the extent to which patients should be included are rich areas for research.

DECISION-MAKING AND DIAGNOSTIC ERRORS

Identifying evidence-based methods that facilitate effective decision-making and reduce diagnostic errors is the new frontier for patient safety [153]. Leape et al. [154] categorized medical errors into four types: diagnostic, treatment, prevention, and others (including communication or system related). Diagnostic error includes delayed, missed, or wrong diagnosis, failure to use indicated tests, and failure to act on the results of monitoring or testing. Berner and Graber [155] noted that such errors occur in every specialty, ranging from 2% in perceptual specialties (such as radiology and pathology) to as much as 15% in the clinical specialties. Their review of the literature led them to conclude that overconfidence, a trait of human nature, does exist among physicians. Such overconfidence contributes to diagnostic error. Physicians believe that diagnostic error exists but underestimate the likelihood of their occurrence, especially in their own decision-making processes. This is evident in physician disregard for decision aids or tools or diagnostic or treatment guidelines or algorithms. If a clinician is uncertain about a clinical situation, then formal or informal consultative assistance is more likely to be requested, especially when the case is complex. However, Berner and Graber believe most cognitive errors arise when cases seem to be routine and physicians are certain about the decisions they have made.

Newman-Toker and Pronovost [153] define misdiagnosis-related harm as preventable harm resulting from delay or failure to treat a condition that is actually present or to treat a condition that does not actually exist. Diagnostic errors are frequently not recognized and underreported and methods for detecting them are lacking. Such errors are often classified as cognitive errors rather than systems errors, a perspective that facilitates attribution of individual blame. Newman-Toker and Pronovost suggest a different approach, taking a 5-point action plan that includes (1) developing systems such as computer-based decision support systems to facilitate cognition, (2) grouping errors based on clinical context rather than cognitive defect, (3) emphasizing misdiagnosis-related harm instead of diagnostic error, (4) taking a systems approach to improving workflow, and (5) building cost-effective diagnostic tools or decision aids that may not be perfectly accurate but assist the human mind.

Medical decision-making involves a series of cognitive steps from outlining the goal and desired outcome, gathering the data, evaluating choices and alternatives, considering pros and cons to each, making the decision, implementing the decision, and learning from the decision. Most diagnoses are clear and unambiguous. However, when a situation is uncertain, complex, and time pressured, then major decisions are frequently made rapidly and subconsciously and bypass the cognitive steps. Such rapid decisions are highly influenced by biases of prior experience and memory, unconscious reasoning, and intuition [156]. Croskerry et al. [157] contend that humans spend about 95% of their time behaving intuitively. Judgments and decisions arising are aided by heuristics—mental rules, rules of thumb, maxims, or shortcuts—that allow one to size up and manage a situation rapidly. Croskerry [156] grouped biases and failed heuristics under the term “cognitive disposition to respond” (CDRs), removing the stigma of bias and clearing the way to accept the “capricious nature of decision-making.” He identified at least 30 CDRs and contended there were probably more. Fargen and Friedman [158] more recently identified that a subset of CDRs that they found were applicable to neurosurgeons. These are generally applicable to surgeons (see Table 10.4).

There are strategies to facilitate “cognitive debiasing,” a term coined by Croskerry et al. [157,159], referring to controlled analytic thought processes to overcome biases, the so-called cognitive pills for cognitive ills [156]. Educational strategies can help improve future decision-making such as learning about cognitive bias and its impact on medical decision-making, being aware of one’s own biases, and training in techniques for overcoming bias, including use of simulation-based training. Simulation of diagnostic error-related cases offers safe and practical means by which to better understand the factors contributing to cognitive error in contextually relevant settings and identify solutions for preventing or mitigating their effect [160]. Likewise, simulation is a practical and safe means by which to assess the efficacy of diagnostic and decision support interventions before they are implemented on a system-wide basis in the clinical setting. Workplace strategies for cognitive debiasing can help facilitate decision-making in the moment of problem-solving. These strategies include slowing down activities such as procedural time-outs or diagnostic time-outs, taking time to pause and reflect on the working diagnosis and supporting evidence, gathering more information, deliberately being more skeptical, seeking other’s opinions, and recalibrating one’s perspective. Force function strategies for cognitive debiasing also facilitate clinicians’ ability during the moment of problem-solving to consciously consider alternatives, thereby mitigating error. These strategies include the use of cognitive aids, checklists, algorithms, practice guidelines, protocols or similar tools, and the technique of deliberately taking time to rule out the worst-case scenario or intentionally consider a diagnosis opposite to the initial impression.

Table 10.4 Cognitive Dispositions to Respond: Applicable to Surgeons

Cognitive disposition to respond	**Description**
Anchoring	Tendency to weigh initial data too heavily and failure to adapt the diagnosis once more information is available, sticking with the diagnosis.
Availability bias	Tendency to judge diagnosis more likely if one has been recently seen or experienced.
Commission bias	Tendency to promote patient beneficence through action rather than inaction, performing a treatment or procedure because the patient is ill.
Confirmation bias	Tendency to look for evidence that confirms a diagnosis rather than look for evidence to refute.
Diagnosis momentum	Tendency to label a diagnosis for gaining traction with the patient and health-care workers so that it is perceived as definite rather than possible.
Fundamental attribution error	Tendency to blame patients for their situation or illness rather than examine their actual circumstances.
Hindsight bias	Being aware of the outcome influences the perception of past events such that the role of an individual is under- or overestimated.
Omission bias	Tendency to avoid doing something wrong through inaction rather than action.
Order effects	Tendency to remember the beginning and end during information transfer, neglecting data exchanged in the middle.
Overconfidence bias	Tendency of an individual to believe themselves to be more knowledgeable than they really are, leading to action based on inadequate information or intuition without appropriate supporting evidence.
Premature closure	Tendency to accept a diagnosis as true before it has been fully verified.
Search satisfying	Tendency to stop looking for other problems once one is identified, leading to missed diagnosis or injuries.
Visceral bias	Tendency to have decisions influenced by an emotional or affectively labile state; countertransference, negative or positive feelings toward a patient, leading to missed diagnosis or injuries.

Source: Modified from Fargen KM and Friedman WA, *World Neurosurg*, 82(1–2), e21, 2014.

DISCLOSURE AND APOLOGY OF ADVERSE EVENTS AND ERRORS

Since errors are inevitable wherever humans are involved, surgery-related errors and adverse events will happen. Methods for managing their aftermath should ensure information is fully disclosed to patients and their families and preserve trust in the patient–doctor relationship and action will be taken to help prevent recurrence of similar errors. Just as the paradigm of surgical education and training has shifted from an apprentice model to one of the simulation-based learnings and practices, health-care education and specialty training have come to appreciate the importance of formally teaching trainees techniques of effective communication and how best to manage difficult conversation and apologize to a patient who has experienced harm due to errors and adverse events. Disclosure has come to be seen as an integral component of patient-centered care and elemental in promoting quality and safety of healthcare [161]. The Joint Commission stepped forward in 2001 to set standards for disclosing unanticipated outcomes of patient-related events by the provider or institutions [162]. The Patient Safety and Quality Improvement Act of 2005 [163] established a confidential, voluntary system in the United States for clinicians to report adverse medical events. Health-care institutions in the United States and worldwide have since established or are instituting policies for such disclosure and incident reporting systems to capture information about adverse events and near misses [164–166].

Disclosure is telling patients important information about their medical care or condition that affects or has the potential to affect their current or future well-being. The physician is expected to conduct the conversation but may be accompanied by other members of the team, or there may be occasion for some other team member to lead the discussion. Patients prefer to know about unanticipated outcomes and adverse events that may have occurred [167]. Kaldjian et al. [168] identified a gap between physicians’ attitudes toward disclosure and what they practice. Surveys sent to physicians, residents, and medical students in the Northeast, Mid-Atlantic, and Midwest of the United States revealed that 97% of responders would disclose a hypothetical error resulting in minor harm and 93% would disclose a hypothetical error resulting in major harm to patients. However, 41% of responders had disclosed an actual error involving minor harm, and only 5% had disclosed an actual medical error involving major harm/death or disability to a patient. These results indicated a discrepancy between the willingness to disclose medical errors and the actual disclosure of errors by physicians. Waterman et al. [169] investigated the impact of medical error on physicians in the United States and Canada. They reported that physicians experienced anxiety about future errors, loss of confidence, difficulties sleeping, and some feared damage to their reputation. Barriers to disclosure include psychological issues such as the fear of retribution from the patient and colleagues; fear that conversations won’t go well; fear of the emotional impact to the patient and self; and beliefs that disclosure is unnecessary, that the unanticipated outcome would have happened anyway, and that the outcome is not directly related to the clinician’s actions. Legal barriers to disclosure include lack of legal protection about the information conveyed, lack of clarity about what needs to be disclosed and when, and belief that disclosing will not be beneficial if case becomes a malpractice claim. However, from the ethical perspective, patients have a right to know about what happened. Disclosure of unanticipated outcomes, adverse events, or near misses is the ethical imperative. Furthermore, Leape stresses the therapeutic aspects of disclosure, stating that full disclosure is essential for healing for the patient, the patient–doctor relationship, and the clinician involved [170]. Surgeons face unique challenges to providing full, appropriate disclosure of surgical adverse events to patients due to the high frequency of such events, current structure of the medicolegal system and variability in legal protections, team structure of surgical care, and lack of clear, reasonable, and specialty-specific standards for guiding disclosure in surgery [171]. Strategies for improvement include training and coaching for disclosure conversations, providing organizational peer support programs and resources for clinicians, improving clinicians’ understanding of the relationship between disclosure and litigation, and establishing organizational programs for communication and resolution, coupled with patient compensation when indicated. Additional strategies offered by Lipira and Gallagher [171] include facilitating collective accountability for individuals and systems in taking responsibility for disclosure conversations, participating in measures to understand why the adverse event happened and how to prevent its recurrence, and establishing standards for disclosure by surgical specialty and subspecialty professional organizations.

Much progress has been made over the past two decades toward better understanding the need for transparency with patients about medical errors and adverse events, yet challenges remain in putting policies and procedures into practice [166]. Even countries known for having supported disclosure on a national level are still challenged by (1) putting policy effectively into large-scale practice, (2) managing conflicts between patient expectations and patient safety theory, (3) resolving conflicts between open disclosure and legal privilege and protections, (4) aligning open disclosure with compensation, and (5) effectively measuring the occurrence of disclosure and its quality. Much remains to be done to overcome these challenges and advance the patient safety agenda.

Apology is the expression of regret or remorse for the unanticipated outcome, adverse event, or near miss. Apology shows the humanity and fallibility of clinicians, a therapeutic necessity for healing and making amends [170]. Lazare [172] in 2006 stated that an effective apology should (1) acknowledge the offense, (2) explain the commitment of the offense, (3) express remorse, and (4) offer reparation for the offense. Properly conveyed, the apology should touch on all these elements and be relayed with sincerity, preserving the patient's dignity and providing reassurance that the clinician cares about the patient's well-being. Performed this way, such apologies facilitate the healing process. Cravens and Earp [173] in 2009 highlighted the following "five R's" and "five A's" for guiding effective disclosure and apology (see Table 10.5).

Table 10.5 Five "R's" of Apology and "A's" of Making Amends

Five "R's" of apology	
Recognition	Understand the patient's feelings and your feelings, the basis for them, and recognize when apology is in order.
Regret	Respond with empathy; acknowledge the patient's feelings. Tell them you regret what they are experiencing. Apology does not imply guilt.
Responsibility	Take responsibility for what happened and disclose all the details that led to the outcome.
Remedy	Make clear to the patient what is being done to remedy the situation, including financial costs or compensation if appropriate.
Remain engaged	Continue to provide care for your patient after the outcome, reassuring them you will remain engaged and available.
Five "A's" of making amends	
Accurate	Truthfully and accurately tell the patient that an error has occurred.
Answers	Anticipate the patient's needs for answers about the error and what impact it may have on their clinical situation.
Accountable	Explain what is known about how the error occurred and accountable about future actions taken to prevent similar errors from occurring.
Apology	Apologize to the patient for the error.
Acknowledge	Acknowledge the patient's responses about the error and its occurrence, addressing their concerns as they arise.

Source: Adapted from Cravens C and Earp JL, *NC Med J*, 70(2), 140, 2009.

A genuine apology can go a long way toward defusing a patient's anger, showing them respect and empathy, and further facilitate the healing process for all involved. Legislative initiatives that provide legal protection for disclosure and an expression of sympathy or full apology have been drafted or passed, varying in scope and breadth from region to region worldwide [166]. Pelt and Faldmo [174] reported in 2008 that 35 states within the United States had enacted apology statutes and 3 had legislation pending. They regarded such statutes as still in their infancy and unclear as to how well they would stand up in court. Since then, Saitta and Hodge [175] published in 2012 that 34 states and the District of Columbia had enacted laws prohibiting a physician's apology with disclosure from being admissible evidence in legal proceedings. They highlighted emerging evidence from Michigan [176], Colorado [177], and Kentucky [178] that apologies have reduced the cost of litigation per claim since the implementation of an apology and disclosure program. They emphasized the importance of being aware of the statutes applying to a specific jurisdiction and practice location because the laws of each state have their own nuances. One's own institutional risk managers can provide guidance and help clarify what to say and when and how best to proceed.

SUMMARY

Ensuring safety and quality is the responsibility of every member of the surgical team. Achieving a balance of expert knowledge, technical skills, sound decision-making, and optimal teamwork behaviors offers the best approach toward assuring reliably safe, high-quality care of our surgical patients. As surgeons, we aspire to provide the safest, highest-quality health-care services. The literature reviewed here underscores the importance of a patient safety culture and supports surgical teamwork training and simulation for practicing routine and critical procedures and events, improving technical proficiency and team interactions, and error reduction, recognition, and management. The paradigm of surgical education has indeed shifted from the apprenticeship style of learning. More research is needed to advance our understanding of what environments best facilitate excellence in training and proficiency in technical and teamwork skills, skills that are translatable to the surgical arena. Sound educational objectives serve as the best guide for the ongoing development of simulator technology and the extent of its realism and fidelity. This chapter identified several ways by which to prevent medical errors or mitigate their effects given that all human beings are subject to making errors. Effective disclosure and apology is vital to the process of error management. A thorough understanding of where surgical practice is vulnerable to error best informs design of systems-based approaches to mitigate the clinical demands that weaken our defenses and facilitate provision of the safest, highest-quality surgical care for our patients.

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Section II

Role of Patient Reported Outcome Measures and Health Economics

11

Section Introduction: The Role of Patient-Reported Outcome Measures and Health Economics

Cornelius J. Kelleher

Understanding the patient perspective of any medical condition allows us to treat our patients more effectively, compassionately, and completely. Lower urinary tract dysfunction and genital prolapse can be described by objective investigations and clinical examination. Treatment outcomes can be assessed in a similar manner. Ignoring the patient perspective can, however, lead to inappropriate conclusions regarding treatment desire, appropriate treatments to select, and treatment efficacy. How conditions affect patients' lives and how they hope to benefit from interaction with the medical world can only be answered by the patients themselves. This chapter hopes to discuss our current understanding of patient-reported outcomes (PRO) assessment.

In Chapter 12, Coyne and Sexton introduce the concept of patient-reported outcomes, from their development through their selection and usage for clinical trials and clinical practice. In this chapter, the authors describe the evolution of the PRO to encompass many aspects of the patient pathway, from the initial assessment of the symptoms and the bother they cause to the multifaceted assessment of treatment outcome. Increasingly, the patient perspective of treatment success is recognized as the most important goal of medical interventions. Whether the patient is satisfied with their treatment, whether it improves their symptoms sufficiently, and whether they wish to persist with treatments outside the context of clinical trials are all hallmarks of a successful intervention. The authors describe how the bother caused by a problem can be addressed and measured in a reproducible way and how to select the best tools to use in various different settings.

In Chapter 13, the individual questions used to measure the quality-of-life outcomes of patients with lower urinary tract dysfunction are described in greater detail. Understanding as much as possible about the content of the questionnaire, its previous usage, size, etc., ensures that the correct tool can be chosen for the correct purpose.

Kopp and Evans focus on patient satisfaction, expectations, and goal achievement in Chapter 14, a new edition to this volume of the textbook. It is now increasingly recognized that setting realistic patient goals and expectations for treatment are of paramount importance to satisfactory treatment outcome. Addressing patient goals before an intervention supports dialogue with a patient and ensures that they understand what a treatment is likely to achieve and helps the clinician understand what a patient would like the treatment to do. This is a very important chapter and highlights the fact that clinicians and patients are not always on the same wavelength regarding the expectation of an intervention and what signifies treatment success. How to measure goals and patient satisfaction has evolved considerably, and while we all undoubtedly address various aspects of this in our clinical practice, how best to do it and what instruments are available to do it properly may not be so clear.

In Chapter 15, Domoney and Symonds have updated their chapter from the previous edition of this textbook to include new questionnaires to assess sexual function. The assessment of sexual function in a standardized fashion is crucial to understand the problems that patients are experiencing, and whether treatments impact positively or indeed negatively on this important aspect of their lives. So many of the problems affecting the lower genital and urinary tracts impact on sexual function, and so often it is assumed that treatments improve it. Without being able to measure it in a reproducible and meaningful way, we are unable to draw these conclusions. This is a must-read chapter that will complement chapters one to three.

In Chapter 16, Mohamed, Chatoor, and Williams describe questionnaires used to assess bowel function. Many patients with lower urinary tract dysfunction and genital prolapse have associated bowel symptoms. Increasingly, we are working as part of a multidisciplinary team to assess and treat all aspects of a patient's concerns from the outset. The inclusion of clinicians trained in the clinical assessment and treatment of lower bowel dysfunction is recognized as well as the use of questionnaires to identify bowel problems as part of the initial patient evaluation. Specific tools for this purpose have evolved along a similar pathways to those used to measure lower urinary tract dysfunction. Currently, available questionnaires are discussed in this chapter.

In Chapter 17, further evolution of the International Consultation on Incontinence (ICI) modular questionnaire is described by Cotterill and Abrams. This chapter should be useful when designing a study or clinical trial. Many of the questionnaires adopted by the ICI appear in various other chapters of this book and several have been specifically designed by the ICI when suitable tools were not available elsewhere. The idea of a modular questionnaire is essential to the assessment of the many different aspects of the typical conditions that we see and treat. The chapter guides the reader through selection of the recommended instruments in order that the best tool for each desirable outcome can be used with as little overlap of the tools as possible.

Increasingly, we are living in an electronic world where paper is replaced by computers and keypads. While not all of our patients are computer literate and the expense of computerized assessment not always affordable, questionnaire completion has moved into the computer age. Radley and Gopinath, in Chapter 18, describe the ePAQ questionnaire as one of the leaders in this field. The ePAQ can be used as a self-completion tool to reduce clinician workload in initial assessment as well as measure outcomes in clinical practice and clinical studies. Progress is always important and I suspect in the coming years we will be losing our paper notes and the computer era will be upon us. Ultimately, the inclusion of many of the questionnaires already discussed in this section will be amenable to computerized completion and scoring, which is already the case in many clinical trials.

Prolapse questionnaires have evolved considerably over the last decade, possibly in response to the huge interest in new ways to treat this condition. The last decade witnessed an explosion in the use of mesh kits to treat prolapse and a subsequent and almost as rapid decline as fear over complications arose. Understanding how and whether patients are bothered by their anatomically demonstrable prolapse has allowed us to reevaluate the success of our prolapse surgery. The fact that patient satisfaction after prolapse surgery does not always correlate with anatomical correction will allow us to better understand what patients want from surgery and avoid the pitfalls of treating anatomical defects rather than patient’s symptoms and expectations. In Chapter 19, Digesu describes questionnaires currently available to assess patients with prolapse in the hope that we can better understand the patient perspective of this common condition.

Chapter 20, the final chapter in this section, discusses the important aspect of health economics. Having recently witnessed a world financial recession at the same time as an ever-increasing expectation of successful healthcare, we need to be certain that our treatments are cost-effective and affordable. It is not always the most expensive option that is the best, and sensible rationing to achieve as much as possible for as many as possible is the key to sensible management of our health-care budgets. In this chapter, Moore offers an interesting insight into financial conundrums in healthcare and describes the terminology and processes to allow us to better understand how they pertain to our own medical management decisions.

Hopefully, the reader will find this section both useful and informative. Inevitably, there are some areas of overlap but wherever possible these have been minimized. By reading this section, you will be in a better position to understand questionnaire usage, selection, and analysis, both in your clinical practices and clinical studies and trials.

12 Patient-Reported Outcomes: From Development to Utilization

Karin Coyne and Chris Sexton

INTRODUCTION

A patient-reported outcome (PRO) is any report coming directly from patients, without interpretation by physicians or others, about how they function or feel in relation to a disease or treatment [1,2]. The field of PRO research has evolved considerably over the last 30 years from an initial focus on quality of life (QOL) to a more multifaceted study of different aspects of disease and therapeutic impact with a comprehensive theoretic framework, accepted methods, and diverse applications [3]. As medical treatments have progressed from lifesaving benefits to QOL-improving benefits, PROs have become increasingly important to patients and health-care providers.

Traditionally, the clinical history has been used to gain a summary view of the symptoms patients experience; however, clinical histories often do not assess patient impact or patient perception of their condition. As such, patient-administered PRO measures have increasingly been used to support the clinical history and provide information about outcomes patients consider important. By facilitating comparisons of treatments in the context of research and routine clinical care, PROs can help patients and clinicians make better decisions about treatment and may even reshape how health care is conducted [4]. The science of developing and validating such PRO measures is the focus of this chapter.

In providing a method for the standardized collection of data or an objective assessment of a subjective phenomenon, PROs represent the most important clinical review of the patient experience of a condition, disease, or set of symptoms. In the clinical setting, PROs can be used to inform clinicians' and patients' decisions about treatments [5,6]. In the context of research and clinical trials, PROs can serve as a primary efficacy or key secondary endpoint in order to evaluate treatment effects from the patient perspective [2,7].

Importantly, patients' perceptions of outcomes associated with urogynecological health are greatly influenced by their personal beliefs about their condition and their understanding of the availability of various treatments [8]. Assessment of patient goals may be useful to patients and their clinicians in determining treatment options. For example, women with pelvic floor dysfunction who undergo treatment have been shown to have a variety of desired subjective goals that relate to their short- and long-term treatment satisfaction [9].

PROs are especially valuable in assessing symptoms that may be bothersome but cannot be fully assessed without direct report from the patient, such as pelvic floor disorders, urinary symptoms, fatigue associated with gynecological cancer, and aspects of bowel and sexual function. The use of PROs in the measurement of urogynecological health can help provide a context for what is driving treatment-seeking behavior and inform decisions about treatment options. Although urogynecological symptoms perceived by the patient or caregiver or partner do not necessarily translate into a definitive diagnosis [10], the quantification of symptoms and their impact coupled with observations in the clinical setting can be used to better consider treatment options and to assess treatment outcomes. This chapter will provide an overview of the types of PRO measures and review the PRO development and validation process from a scientific and regulatory perspective.

TYPES OF PATIENT-REPORTED OUTCOMES

Generic and Condition-Specific PRO Measures

PRO measures generally fall into two broad categories: generic and condition specific. Generic measures are designed to assess outcomes in a broad range of populations (e.g., both healthy and ill individuals). These instruments are generally multidimensional and tend to assess the physical, social, and emotional dimensions of life. An example of this type of instrument is the Medical Outcomes Study SF-36 Health Status Profile [11].

Condition-specific measures are designed to assess the impact of specific diseases or conditions and include items more specific to the particular condition or population being studied. Condition-specific measures can be similar to generic instruments in that they assess multiple outcome dimensions. Examples of frequently used condition-specific instruments in gynecology and urogynecology include the Functional Assessment of Cancer Therapy-Ovarian [12], the Pelvic Floor Impact Questionnaire [13], the Incontinence Impact Questionnaire, the King's Health Questionnaire (KHQ) [14], and the Overactive Bladder Questionnaire (OAB-q) [15]. In general, there has been a growing trend to include condition-specific outcome measures in the clinical trial and research setting due to their enhanced sensitivity to change and the need to minimize participant burden.

Importantly, the type of measures selected for inclusion in a research study will depend on the goals of the intervention and the specific research questions to be addressed. Important considerations about the instrument include what is being measured (concept and form), who is being assessed (target population), when the assessment is occurring (study design and frequency of assessment), and how it is being administered (mode) [7]. In practice, clinical trials that include PROs usually incorporate a combination of PRO measures most relevant to the study population and intervention and prioritize the selection of these instruments according to the resource constraints and staff and participant burden. In the clinical setting, PROs can be used to provide information about symptoms of disease to aid physicians in selecting therapies.

CLASSIFICATIONS OF PATIENT-REPORTED OUTCOMES

The term PRO is often used to refer to a number of different aspects of patient-based assessment. It is important to distinguish between the concept being measured, the instrument used to assess the concept, and the outcome as analyzed in a clinical trial or "endpoint" [2]. For example, when assessing urogenital pain in relation to sex, urogenital pain intensity is the concept, decrease in pain intensity is the outcome, and change over a certain time interval in pain intensity (as represented by a 10 cm visual analog scale) is the data point that is used in the statistical analysis.

As shown in Figure 12.1, outcomes that can be assessed directly from the patient frequently overlap. The most broad category is the health-related quality of life (HRQL), which, at a minimum, measures physical, psychological (including emotional and cognitive), and social functioning. Examples of urogynecologic-specific HRQL measures were provided earlier. Outcomes that frequently overlap with HRQL include the experience and frequency of symptoms (e.g., pain, urinary incontinence [UI]), the bother and discomfort associated with these symptoms, the impact of symptoms on activities of daily living (ADLs), the treatment satisfaction, and the cost considerations, such as work productivity, cost, and quality-adjusted life-years (QALYs). A brief description of each of these outcomes, with examples of instruments used in urogynecology, is provided in the following text.

While some outcomes are specific to a therapeutic area, other measures of physical and mental health and social functioning may be relevant across diseases. The National Institutes of Health Patient-Reported Outcomes Measurement Information System (PROMIS) is a cooperative group of research centers that conducts qualitative and quantitative research to create domain-specific measures of physical, mental, and social health for use across diseases [16]. Many of these conceptual frameworks and item banks have the potential to be useful in areas of urology and urogynecology. For example, qualitative research with women with UI suggests that while many of these existing PROMIS domains are relevant to UI patients, additional domains are needed to improve the comprehensiveness of these assessment frameworks [17].

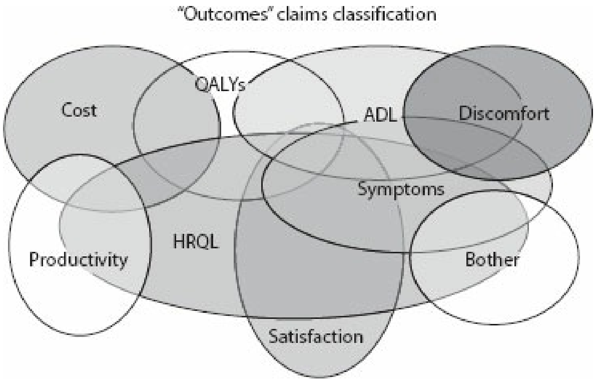

Figure 12.1 Patient-reported outcomes assessment areas. (From Burke L, Evidence Review Branch DDMAC, FDA, *DIA Workshop on Pharmacoeconomic and Quality of Life Labeling and Marketing Claims*, New Orleans, LA, October 3, 2000.)

Symptom Frequency and Bother

As stated previously, many symptoms in urogynecology are best understood based on direct report from the patient. For example, symptoms are defined by the International Continence Society as "the subjective indicator of a disease or change in condition as perceived by the patient, caregiver or partner and may lead him/her to seek help from health care professionals" [10]. Instruments designed to elicit patient-reported symptoms can assess a number of different dimensions, including presence/absence, frequency (e.g., how often patients experience a specific symptom; e.g., Pelvic Floor Distress Inventory [PFDI-20]) [18,19], and severity or bother (e.g., the symptom bother scale of the OAB-q [15] and the Urogenital Distress Inventory [20]).

Discomfort and Activity of Daily Living

Discomfort and/or pain are common outcome measures for many therapeutic areas. As such, measures of pain or discomfort are typically adapted from other generic measures (e.g., Brief Pain Inventory [21,22]) for specific urogynecology conditions. ADLs (e.g., the ability to dress and feed oneself) are infrequently assessed within urogynecology as such concepts, if pertinent, are incorporated into condition-specific HRQL measures.

Treatment Satisfaction

Patient satisfaction of treatment is the subjective, individual evaluation of treatment effectiveness and/or the service provided by the health-care system. At its most basic level, satisfaction is a comprehensive evaluation of several dimensions of health care based on patient expectations and provider and treatment performance. Measures of satisfaction can include evaluation of accessibility/convenience, availability of resources, continuity of care, efficacy, finances, humaneness, information gathering and giving processes, pleasantness of surroundings, and perceived quality/competence of health-care personnel [23]. As an outcome measure, patient satisfaction allows health-care providers to assess the appropriateness of treatment according to patient expectations. In chronic diseases, where patients must continually adhere to treatments, patient satisfaction may be the distinguishing outcome among treatments with comparable efficacy [24]. Two examples of patient satisfaction outcome measures that have been used in urogynecology are the Benefit, Satisfaction, and Willingness to Continue (BSW) measure [25] and the Overactive Bladder Satisfaction (OAB-S) measure [26,27]. The BSW is a single-item overall satisfaction measure, whereas the OAB-S is a multi-item, multidomain satisfaction measure. Another commonly used generic treatment satisfaction tool is the Treatment Satisfaction Questionnaire for Medication (TSQM) [28]. Generally, responsiveness cannot be assessed in this domain as there is no baseline assessment of patient satisfaction with treatment as no treatment has been given.

Productivity

The assessment of work productivity is particularly relevant for conditions that impact patients in their working years (<65). Currently, there are no condition-specific PROs for work productivity for urogynecological conditions; however, generic measures, such as the Work Productivity and Activity Impairment (WPAI) [29], are typically adapted to the specific patient population (e.g., the WPAI: irritable bowel syndrome) [30]. Productivity impact is an important construct to measure; however, there are many cultural and gender considerations in assessing this construct. Particularly notable is the complexity surrounding the assessment of productivity for those who work in the home but are not currently employed—a heterogeneous group predominantly composed of women and older people.

Cost and Economic Assessments

Cost and economic assessments are not necessarily PROs as many cost evaluations are conducted using currently existing economic data and claims databases. However, cost data are occasionally collected from patients to obtain cost information that is relevant to the patient (e.g., costs paid by the patient such as UI pads). The key to obtaining cost data from patients is to ensure that the questions asked are clear, easy to read, and understandable. Additionally, other relevant cost information must be collected as needed from other sources (e.g., claims databases) to fully evaluate economic impact.

Quality-Adjusted Life-Year

Increasingly, HRQL outcome measures are being used in the development of QALY measures. A QALY is a universal health outcome measure applicable to all individuals and all diseases, which combines gains or losses in both life quantity (mortality) and life quality (morbidity) and enables comparisons across diseases and programs. QALYs are widely used for cost–utility analysis [31]. In the past decades, economic evaluation has been increasingly important for the decision maker to decide which treatment or intervention is more cost-effective in order to allocate limited health-care resources soundly. The aim of economic evaluation is to compare interventions in terms of their costs and benefits, including their patient outcome impact. Health benefits can be quantified as QALYs, which has become a standard measure and is now recommended in most of health economics guidelines as the method of choice [32]. For example, algorithms have been derived to convert the OAB-q and KHQ to QALYs [33,34].

Conceptual Congruency

As described earlier, there are a variety of PRO instruments that differ in underlying construct measured. Thus, an essential component of selecting a PRO is to ensure consistency with the clinical purpose and objectives of the study. For example, if the goal is to assess treatment satisfaction, then a treatment satisfaction measure must be incorporated into the study design as a PRO. The matching of appropriate PRO selection with one's desired outcome is critical to success when assessing PROs.

PRO QUESTIONNAIRE DEVELOPMENT AND VALIDATION

To ensure that the results obtained with PROs are clinically useful, data must be gathered using valid and reliable instruments. The development of a PRO is a rigorous, scientific process designed to provide confidence that the PRO is measuring what it is intended to measure, that it does this reliably, and is appropriate for use in the patient or population group under investigation. The process begins by determining the intent and purpose of the PRO and culminates in studies that demonstrate the measure's validity, reliability, and responsiveness in the intended patient population. A task force for the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) has developed a description of recommended research practices to establish content validity of newly developed PROs [35,36]. The specific steps required for developing a PRO questionnaire based on these recommendations and guidelines issued from the FDA are outlined in Figure 12.2.

Determining Questionnaire Intent and Purpose

The first task in developing a PRO measure is to determine why a new outcome measure is needed. Given the current number of disease-specific questionnaires available in the field of incontinence and related pelvic disorders, a new PRO measure must fill a need that has not already been met by an existing instrument. Once the need for the measure is recognized, its purpose and clinical usefulness need to be considered in order to inform the validation design. For example, a symptom measure would be developed and validated differently from a treatment satisfaction measure because of the different concepts evaluated by these outcomes.

The development stage would focus on the outcome of interest (e.g., symptoms patients experience and the significance of each symptom, or what issues patients consider when determining how satisfied they are with the treatment), with the items derived directly from patient statements and relating to the outcome of interest.

Developing Items and Assessing Content Validity

Designing a clinically useful PRO measure involves more than just developing a series of questions. In addition to obtaining clinician input and reviewing the literature to better understand the disease, questionnaire items should be developed based on carefully planned qualitative research with patients [35–37]. Qualitative research is critical to documenting the content validity of an instrument. Content validity refers to the qualitative assessment of whether the questionnaire captures the range of the concept it is intended to measure among the patient population for which it is intended [38]. For example, does a measure of symptom severity capture all the symptoms that patients with a particular condition have, and if so, is the measure capturing the items in a manner meaningful to patients? To obtain content validity, patients (and clinical experts to some extent) review the measure and judge whether the questions are clear, unambiguous, and comprehensive [7].

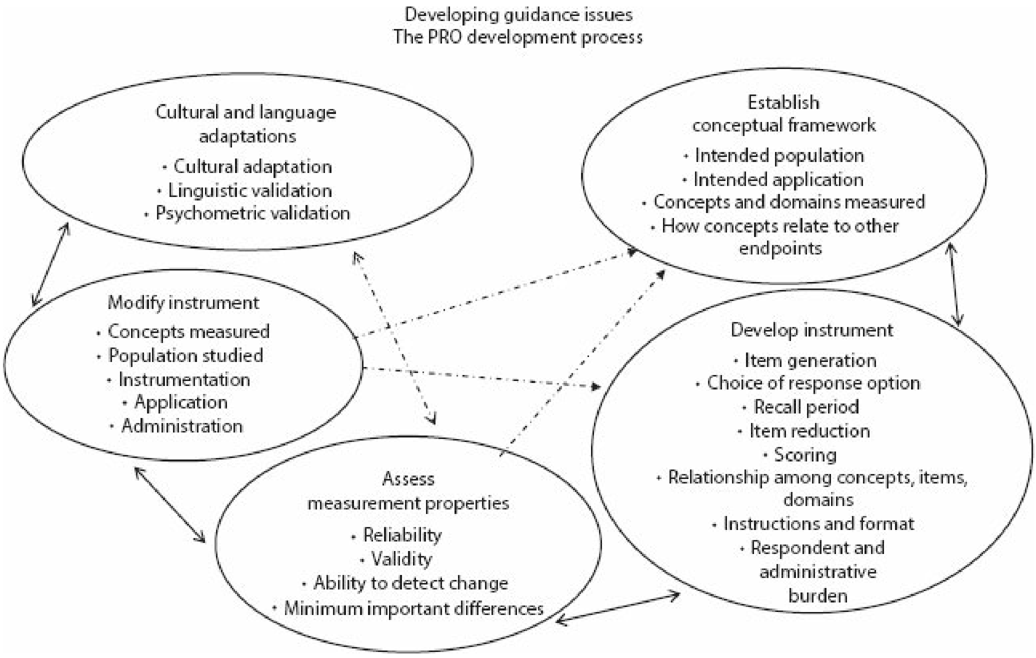
Developing guidance issues
The PRO development process
Cultural and language adaptations
• Cultural adaptation
• Linguistic validation
• Psychometric validation
Establish conceptual framework
• Intended population
• Intended application
• Concepts and domains measured
• How concepts relate to other endpoints
Modify instrument
• Concepts measured
• Population studied
• Instrumentation
• Application
• Administration
Develop instrument
• Item generation
• Choice of response option
• Recall period
• Item reduction
• Scoring
• Relationship among concepts, items, domains
• Instructions and format
• Respondent and administrative burden
Assess measurement properties
• Reliability
• Validity
• Ability to detect change
• Minimum important differences

Figure 12.2 The development of a patient-reported outcome is a multistep process. (From FDA, Guidance for industry: Patient-reported outcome measures: Use in medical product development to support labeling claims, FDA, Silver Spring, MD, 2006.)

Patrick et al. [35] have outlined five steps to elicit concepts for a new instrument: (1) determine the context of use, (2) develop the research protocol for qualitative concept elicitation and analysis, (3) conduct the concept elicitation interviews and focus groups, (4) analyze the qualitative data, and (5) document concept development and elicitation methodology results (Table 12.1).

Table 12.1 Example of Saturation Grid

Stress urinary incontinence symptoms	**Group 1**	**Group 2**	**Group 3**
Leak urine while coughing	×		×
Leak urine while laughing	×		
Leak urine when sneezing	×	×	×

Leak urine when lifting something	×	×

Notes: No new concept emerged after Group 2; conceptual saturation for this set of concepts is demonstrated; the highlights indicate that the new concept was spontaneously mentioned, rather than probed about.

Qualitative research methods typically involve focus groups, semi-structured one-on-one interviews, and cognitive interviews [1,37,39]. Focus groups, which typically involve six to ten people with a common attribute, such as a disease, can have advantages over individual interviews in that descriptions of the patient experience are enriched by participants' responses to the comments of others [7]. Conversely, personal or sensitive topics may be better suited for one-on-one interviews or gender-specific groups. Focus groups and one-to-one interviews should be conducted by moderators with experience in qualitative methods, following a semi-structured interview or discussion guide.

There are three types of focus groups and/or semi-structured interviews commonly used to inform PRO instrument selection or development: exploratory, developmental, and confirmatory [7]. *Exploratory* focus groups or semi-structured interviews are conducted before instrument selection or development to provide insight into the patient experience of a disease in order to better understand a PRO concept(s). Data collected at this stage can be used to determine the relevance of concepts to patients. Building on this, *developmental* focus groups are designed to explicitly capture patient descriptions of the proposed concept of measurement, including the themes, topics, and language that patients use in describing their experience. Careful consideration at this point should be given to the questionnaire intent and purpose [35]. For example, if a measure is intended to assess symptom bother, interview questions should be designed to elicit the words and phrases patients use to describe the impact of their condition. Rather than using clinical terminology that patients may not understand, the words used during the focus groups or interviews should be common to patients. Moderator prompting should be designed to elicit emergent information rather than leading participants to prespecified responses. Finally, evaluative or *confirmatory* focus groups or interviews can be conducted to provide documentation that an existing instrument is appropriate for a given purpose and patient population. Qualitative data obtained in confirmatory focus groups can be used to map content, words, phrases, and themes to items from existing and/or newly developed instruments.

Saturation is defined as the point at which no substantially new themes, descriptions of concepts, or terms are introduced as additional focus groups or interviews are conducted [40]. The exact number of focus groups or interviews needed to reach saturation is determined by the number of concepts elicited, the complexity of these concepts, and the attributes of the patient population (e.g., age, severity). Although larger sample sizes (i.e., additional focus groups/interviews) may provide additional confirmation of the findings, it is important to recognize that there is a point at which additional qualitative research fails to provide new information—this is the point of saturation [7]. Saturation of concepts can be documented through a saturation grid (see Table 12.1).

After questionnaire items have been generated, the newly drafted questionnaire should be reviewed by other patients and experts to ensure its *readability* and provide additional evidence of *content validity*. Cognitive interviews are one-on-one interviews designed to uncover problems in the social-cognitive processes involved in completing a questionnaire [41]. The ISPOR task force [36] has outlined five good practices related to the use of cognitive interviews: (1) develop items based on findings from concept elicitation, (2) design cognitive interview process for the planned context of use, (3) conduct cognitive interviews, (4) make decisions to revise the PRO instrument (includes assessment of saturation), and (5) document cognitive interview results for evaluation of content validity (includes development of complete item-tracking matrix) (Figure 12.1).

During cognitive interviews, patients are typically asked to review and respond to the questionnaire items and are then interviewed about what each item meant to them as they completed the questionnaire. The results are used to make modifications in the words or phrases in the items, response options, recall period, and instructions or format of the instrument in order to improve ease of administration and enhance the validity [7]. This process is also important when reviewing or adapting an existing measure to meet the needs of a new patient population. The adapted questionnaire must be validated on its own in the target population; the validity of the original questionnaire does not apply to an adapted measure. Saturation should be demonstrated in the cognitive interviewing process in a similar way to that used in the initial focus group or one-on-one interview process used to generate items. Also valuable for content validity review is a listing of all changes made to each item in the instrument development process, the rationale for decisions to drop or change items, and a record of items added or dropped [2]. The development of the final PRO can be illustrated in an item-tracking matrix, which includes the final item, final response scale, any preliminary domain assignment, description of intent of item, and patient quotes supporting item intent [36].

Determining the Mode of Administration of a Questionnaire

Once items have been generated, the mode of administration must be considered. Will the measure be completed by the patient (i.e., self-administered) or administered by an interviewer (i.e., interviewer administered)? How the questionnaire will be completed needs to be determined before the validation stage because the mode of administration can affect patient responses. For highly personal or intimate questions or questions regarding satisfaction, a self-administered questionnaire is recommended to avoid response bias. Questionnaires that are self-administered are preferable to interviewer-administered questionnaires because the data collection burden is reduced and patients are more likely to provide unbiased information on self-administered questionnaires. Importantly, if a questionnaire has been validated for a particular mode of administration, this does not make the questionnaire valid for all modes of administration. Each mode of administration should be validated separately. This applies to varying modes of self-administration such as going from pen and paper to electronic; the new mode of administration needs to be demonstrated as equivalent to the initial mode of administration.

PRO PSYCHOMETRIC PROPERTIES

All PRO measures must demonstrate *reliability*, *validity*, and *responsiveness*, which are described in detail in the following text. This can be accomplished in several ways:

1. Perform a stand-alone cross-sectional study to validate the questionnaire in the patient population for which it was designed.
2. Administer the untested questionnaire in a clinical trial and use the baseline data to perform psychometric validation (the end-of-study data can also be used to evaluate responsiveness).
3. Perform a stand-alone longitudinal study with an intervention to determine the instrument’s psychometric performance and responsiveness in a nonclinical trial setting.

The following psychometric properties must be tested for and demonstrated in a validated questionnaire:

Reliability refers to the ability of a measure to produce similar results when assessments are repeated (i.e., is the measure reproducible?) [42–44]. Reliability is critical to ensure that change detected by the measure is due to the treatment or intervention and not due to measurement error [43].

Test–retest reliability, or reproducibility, indicates how well the results can be reproduced with repeated testing. To assess test–retest reliability, the same patient completes the questionnaire more than once, at baseline and again after a period of time during which the impact of symptoms is unlikely to change (e.g., a few days or weeks) [43]. The Spearman’s correlation coefficient and intraclass correlation coefficient are used to demonstrate reproducibility. For group data, a Spearman’s correlation coefficient or an intraclass correlation coefficient of at least 0.70 demonstrate good test–retest reliability [43].

Internal consistency reliability is another measure of reliability that indicates how well individual items within the same domain (or subscale) correlate [42,45]. Cronbach’s alpha coefficient is used to assess internal consistency reliability, with higher alphas indicating greater correlation [46,47]. Typically, Cronbach’s alpha should be greater than 0.70 to indicate good internal consistency reliability [3,43].

Interrater reliability indicates how well scores correlate when a measure is administered by different interviewers or when multiple observers rate the same phenomenon [42]. Demonstration of interrater reliability is not necessary for self-administered questionnaires but is necessary for instruments based on observer ratings or using multiple interviewers. A correlation of 0.80 or higher between raters indicates good interrater reliability [48].

Validity refers to the ability of an instrument to measure what it was intended to measure [3,42,43]. A measure should be validated for each specific condition or outcome for which it will be used. For example, a measure designed to assess stress incontinence would not be valid for OAB unless it was specifically validated in patients with OAB symptoms.

Evidence of content validity, convergent validity, discriminant validity, and criterion validity typically are required to validate a questionnaire [42]. As described previously in relation to qualitative research, content validity is a qualitative assessment of whether the questionnaire captures the range of the concept it is intended to measure. Construct-related validity refers to evidence that an instrument behaves in a way that is consistent with the theoretical implications associated with the constructs being measured [3].

Convergent validity is demonstrated by the extent to which the measure correlates with other measures designed to assess similar constructs [49]. *Discriminant validity* refers to the degree to which the scale does not correlate with other measures designed to assess dissimilar constructs or is able to discriminate between constructs that should be related [49]. Stronger relationships should be seen with the most closely related constructs and weaker relationships seen with less-related constructs [43]. Another common method for examining construct-related validity is to evaluate whether a questionnaire can differentiate between known patient groups (e.g., those with mild, moderate, or severe disease) [3]; generally, measures that are highly discriminative are also highly responsive [50].

Criterion validity reflects the correlation between the new questionnaire and an accepted reference or gold standard [3,51]. One difficulty in establishing criterion validity is that a gold-standard measure might not be available [3]. When criterion validity can be established with an existing measure, the correlation should be 0.40–0.70; correlations approaching 1.0 indicate that the new questionnaire may be too similar to the gold-standard measure and therefore redundant [3].

Responsiveness indicates whether the measure can detect change in a patient’s condition [3,43]. An important aspect of responsiveness is determining not only whether the measure detects change but whether the change is meaningful to the patient. This can be done by determining the *minimal important difference* (MID) of the measure. The MID is the smallest change in a PRO questionnaire score that would be considered meaningful or important to a patient [52,53]. A treatment that is statistically significantly better than another may not necessarily have a meaningful difference to the patient; the MID indicates whether the treatment made such a difference from a patient perspective [52,53].

Unfortunately, there is no scientific test for MID as it is an iterative process that typically involves two methodologies: an anchor-based approach and a distribution-based approach [54,55]. With the anchor-based approach, the MID is determined by comparing the measure to other measures (or “anchors”) that have clinical relevance, such as a global measure of well-being or perception of treatment benefit [52]. With the distribution-based approach, the MID is determined by the statistical distributions of the data, using analyses such as effect size, one-half standard deviation, and standard error of measurement [54,55].

LINGUISTIC AND CULTURAL VALIDATION

Increasingly, PRO questionnaires are required to be used in a number of different populations and settings; however, questionnaires and their psychometric properties are not necessarily transferable [56,57]. A measure that is valid and reliable for a particular language and culture may not prove so when used in a different population. Linguistic and cultural adaptation of a questionnaire occur during the development phase before validation, or it can be done after the questionnaire is validated in the language in which it was initially developed, with the latter being the more common approach. Ensuring the linguistic and cultural validity of a questionnaire is especially important for measures used in multinational clinical trials.

The principal steps in adapting a measure for different languages and cultures are as follows:

1. Two forward translations of the original instrument into the new language
2. Quality-control procedures that may include a backward translation (translating the instrument back into the original language) [58]
3. Adjudication of all translated versions
4. Discussion by an expert panel to ensure clarity of the translated questionnaire
5. Testing the translated instrument in monolingual or bilingual patients to ensure that it measures the same concepts as the original instrument [45,56,58]

However, if a backward translation of the measure does not produce a semantically equivalent instrument, then the instrument may need to be developed in the target language, rather than just translated [58].

After cultural and linguistic validation, PROs should also be psychometrically validated within the target language. Thus, reliability, validity, and responsiveness need to be assessed with each language translation to confirm the same measurement properties are present in the translated language(s) to ensure psychometric equivalence. If psychometric equivalence is not present (e.g., not achieving similar or better results in new language translation), the cultural and linguistic translations need to be reevaluated and perhaps revisions made to the existing instrument or a new instrument may need to be developed.

Regulatory Oversight

As clinicians and scientists have begun to appreciate and accept PROs as appropriate outcome measures, regulatory authorities have issued guidance documents on current best practices in the development and implementation of PRO in clinical trial settings [1,59]. Both the FDA and the European Agency for the Evaluation of Medicinal Products (EMEA) have released documents acknowledging the importance of PROs in clinical trials and providing recommendations about their use [1,37]. For PROs to be acceptable outcome measures for regulatory authorities, documentation of measurement properties must be present as well as qualitative evidence of inclusion of the patient perspective and understanding of the PRO. Importantly, a cohesive conceptual framework that stipulates how the PRO is related to the specific intervention must also be developed and presented to the regulatory authorities. It is strongly suggested that regulatory authorities be contacted early in the process of selecting a PRO for clinical trials to ensure regulatory acceptance of the PRO measure.

Questionnaire Modification

Most PROs have been developed for use with members of the general population or urology/gynecology patients with the specific condition (e.g., incontinence, OAB, POP). However, specific patient groups may experience particular problems or have unique needs that need to be addressed within the PRO (for example, children, frail elderly, spinal cord injuries, or those who are severely disabled). As such, a new questionnaire or modifications to an existing questionnaire may be needed that would require additional investigation and to establish relevance and content validity among the specific patient group. This situation also occurs when using a PRO to assess an outcome within a new patient population for which the PRO was not developed. Coyne et al. [60] evaluated several sexual health outcome measures to establish content validity of the PROs among women with OAB [61]. Since none of the PRO had been developed among women with OAB, this qualitative step was essential to evaluate relevance of the sexual health measures among this patient group.

Importantly, any modifications of established questionnaires may result in changes (sometimes substantial) in the psychometric performance of the instrument. Consequently, all modified instruments should be qualitatively reviewed first by the target patient population to ensure patient understanding and relevance as well as be subjected to the same psychometric testing as that employed in developing a completely new instrument. Specifically, modified instruments should report information regarding the instrument’s content validity, construct validity, reliability, and test–retest reliability, at a minimum, and sensitivity to change, in intervention studies.

SELECTING PRO MEASURES FOR CLINICAL TRIALS AND CLINICAL PRACTICE

The previous sections have provided an overview of PRO measure development and validation. But how does a researcher choose which instruments are most appropriate for a particular research study and/or clinical assessment? As there are many available PROs, it is of utmost importance to select the PRO measure that is relevant and applicable to one’s desired outcome. The goal is to develop a conceptually adequate yet practical PRO battery given the study population, the specific intervention, and the study design. If an intervention is designed to reduce symptom bother, then a relevant PRO would be a symptom bother measure. Multiple PROs can be included in a research study; however, the designation of the PRO as a primary or secondary endpoint must be *a priori*. In addition, issues of staff and participant burden, time constraints, and resources should be considered in the selection of a PRO measure.

Study Design Considerations

There are several protocol concerns that must be taken into account when implementing PRO measures in research studies, including the length of the study, the frequency of contact with the study participants, the timing of clinical assessments, the complexity of the trial design, the number of participants enrolled, and the participant and staff burden. The goal of the PRO investigation is to “fit” the PRO measures to the protocol without compromising either the study objective or the design. For example, if the study design is complex with frequent participant contacts and multiple clinical measures, it may be necessary to keep the PRO measures at a minimum or to reduce the number of times the PRO is assessed (e.g., baseline and end of study rather than during all participant contacts) to minimize participant and staff burden. At the same time, however, PROs must be viewed as an important variable in the overall trial design and cannot be devalued in the data collection process. Consequently, PRO measures cannot be altered or reduced to accommodate study design as such alterations may yield potentially less reliable measures or may seriously diminish the integrity of the overall study design and yield useless information. The frequency with which PRO will need to be assessed in a research study will depend upon the nature of the condition or intervention being investigated and the expected effects (both positive and negative) of treatment. At a minimum, as with all measurements collected in a research study, a baseline and end of study assessment should be completed. In addition, other PRO assessments should be timed to match expected changes in functioning due to the intervention, the condition, or the disease itself.

It is critical to specify the key population demographics that could influence the choice of instruments, the relevant dimensions of PRO to be assessed, and the mode of administration. Thus, age, gender, educational level, the language(s) spoken, and cultural diversity should be carefully considered prior to selecting PRO measures. For example, a cohort of patients over the age of 70 may have more vision problems than the middle-aged persons, making self-administered questionnaires potentially difficult. Ethnically, diverse groups also require measures that have been validated across different cultures and/or languages.

CONCLUSION

PROs provide vital information regarding disease impact and treatment outcomes from the patient’s perspective that is critical for urogynecologists. The development of a PRO questionnaire is an iterative, time-consuming process that involves many steps. As such, developing a new questionnaire is not a task that should be undertaken lightly. Prior to questionnaire development, ensure that a need for a new questionnaire exists and that existing PRO measures do not meet current needs or cannot be modified to meet current needs. If a new scale needs to be developed, ensure that the guidelines proposed by the FDA and EMEA on developing PROs are followed and that the appropriate expertise in questionnaire development and psychometrics is available to your research team in order to guide the questionnaire development process.

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13

Patient-Reported Outcome Questionnaires to Assess Health-Related Quality of Life and Symptom Impact

Cornelius J. Kelleher, Ramandeep Basra, and Alexandra E. Ridout

Over the last decade, there has been tremendous growth in the number and breadth of patient-reported outcome (PRO) measures available for use in clinical practice and research, allowing assessment of a broad range of concepts. A PRO is “any report of the status of a patient’s health condition that comes directly from the patient, without interpretation of the patient’s response by a clinician or anyone else” [1].

It would be unusual for any clinical study of patients with lower urinary tract symptoms (LUTS) to not include at least one PRO questionnaire.

This chapter will cover three types of PRO, namely health-related quality of life (HRQL), symptom bother, and urgency specific measures. (Screener satisfaction and goal assessment tools are described in Chapter 14. PROs to evaluate bowel and sexual dysfunction are described in Chapters 15 and 16.) There is inevitable overlap between this chapter and that regarding the International Consultation on Incontinence (ICI) modular questionnaire in Chapter 17, however, where possible repetition has been avoided.

The *design, validation, and use* of PROs have been described in detail by Coyne and Sexton in Chapter 12 and therefore will not be repeated here.

All of the questionnaires included in this chapter are largely Grade A or B as outlined in the recently published Fifth International Consultation on Incontinence. Recently, the addition of a+ sign has been added to indicate when published content validity is available for an instrument. For the sake of clarity, the grading of questionnaires adopted from the ICI fifth consultation is outlined in the following texts. Where possible it is advisable to use questionnaires of the highest possible grade, providing they meet the requirements of the study or evaluation being undertaken.

- Questionnaires were “highly recommended” and given a *Grade A* if the ICI committee found “published data indicating that the questionnaire is valid, reliable, and responsive to change following standard psychometric testing.” Evidence must be published on all three aspects, and questionnaires must be relevant for use with persons with incontinence. *Grade A+ indicates there is additional evidence of published content validity*.
- Questionnaires were “recommended” and given a *Grade B* if the committee found “published data indicating that the questionnaire is valid and reliable following standard psychometric testing.” Evidence must be published on two of the three main aspects (usually validity and reliability). *Grade B+ indicates there is additional evidence of published content validity*.
- Questionnaires were considered to have “potential” and given *Grade C* if the committee found “published data (including abstracts) indicating that the questionnaire is valid or reliable or responsive to change following standard psychometric testing.” *Grade C+ indicates there is additional evidence of published content validity*.

As there are so many PROs, it is of utmost importance to select the measure that is relevant and applicable to one’s desired outcome. If an intervention is designed to reduce symptom bother, then a relevant PRO would be a symptom bother measure. Multiple PROs can be included in clinical practice or in a research study; however, the designation of the PRO as a primary, coprimary, secondary, tertiary, or exploratory endpoint must be noted. In addition, issues of staff and participant burden, time constraints, and resources should be considered in the selection of a PRO measure. Once it has been decided which outcomes are to be assessed, it is important to choose a questionnaire that has been scientifically developed and validated.

As a general rule, most studies will use a HRQL measure and additional symptom specific scales. Care must be exercised to avoid questionnaire overload, and only questionnaires that are deemed useful should be chosen.

But how does a researcher choose which instruments are most appropriate for a particular research study and/or clinical assessment? Clearly, there are many questionnaires to choose from, and determining the most fitting option requires some guidance. The goal of the PRO assessment is to “fit” the PRO measures to the protocol without compromising either the study objective or the design. Having well-developed research goals and questions regarding PROs will help to guide you in the selection of measures for a study. The aim is to develop a conceptually adequate, yet practical PRO battery given the study population and design and the specific intervention.

1. *Try to select a Grade A/Grade A+ questionnaire if available.*
2. *Understand the questionnaire content.*

   There is no replacement for reading and understanding the content of the questionnaire, the layout of the questionnaire, the scoring system, the presentation, and how the questionnaire is completed.
3. *What is the target population?*

   It is critical to specify key population demographics that could influence the choice of instruments, the relevant dimensions of the PRO to be assessed, and the mode of administration.

   What is the intended age range, and are the respondents men, women, or both? Are the target population patients with specific LUT problems or patients with mixed diagnoses?
4. *Where is the study to be carried out?*

   Is there a need for linguistically validated versions of the questionnaire, of particular importance for multinational studies, or inner city studies with mixed cultural populations?
5. *How often will the questionnaire be completed?*

   Is there any benefit in using a complex and longer questionnaire when a short-form (SF) questionnaire would offer adequate information? This is particularly important in busy clinical settings or when patients are expected to complete many other questionnaires at the same time.
6. *Has the questionnaire previously been used successfully?*

   If possible, use questionnaires that have a proven track record in the area that you intent to study. If many studies of stress incontinent (SI) patients or patients with overactive bladder (OAB) have utilized a questionnaire, did it respond as expected and was the choice of questionnaire good?
7. *Are there specific issues that you need to investigate?*

   If you need to investigate certain issues, make sure the questionnaire you choose has appropriate questions and covers the problem in sufficient depth. If, for example, a study of nocturia is performed, does the questionnaire suitably cover aspects of sleep deprivation, tiredness, work impact, etc.?
8. *Is the questionnaire recognized by the audience, governmental, or regulatory body that will review and credit the results?*

   This may seem obvious but is extremely important. Check before starting clinical trials and studies that the outcomes used will be accepted if necessary by the appropriate regulatory agencies. Stringent criteria for design and validation of questionnaires are usually required, and it is normally desirable that validation data are available in a country-specific fashion. Is the questionnaire recognized and widely used in the country where the study is to be conducted? Will the audience recognize and understand the questionnaire and results when you present your study?

HEALTH-RELATED QUALITY OF LIFE MEASURES

HRQL measures help to assess the impact of disease and treatment on those aspects of quality of life related to health. The term “quality of life” is linked to the WHO definition of health that refers to a state of physical, emotional, and social well-being and not just the absence of disease or infirmity [2].

HRQL PROs are multi-item questionnaires that usually collect information on various aspects or “domains” relating to a patient’s life. These domains may relate to sleep, energy, emotions, social life, work life, sexual problems, etc., but vary to some extent between the different questionnaires. The results are usually presented as impairment in individual domains (e.g., physical or emotional function) and for intervention studies improvement in the respective domains after treatment. It is possible for some of the questionnaires to provide a summary score "overall HRQL" but this means that the value of measuring the individual domains is lost in the overall presentation of results. Such questionnaires are useful in health economic studies where a summary score is desirable.

There are two major types of HRQL PRO: generic and condition specific. These are discussed by Coyne in Chapter 12.

Generic questionnaires are designed to assess all patients with all conditions and are also used as population survey tools. They allow comparison of different groups of patients and different illnesses. Generic measures are designed to assess outcomes in a broad range of populations (e.g., both health and ill individuals). These instruments are generally multidimensional and assess at least the physical, social, and emotional dimensions of life. They are often, however, insufficiently sensitive to measure clinically relevant change when applied to patients with lower urinary tract dysfunction. For the purpose of this chapter, only condition-specific HRQL questionnaires are discussed (i.e., in this context questionnaires designed for the assessment of HRQL among patients with LUTS).

The condition-specific measures can be similar to generic instruments in that they assess multiple outcome dimensions but are also designed to include items more specific to the particular condition or population being studied. Examples of condition-specific instruments in the study of lower urinary tract dysfunction include the Incontinence Impact Questionnaire (IIQ) [3], the King's Health Questionnaire (KHQ), [4] and the Overactive Bladder Questionnaire (OAB-q) [5].

In general, the growing trend has been to include condition-specific outcome measures in clinical trials due to their enhanced sensitivity to change and the need to minimize participant burden. Importantly, the type of instruments selected for inclusion in a research study will depend on the goals of the intervention and the specific research questions to be addressed.

As HRQL questionnaires cover many different domains, they tend to be longer and consequently require greater time for completion than single item or summary measures. When time constraints exist and/or questionnaires are to be completed on many different occasions, or multiple questionnaires are to be used, this may be an important consideration. Overall, the value of such questionnaires far outweighs these considerations. Some of the questionnaires do have a SF version, which allows them to overcome this potential problem. It is important to look at the SF version in detail to ensure that you are able to collect the information you require and do not sacrifice clarity for the sake of brevity.

Coyne and Sexton discuss the issue of questionnaire responsiveness in their chapter with reference to minimal important difference (MID). This refers to the smallest change in PRO score that would be deemed clinically meaningful to a patient. MID values have been calculated for both the KHQ and the OAB-q and are commonly used in data analysis and presentation of PRO results [6].

One drawback of multidomain questionnaires is their inability to probe with great detail into any specific problem. This issue is discussed by Domoney and Symonds in their chapter on sexual dysfunction. Greater detail requires a greater number of questions, which would make HRQL questionnaires excessively lengthy and cumbersome. It is for this reason that studies will often employ a HRQL questionnaire in addition to specific questionnaires to measure in greater depth problems such as sexual dysfunction, sleep disorder, and depression when these issues are selective important outcomes to measure.

Increasingly, HRQL outcomes measures are being used in the development of quality-adjusted life-year (QALY) measures. A QALY is a universal health outcome measure applicable to all individuals and all diseases, which combines gains or losses in both life quantity (mortality) and life quality (morbidity) and enables comparisons across diseases and programs (reference development of QALY from KHQ [7]). This topic is addressed in detail by Kate Moore in her chapter on health economics.

In Table 13.1, the major condition-specific HRQL questionnaires for the assessment of patients with lower urinary tract dysfunction are listed in alphabetical order. Their purpose, psychometric properties, translation availability, and recommended ICI grade are also listed. Some of the more commonly used Grade A questionnaires are listed later.

BFLUTS and BFLUTS-Short Form

The long form of the Bristol Female Lower Urinary Tract Symptoms (BFLUTS) [8,9] was developed for use with women, following the pattern established for the questionnaire developed for the international continence society benign prostatic hyperplasia (ICS-"BPH") study. The questionnaire covers the occurrence and bothersomeness of symptoms relating to incontinence and other LUTS. It has shown good levels of validity and reliability and has been increasingly used in epidemiological and outcome studies [10–13]. Validity, reliability, and responsiveness have been demonstrated, and a scored SF has been produced, which is now the recommended version [14,15].

Danish Prostatic Symptom Score

This questionnaire was designed in Denmark to measure the degree to which men are bothered by urinary symptoms [16,17]. A composite score is achieved by the multiplication of the "symptom" by the "bother" score, with a total range of 0–108. A computer version of this questionnaire has been validated and patients seemed to appreciate more of this new version than the paper version [18]. It is primarily a questionnaire for the assessment of the occurrence and bothersomeness of a wide range of LUTS in men including symptom assessment after stroke [19], in patients with Parkinson's disease [20], and in the assessment of sexual dysfunction associated with BPH [21]. There are 10 linguistic versions of the scale [22].

International Continence Society *Male* and ICS *Male* SF

The ICS *Male* questionnaire contains 22 questions on 20 urinary symptoms and, for most questions, the degree of problem that the symptom causes [9]. It has exhibited acceptable levels of validity, reliability, and sensitivity to change following a range of treatments including surgery, minimally invasive therapies, and drug treatments [9,23,24]. This long version has been largely replaced now by a scored SF—ICS *male* SF [25]. It is primarily a questionnaire for the assessment of the occurrence and bothersomeness of a wide range of LUTS in men.

IIQ and IIQ-7

This questionnaire was developed to assess the psychosocial impact of urinary incontinence in women and consists of 30 items (24 on the degree to which incontinence affects activities and six on the feelings engendered) [3,26,27]. Scores are obtained overall or for four subscales determined by factor and cluster analyses: physical activity, travel, social relationships, and emotional health. The IIQ has been found to have acceptable levels of reliability and validity across a range of studies [28,29] and has been recommended for use by the National Institute for Health and Care Excellence (NICE) [15]. The IIQ has also been produced in an SF comprising seven items, also with evidence of validity and reliability [30]. Responsiveness of the IIQ has been assessed in several intervention studies [31].

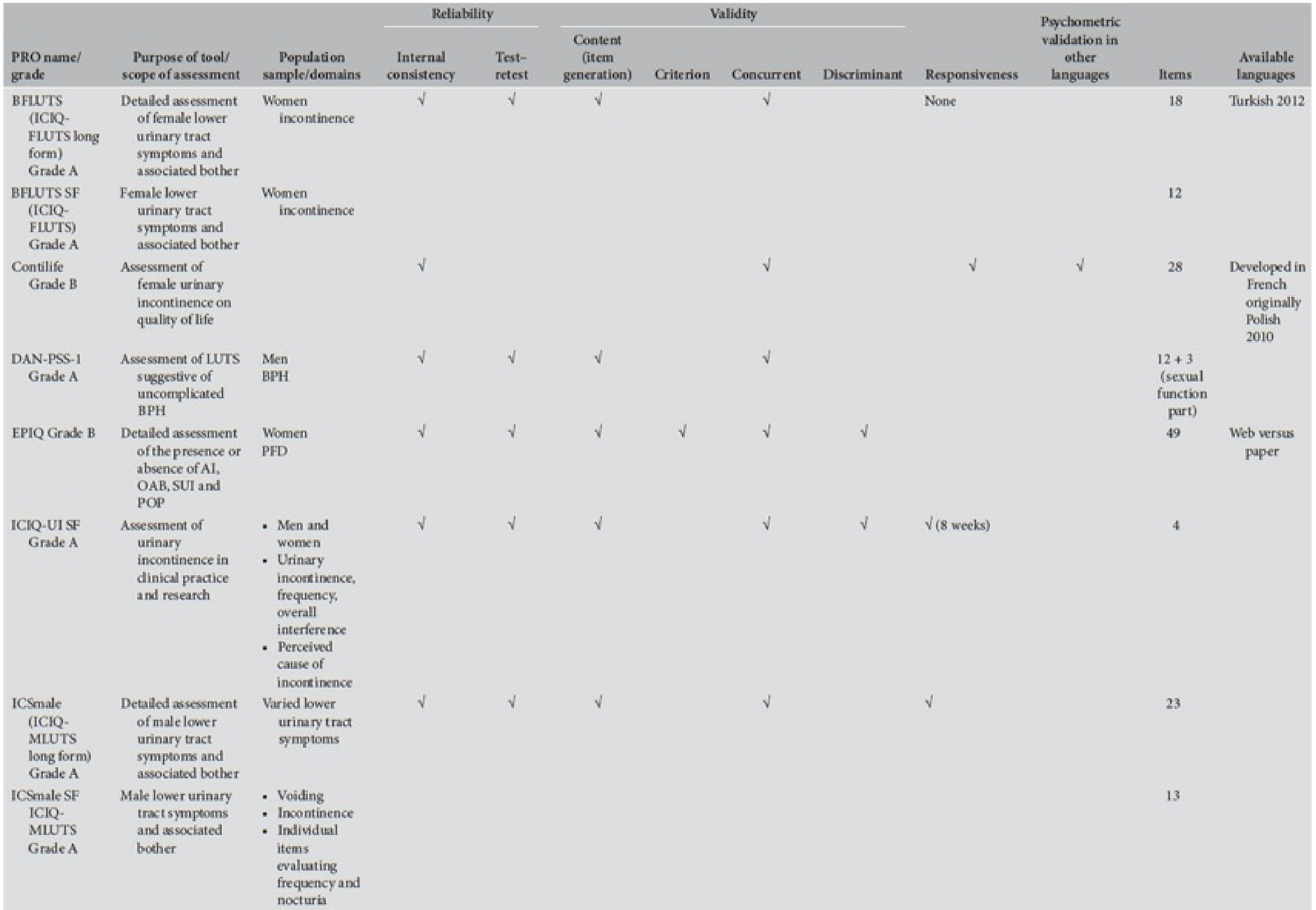
International Quality of Life

This questionnaire was designed to be used in clinical trials to measure the impact of incontinence on men and women [32]. Psychometric information on translated versions of the International Quality of Life (I-QOL) have been reported for French, Spanish, Swedish, German, Korean, and Thai language versions [33–35]. Other cultural and linguistic adaptations are available but have not been validated. In all countries, the use of three subscales, and an overall summary score was confirmed to be useful. The I-QOL has been recommended for use by NICE in the assessment of LUTS and quality of life impact [15].

KHQ

The KHQ consists of three parts [4]. The first section contains two questions measuring general health and overall health related to urinary symptoms. The second section includes 19 questions divided into seven domains of quality of life: incontinence impact, role limitations, physical limitations, social limitations, personal relationships, emotions, sleep and energy, severity coping measures, general health perception, and symptom severity. The third section of the questionnaire comprises 11 questions measuring the bother or impact of urinary symptoms. The KHQ has demonstrated reliability and validity in men and women and is available in 39 languages [36–39].

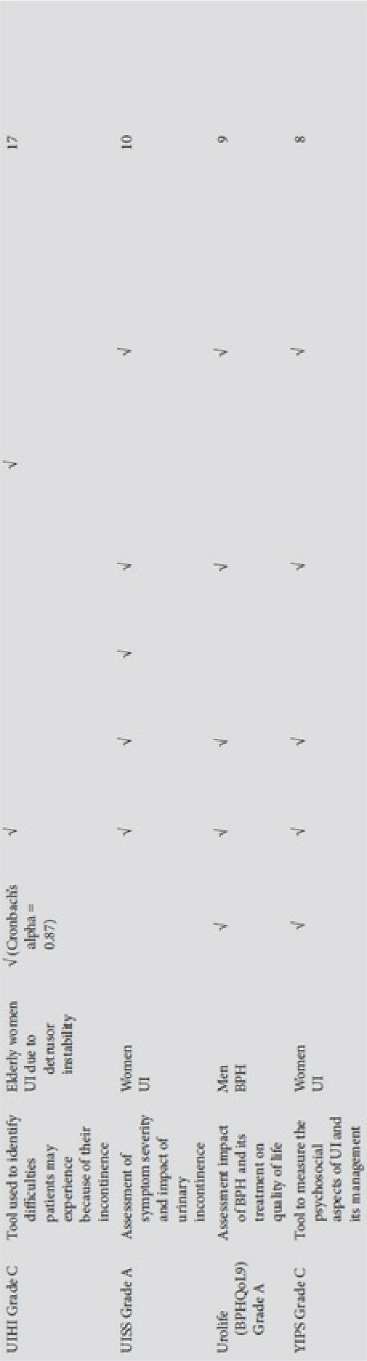
Table 13.1 Summary of Patient-Reported Outcome Measures in Patients with Urinary Incontinence, Overactive Bladder, and Lower Urinary Tract Symptoms: Health-Related Quality of Life



PRO name/ grade	Purpose of tool/ scope of assessment	Population sample/domains	Reliability		Validity				Responsiveness	Psychometric validation in other languages	Items	Available languages
			Internal consistency	Test-retest	Content (item generation)	Criterion	Concurrent	Discriminant				
BFLUTS (ICIQ-FLUTS long form) Grade A	Detailed assessment of female lower urinary tract symptoms and associated bother	Women incontinence	√	√	√		√		None		18	Turkish 2012
BFLUTS SF (ICIQ-FLUTS) Grade A	Female lower urinary tract symptoms and associated bother	Women incontinence									12	
Contilife Grade B	Assessment of female urinary incontinence on quality of life		√				√		√	√	28	Developed in French originally Polish 2010
DAN-PSS-1 Grade A	Assessment of LUTS suggestive of uncomplicated BPH	Men BPH	√	√	√		√				12 + 3 (sexual function part)	
EPIQ Grade B	Detailed assessment of the presence or absence of AI, OAB, SUI and POP	Women PFD	√	√	√	√	√	√			49	Web versus paper
ICIQ-UI SF Grade A	Assessment of urinary incontinence in clinical practice and research	• Men and women • Urinary incontinence, frequency, overall interference • Perceived cause of incontinence	√	√	√		√	√	√ (8 weeks)		4	
ICSmale (ICIQ-MLUTS long form) Grade A	Detailed assessment of male lower urinary tract symptoms and associated bother	Varied lower urinary tract symptoms	√	√	√		√		√		23	
ICSmale SF ICIQ-MLUTS Grade A	Male lower urinary tract symptoms and associated bother	• Voiding • Incontinence • Individual items evaluating frequency and nocturia									13	

ICSQoL Grade A	Assess impact of LUTS on patients' lives	Men LUTS Possible BPH	√	√	√		√			√	8	
IIQ Grade A	Assessment of severity of UI on HRQL	Women UI SUI		√	√		√		√ (12 weeks)	√	30	
IIQ-7 (SF) Grade A	Assess impact of UI on HRQL	Men after radical prostatectomy who had UI	√	√	√	√	√	√		√	7	
IOQ Grade B	Assessment of female quality of life after surgery for stress urinary incontinence	Women SUI	√		√	√			√	√	27	
I-QOL (ICIQ-Uiqol) Grade A			√	√	√			√	√		22	20
ISI Grade C	Recommended by the WHO for studying the epidemiology of incontinence and other LUTS	Women				√	√				2	
ISQ Grade C	Assessment of psychological stress associated with urinary incontinence	Women	√	√							40 (20 sf)	
ISS Grade A	Self-assessment of severity of female urinary storage and voiding symptoms	Women		√			√		√ (duration not specified)		8	
KHQ (ICIQ-LUTSqol) Grade A+	HRQL issues associated with urinary symptoms and related bother	• Life restrictions • Emotional aspects • Preventive measures	√ (except severity measure)		√	√	√	√	√ (12 weeks)		21	39

LIS Grade A	Assessment of quality of life for males and females with urinary store symptoms of urgency, frequency, nocturia, and incontinence		√	√	√		√		√	21	
N-QoL (ICIQ-Nqol) Grade A+	Detailed assessment of HRQL issues associated with nocturia	• Issues associated with sleep disturbance • Life restrictions • Preventative measures • Men and women	√	√	√		√	√	√	13	
OAB-q (ICIQ-OABqol) Grade A	Detailed assessment of HRQL issues associated with overactive bladder	• Coping • Concern/ worry • Sleep • Social interaction • Continence and incontinence OAB	√	√ (ICC = 0.93 for 4-week recall period)	√	√	√		√ (12 weeks)	25	
OAB-q SF Grade A	Shortened version of OAB-q used to evaluate both continent and incontinent symptoms of OAB and their impact on HRQL	• OAB • Men and women	√	√	√		√	√	√ (12 weeks)	19	14
PRAFAB Grade A	Assessment used widely in the Netherlands to evaluated treatment effects for UI in women	Women UI	√	√	√		√	√	√	5	



UIHI Grade C	Tool used to identify difficulties patients may experience because of their incontinence	Elderly women UI due to detrusor instability	√ (Cronbach's alpha = 0.87)	√				√		17
UISS Grade A	Assessment of symptom severity and impact of urinary incontinence	Women UI		√	√	√	√		√	10
Urolife (BPHQoL9) Grade A	Assessment impact of BPH and its treatment on quality of life	Men BPH	√	√	√		√		√	9
YIPS Grade C	Tool to measure the psychosocial aspects of UI and its management	Women UI	√	√	√		√		√	8

Sensitivity to change has been shown successfully in clinical trials where it has been used to assess the HRQL improvement following treatment for patients with OAB, urodynamic stress incontinence (USI), and mixed incontinence symptoms [40–43]. Its use in the assessment of LUTS and quality of life impact is recommended by NICE [15]. A minimally important difference has been derived to establish clinically meaningful interpretations of the KHQ scores, and a QALY measure has been derived from KHQ scoring [6,7].

Leicester Impact Scale

The Leicester Impact Scale (LIS) is a condition-specific HRQL measure for men and women assessing the symptoms of urgency, frequency, nocturia, and incontinence. It is an interviewer-administered tool, so it is not a true PRO as interviewer administration can introduce potential bias into the patient responses. The LIS has utility in the clinical and research settings [44].

Overactive Bladder Symptom and Health-Related Quality of Life (OAB-q) and OAB-q SF

The OAB-q is a 33-item questionnaire developed to assess the symptom bother (8 items) and HRQL impact of OAB (25 items and 4 domains: coping, concern/worry, sleep, and social interaction) [45]. It has demonstrated reliability, validity, and responsiveness in multiple clinical studies of men and women [46]. A minimally important difference has been derived [47] to establish clinically meaningful interpretations of the OAB-q scores, and a QALY measure has been derived from OAB-q scoring [48]. The 19-item SF (OAB-q SF) is a 6-item symptom bother scale and 13-item HRQL scale that is a single score, which has also demonstrated reliability, validity, and responsiveness to change [49]. The OAB-q was the basis for the OAB-V8 awareness tool to screen for symptoms of OAB [5] and has been used in a Parkinson's disease patient population [50].

UDI and UDI-6

This questionnaire was developed in the United States with women to assess the degree to which symptoms associated with incontinence are troubling [3]. It contains 19 LUTS and has been shown to have high levels of validity, reliability, and responsiveness in community-dwelling women with incontinence and women over 60 years of age [51]. Responsiveness to changes in clinical status as or a result of treatment has been reported in a number of areas: comparing abdominal and vaginal prolapse surgery [52] and the use of a simple urethral occlusive device [53]. A SF version of the Urogenital Distress Inventory (UDI-6 SF) has been shown to be valid and reliable in older adult males and females [54,55], with demonstrated responsiveness to reconstructive pelvic surgery, tension-free vaginal tape [56], and imipramine [57].

ASSESSING SYMPTOM BOTHER AND OVERALL BOTHER

Bother questionnaires assess the impact or bother of symptoms rather than their presence or absence. Although superficially simplistic patients make many valued judgments to score these questionnaires and to patients they are a hugely important assessment of condition severity. These measures, particularly the patient perception of bladder condition (PPBC), are frequently used in clinical studies and clinical trials. They are short and relatively easy to complete and usually appear to be clinically meaningful. Measures that can be used to assess how bothered patients are by urinary symptoms are included in Table 13.2. The PPBC [63] and the UDI are the only Grade A recommended instruments. There are several Grade B and C measures, which assess bother for incontinence and LUTS.

Patient Perception of Bladder Condition Questionnaire

The PPBC is a single-item questionnaire designed to rapidly assess patients' perception of their bladder condition [63]. The questionnaire asks patients to choose one of six statements that best describes their present bladder condition. The scale was validated during two large 12-week clinical studies evaluating the efficacy and tolerability of tolterodine in patients with OAB. Patients taking part in the studies completed the PPBC, OAB-q, KHQ, and bladder diaries. Baseline and week 12 data were used for statistical analysis. PPBC scores were well correlated with OAB-q questionnaire scores and bladder diary variables. Correlations of the KHQ and PPBC were significant for all KHQ domains with the exception of the general health perception domain. The scale was found to be responsive to change in OAB symptoms and to have discriminant validity as reflected in the OAB-q, KHQ score, and bladder diary changes. The PPBC has also shown to have good test–retest reliability [63]. This scale has been widely used in studies evaluating the use of drug therapy in patients with OAB [64–66].

UDI-6

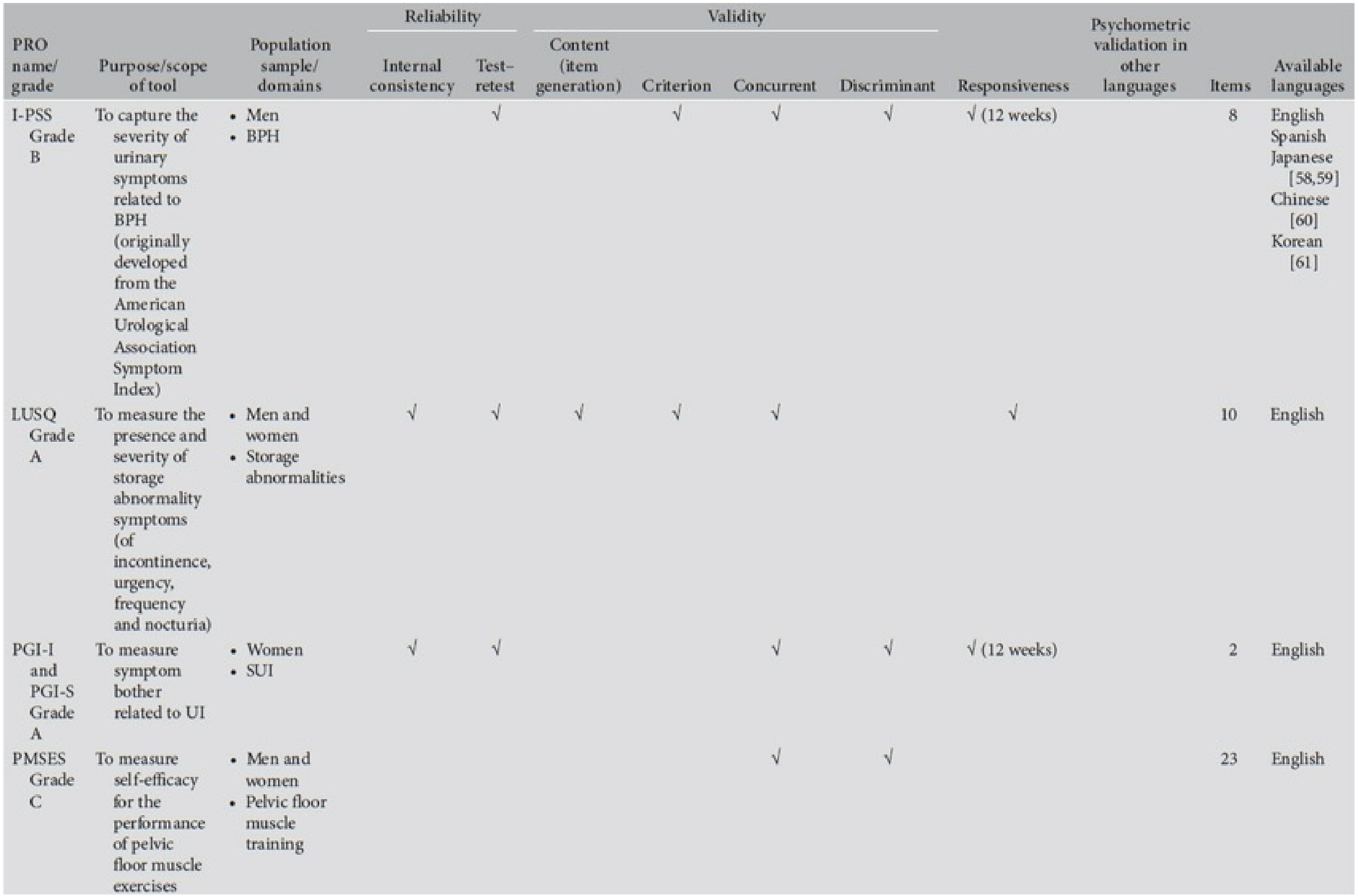
The UDI-6 is a six-item questionnaire that assesses the presence and bother of six LUTS [55]. The UDI-6 assesses the types of incontinence, frequency, difficulty emptying the bladder, and pain/discomfort in the lower abdomen/genitalia. The response options are zero to three. The instrument has demonstrated validity, reliability, and responsiveness [67].

Assessing the Impact of Urgency

Several instruments have been developed specifically to assess urinary urgency, which is defined by the

ICS as “the complaint of a sudden compelling desire to pass urine which is difficult to defer [68].” Urgency is the principal symptom of OAB, and, as such, assessing the effect of treatment on this symptom and its impact on HRQL is important. With any measure designed to evaluate urgency, patients must be able to distinguish between the normal desire to urinate (urge) and the difficulty to postpone the need to urinate (urgency) [69,70]. Wording thus becomes critical in the development of urgency assessment measures. Chapple and Wein [71] make a case for describing urgency as a “compelling desire to void in which patients fear leakage of urine” as a means of distinguishing this abnormal sensation from the normal need to void. However, some patients may have a sensation of urgency without fear of leakage, further complicating attempts to define urgency. Importantly, with some of these scales, patients have the option of indicating that they experienced urge urinary incontinence (UUI) (an event) rather than the strongest feeling of urgency (a sensation) itself. In such cases, patients who have severe urgency, but not UUI, do not have an option for endorsing the highest (worst) value because they are not incontinent. Urgency severity scales that include a UUI response option thus may be less useful than those that do not because such scales are trying to measure two things at once, both urgency and UUI.

Table 13.2 Summary of Patient-Reported Outcome Measures in Patients with Urinary Incontinence, Overactive Bladder, and Lower Urinary Tract Symptoms: Symptom Bother



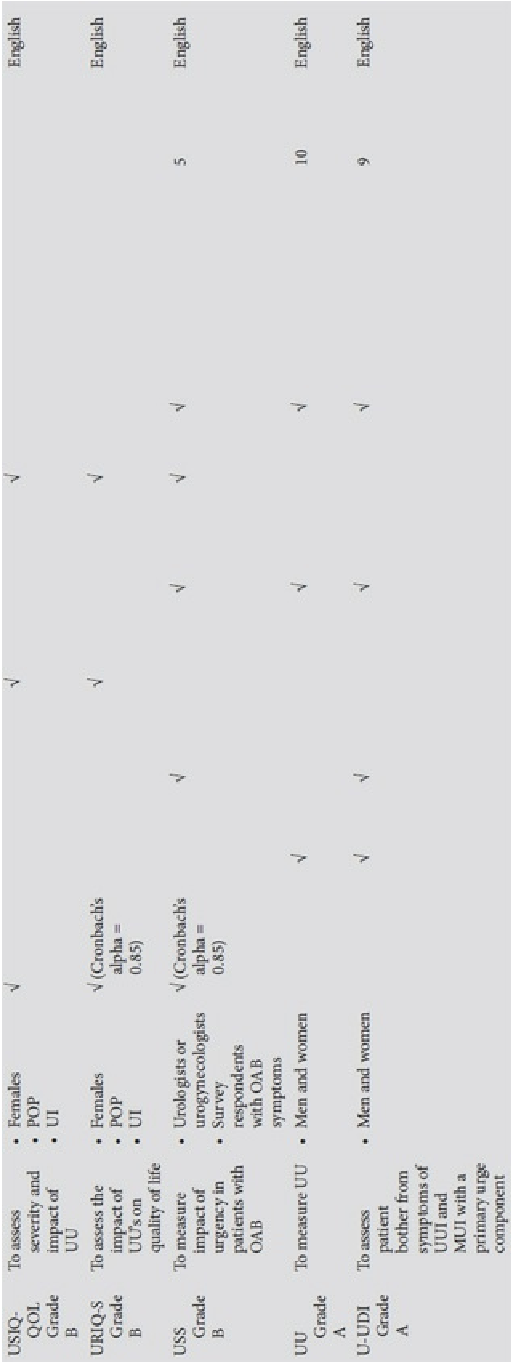
PRO name/ grade	Purpose/scope of tool	Population sample/ domains	Reliability		Validity					Psychometric validation in other languages	Items	Available languages
			Internal consistency	Test–retest	Content (item generation)	Criterion	Concurrent	Discriminant	Responsiveness			
I-PSS Grade B	To capture the severity of urinary symptoms related to BPH (originally developed from the American Urological Association Symptom Index)	• Men • BPH		√		√	√	√	√ (12 weeks)		8	English Spanish Japanese [58,59] Chinese [60] Korean [61]
LUSQ Grade A	To measure the presence and severity of storage abnormality symptoms (of incontinence, urgency, frequency and nocturia)	• Men and women • Storage abnormalities	√	√	√	√	√		√		10	English
PGI-I and PGI-S Grade A	To measure symptom bother related to UI	• Women • SUI	√	√			√	√	√ (12 weeks)		2	English
PMSES Grade C	To measure self-efficacy for the performance of pelvic floor muscle exercises	• Men and women • Pelvic floor muscle training					√	√			23	English

POSQ Grade C	To assess which symptom of OAB is the most bothersome to patients	• Men and women • OAB		√	√						5	English
PPBC Grade A	To assess patients' subjective impression of their current urinary problems (developed as a global assessment of bladder condition)	• Men and women		√			√		√	√	1	English
PFBQ Grade B	To assess symptoms of UI, UU and frequency, urge incontinence, FI, obstructed defecation, dyspareunia, and POP	• Women over the age of 18 • UI, UUI and SUI	√	√	√	√		√			9	English
SPI Grade B	To measure how troublesome patients find their urinary symptoms	• Men • BPH									7	English

SSI and SII Grade B	To measure SI severity/ impact or bothersome of symptoms	• Women undergoing SI surgery		√	√		√			√	3	English
UI-4 Grade C	To assess how bothered patients are by UI	• Women • UI					√				4	English
UDI Grade A	To assess symptom bother related to UI (complement to the IIQ)	• Women • UI and SUI	√	√	√		√	√		√	19	English Italian [62]
UDI-6 Grade A	To assess LUTS including incontinence	• Women	√	√	√	√	√	√	√	√	6	English Arabic

Table 13.3 Summary of Patient-Reported Outcome Measures in Patients with Urinary Incontinence, Overactive Bladder, and Lower Urinary Tract Symptoms: Urgency

PRO name / grade	Purpose/scope of tool	Population sample/domains	Reliability		Validity				Responsiveness (treatment duration)	Psychometric validation in other languages	Items	Available languages
			Internal consistency	Test-retest	Content (item generation)	Criterion	Concurrent	Discriminant				
IUSS Grade A	To quantify the level of urgency associated with void (as measured during standard voiding diaries)	Men and women • OAB with UI		√	(√)	√	√	√	√ (12 weeks)		1	English
PPIUS Grade B	To assess patient perception of urgency intensity	• Women • UUI		√					√		1	English
SUIQ Grade B	To differentiate between SUI and UUI	• Women • UI		√			√				2	English
U-IIQ Grade A	To assess the interference of urine leakage and bladder problems	• MUI • UUI • Developed for use in patients with all types of incontinence	√	√			√	√	√ (12 weeks)		32	English
UPS Grade B	To grade the urge to void and to assess the reason to void	• Men and women	√	√			√	√			5	English
UPS Grade B	To assess the severity of urgency	• Men and women • OAB			√		√	√	√		1	English
UQ Grade B	To assess severity and impact of urinary urgency symptoms on HRQL	• Women • OAB • Use of a VAS scale	√	√	√		√	√	√ (10 days)		15-Likert Scale Item and 4-VAS tool	English
URIS-24 Grade B	To assess UI in older persons	• Older persons • UI	√	√	√		√				24	English



USIQ-QOL Grade B	To assess severity and impact of UU	• Females • POP • UI	√			√		√			English
URIQ-S Grade B	To assess the impact of UU's on quality of life	• Females • POP • UI	√ (Cronbach's alpha = 0.85)			√		√			English
USS Grade B	To measure impact of urgency in patients with OAB	• Urologists or urogynecologists • Survey respondents with OAB symptoms	√ (Cronbach's alpha = 0.85)		√		√	√	√	5	English
UU Grade A	To measure UU	• Men and women		√			√		√	10	English
U-UDI Grade A	To assess patient bother from symptoms of UUI and MUI with a primary urge component	• Men and women		√	√		√		√	9	English

Several instruments have been developed to assess urinary urgency, and these are summarized in Table 13.3. A brief summary of each urgency measure is presented in the following texts.

The *urgency perception scale* was designed for use in clinical trials to evaluate patient-perceived urgency [72]. This instrument consists of a single question asking patients to describe their typical experience when they feel the need to urinate. The three possible responses are as follows: “I am usually not able to hold urine,” “I am usually able to hold urine until I reach the toilet if I go immediately,” and “I am usually able to finish what I am doing before going to the toilet” [72]. This scale was validated in a clinical trial evaluating the efficacy of tolterodine in treating OAB symptoms; however, its limited responsiveness may preclude its usefulness in clinical practice [73].

The *Indevus urgency severity scale* asks patients to rate their level of urgency on a four-point scale, from zero (no urgency) to four (extreme urgency discomfort that abruptly stops all activities/tasks) [74]. The scale has been validated in a clinical trial of trospium in patients with OAB [74], but Chapple et al. [73] question whether this scale actually measures urgency or just the normal urge to void.

The *urinary sensation scale* is a five-point scale ranging from one (no urgency; can continue activities until it is convenient to use the bathroom) to five (urge incontinence; extreme urgency discomfort, cannot hold urine, and have a wetting accident before arriving at the bathroom) [75]. The content validity of this scale was established through a physician survey and patient interviews [75].

The *urgency rating scale*, recommended by the European Medicines Evaluation Agency, consists of a five-point rating scale to be rated with every void, ranging from one (no urgency; I felt no need to empty my bladder but did so for other reasons) to five (urge incontinence; I leaked before arriving at the toilet). This scale was used in a tolterodine clinical trial, in which responses on this scale were used to calculate sum urgency, a measure that accounts for changes in both urgency and frequency [76,77].

CONCLUSION

A questionnaire design is a complex and lengthy process reinventing the wheel unnecessary for the vast majority of cases. A careful read of the chapter by Cotterill and Abrams will reveal that many of the questionnaires discussed in this and the chapter by Kopp have been adopted by the International Consultation as modules for the International Consultation on Incontinence Questionnaire.

There are clearly many different questionnaires and types of questionnaires from which to choose. Plan a study carefully with respect to what you expect to measure and which populations you intend to survey, and read the content of a questionnaire carefully. The value of spending time to make an informed and careful decision will, however, always be worth the effort.

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14

Patient-Reported Outcome Questionnaires to Screen and Measure Satisfaction, Expectations, and Goal Achievement

Zoe S. Kopp and Christopher J. Evans

This chapter reviews PRO questionnaires that assist urogynecologists in patient screening, setting realistic patient expectations that lead to goal achievement and assessing satisfaction. Symptom and condition screeners help identify health conditions to identify patients who may benefit from treatment. Patient expectation, goal assessment, and satisfaction questionnaires help clinicians understand the patients' point of view regarding their treatment goals and expectations so that the clinician can enhance the probability of a satisfactory outcome. Other chapters in this section focus on PROs that assess function and health-related quality of life, the development of PROs, and their effective implementation in clinical trials.

As with other PROs, the development of screeners, expectation, goal assessment, and satisfaction questionnaires must done scientifically, following recommended development guidelines, and have been psychometrically validated to ensure that results are accurate [1–3].

The development process steps from conceptual design through cognitive debriefings, psychometric, and linguistic validation are described in detail earlier in this section. Whether using a PRO in clinical practice or research, it is important to verify the validity of multiple aspects of the tool including the way in which it was developed, administration (paper or electronically), the population in which it is to be used (elderly, surgical, etc.), and the usage setting (clinical practice versus research). When using PROs in multilingual environments, the tool should be linguistically validated instead of merely translated. This chapter introduces you to some useful, validated questionnaires for female urological practice.

SCREENING TOOLS

Patient-completed screeners can facilitate appropriate diagnosis and treatment in urogynecological clinical practice. Most clinicians recognize that many patients find it difficult to articulate their health issues for a variety of reasons such as embarrassment about their problem or lack of medical knowledge or language. Providing questionnaires that screen for common urogynecological conditions to patients before their medical consultation can help focus the medical visit. In this section, validated screeners, their individual strengths and weaknesses, and how to obtain them are presented.

Compared to the other PROs, screeners have additional criteria they must satisfy in order to be considered sound measurement tools. When choosing and interpreting the results of screeners, the sensitivity and specificity of the measures should be considered. Sensitivity is the probability of a positive screener score in a patient with the condition. That is, how likely is someone with the condition to score positive? At the same time, the screener should have a high likelihood of correctly identifying individuals without the condition—specificity. Screeners alone are not diagnostic; clinicians should verify the indicated condition before determining treatment.

LOWER URINARY TRACT SYMPTOMS SCREENERS

To improve the detection of incontinence, overactive bladder (OAB), and other lower urinary tract symptoms (LUTS), several screening questionnaires have been developed (Table 14.1). These tools help patients self-describe symptoms and facilitate diagnosis of LUTS by the clinician. Only the Bladder Self-Assessment Questionnaire (B-SAQ) has been designed to screen for general LUTS rather than solely symptoms of one condition. The majority of patients with LUTS have mixed urinary symptoms, and therefore a questionnaire, which can detect more than one symptom complex, may be more functional as a screening tool in clinical practice than a highly specific questionnaire. There are several condition-specific screeners available, which assess common female urological problems such as OAB, stress urinary incontinence (SUI), and interstitial cystitis (IC). The OAB-V8/V3, Overactive

Bladder Symptom Score, and Questionnaire for Urinary Incontinence Diagnosis are all validated, short, simple to understand, complete, and easy to interpret, which screen for OAB. Importantly, with screeners, responsiveness is not assessed; however, the sensitivity and specificity of each tool is critical. The International Consultation on Incontinence has evaluated many LUTS questionnaires, and you can obtain information about their recommended questionnaires at www.iciq.net [4].

In this section, we describe some commonly used screeners and factors such as which populations the screener can be used in, its reliability and validity, its sensitivity and specificity, and its availability of valid linguistic translation. Details about these screeners and others are included in Table 14.1.

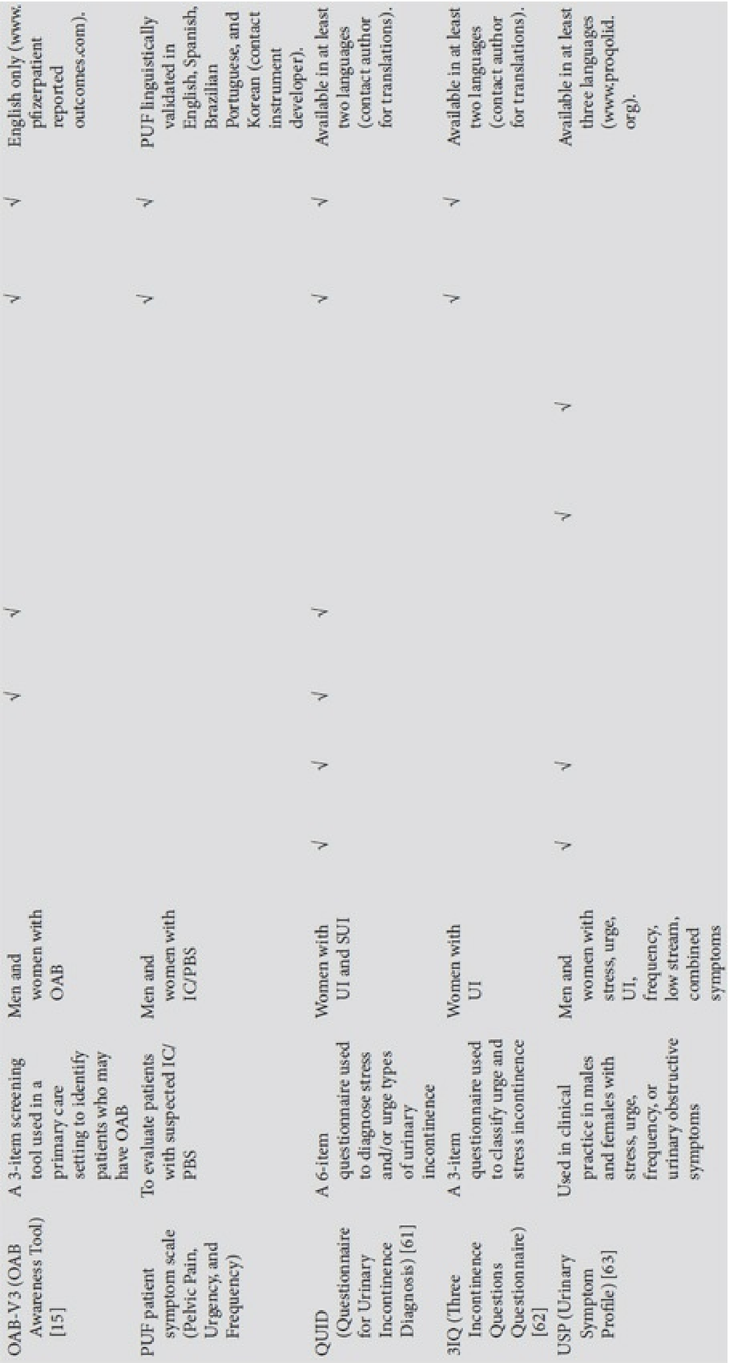
Lower Urinary Tract Symptoms

Bladder Self-Assessment Questionnaire or Bladder Control Self-Assessment Questionnaire

The B-SAQ instrument was developed by a European panel of experts in lower urinary tract dysfunction as a screening tool to evaluate the presence of bothersome LUTS in women [5]. The final instrument was validated and showed good reliability, validity, and sensitivity/specificity. The questionnaire has been translated and validated in at least 14 languages and is for both men and women.

Table 14.1 LUTS Screeners Overview

PRO name	Purpose of tool	Population sample	Reliability		Validity				Sensitivity/ specificity	Validation in other languages	Available languages
			Internal consistency	Test–retest	Content	Criterion	Concurrent	Discriminant			
B-SAQ (Bladder Self-Assessment Questionnaire) or Bladder Control Self-Assessment Questionnaire (BCSQ) [5]	A screening tool for the presence of bothersome lower urinary tract symptoms (LUTS) in women	Women	√	√		√	√	√	√	√	Available in at least 14 languages (contact author for translations).
ICSI (Interstitial Cystitis Symptom Index) [8]	A screening tool for interstitial cystitis (IC) and pelvic pain syndrome (PBS)	Women	√	√	√		√	√		√	Available in at least three languages (contact author for translations).
ISQ (Incontinence Screening Questionnaire) [58]	A 5-item questionnaire developed to screen for incontinence in women	Women with UI		√				√		√	None found
MESA (Medical, Epidemiological, and Social Aspects of Aging Questionnaire) [11]	A 15-item screening tool for UI in the female pelvic medicine and reconstructive surgery patients	Women with UI		√						√	Available in at least two languages (contact author for translations).
OAB-SS (Overactive Bladder Symptom Score) [59]	A 7-item questionnaire validated to measure overall symptom severity due to the four index symptoms of OAB	Men and women with LUTS, with or without OAB	√	√	√			√	√	√	Available in at least five languages (contact author for translations).
OAB-V8 (OAB Awareness Tool) [60]	An 8-item screening tool used in a primary care setting to identify patients who may have OAB	Men and women with OAB			√	√			√	√	OAB-V8 is linguistically validated into 29 languages (www.pfizerpatientreportedoutcomes.com).



OAB-V3 (OAB Awareness Tool) [15]	A 3-item screening tool used in a primary care setting to identify patients who may have OAB	Men and women with OAB			√	√			√	√	English only (www.pfizerpatientreportedoutcomes.com).
PUF patient symptom scale (Pelvic Pain, Urgency, and Frequency)	To evaluate patients with suspected IC/PBS	Men and women with IC/PBS							√	√	PUF linguistically validated in English, Spanish, Brazilian Portuguese, and Korean (contact instrument developer).
QUID (Questionnaire for Urinary Incontinence Diagnosis) [61]	A 6-item questionnaire used to diagnose stress and/or urge types of urinary incontinence	Women with UI and SUI	√	√	√	√			√	√	Available in at least two languages (contact author for translations).
3IQ (Three Incontinence Questions Questionnaire) [62]	A 3-item questionnaire used to classify urge and stress incontinence	Women with UI							√	√	Available in at least two languages (contact author for translations).
USP (Urinary Symptom Profile) [63]	Used in clinical practice in males and females with stress, urge, frequency, or urinary obstructive symptoms	Men and women with stress, urge, UI, frequency, low stream, combined symptoms	√	√			√	√			Available in at least three languages (www.proqolid.org).

Pelvic Pain Syndrome and Interstitial Cystitis

There are two commonly used screeners for pelvic pain syndrome (PBS) and IC, the Interstitial Cystitis Symptom Index (ICSI) and Pelvic Pain and Urgency/Frequency (PUF) questionnaire. Researchers evaluated the ability of the PUF along with the ICSI to screen for IC/PBS among patients attending a urology clinic prior to diagnosis [6]. They found that while both tools could adequately distinguish IC from other urinary tract pathologies and aid in the diagnosis of IC/PBS, neither demonstrated sufficient specificity to serve as a sole diagnostic indicator.

Pelvic Pain and Urgency/Frequency

The PUF questionnaire is an eight-question scale that measures both the severity of IC/PBS symptoms, including pelvic pain, urgency/frequency and dyspareunia, and the degree to which patients are bothered by them [7].

A score of 13 or greater was found to provide the best sensitivity/specificity ratio for the PUF.

Although the PUF was developed to be patient reported, its content was developed by clinicians without patient input. While the scale provides good coverage of the key symptoms of IC/PBS, it includes clinical language such as "urethra" and "perineum," which may not be well understood by patients. Additionally, the layout of the questions may be confusing to patients. Thus, the validity of the PUF as a patient-reported, symptom-based diagnostic tool remains in question.

Interstitial Cystitis Symptom Index

The O'Leary-Sant ICSI assesses global IC symptom severity, with scores ranging from 0 to 20. This is based on four questions that measure the severity of day- and nighttime urinary frequency, urgency, and bladder pain over the past month [8]. The content of the questionnaire was developed from literature review, patient focus groups, and input from clinicians with expertise in the diagnosis and treatment of IC. Internal consistency and test–retest reliability were found to be high for the scale. The ICSI has been further validated as an IC/PBS symptom measure in a randomized, double-blind clinical trial [9]. In addition to good test–retest reliability, internal consistency, and construct validity, the ICSI was found to be responsive to change. A score of 0–6 has been suggested as indicative of mild symptoms, 7–14 of moderate symptoms, and 15–20 of severe symptoms [10].

Urinary Incontinence

Medical, Epidemiological, and Social Aspects of Aging Questionnaire

The Medical, Epidemiological, and Social Aspects of Aging questionnaire is a 15-item tool developed to screen for urinary incontinence and other urinary symptoms in noninstitutionalized women [11]. Frequency of symptoms is measured on a 4-point scale from "never" to "often" with higher scores indicating more frequent symptoms. There are two subscales: six items that assess stress incontinence and nine items for urge incontinence and other urinary symptoms; each subscale was rescored to have a range from 0 to 100 [12].

Overactive Bladder

OAB Awareness Tool V8 and V3

The OAB-V8/OAB awareness tool has been adapted from the Overactive Bladder Questionnaire (OAB-q), which is a 33-item questionnaire, that assesses symptom bother and HRQL impact of OAB [13]. The OAB awareness tool V8 and V3 are an 8-item and a 3-item questionnaires, which evaluate the symptoms of OAB. Responses are graded on a 6-point Likert scale. Patients with an overall score of eight or more on the V8, or four or more on the V3, are directed to seek medical advice. These questionnaires have been validated for use by men and women [14,15].

Sexual Dysfunction (Refer Also to Chapter 64)

There are several screeners that can be used to detect sexual dysfunction. PRO questionnaires have been developed to detect hypoactive sexual desire disorder (HSDD), female sexual arousal disorder (FSAD), female orgasmic disorder (FOD), and satisfaction and pain on intercourse (dyspareunia). Table 14.2 provides an overview of sexual dysfunction questionnaires: their validity, reliability, and availability.

Hypoactive Sexual Desire Disorder Screener

The 4-item HSDD screener was developed to screen specifically for the presence or absence of HSDD in women 18 years and older [16]. Three of the items address desire and one item addresses level of distress. The HSDD screener was developed and validated on women with HSDD as confirmed by clinician diagnosis. The HSDD is self-administered in approximately 2 minutes and has a 5-point Likert scale and a 3-month recall period.

Female Sexual Function Index

The Female Sexual Function Index (FSFI) is a 19-item questionnaire. It has been developed as a brief self-report instrument for assessing sexual function in women [17].

It was developed on a female sample of normal controls and age-matched subjects and provides scores on six domains of sexual function (desire, arousal, lubrication, orgasm, satisfaction, and pain) as well as a total score. The FSFI has been validated on clinically diagnosed samples of women with

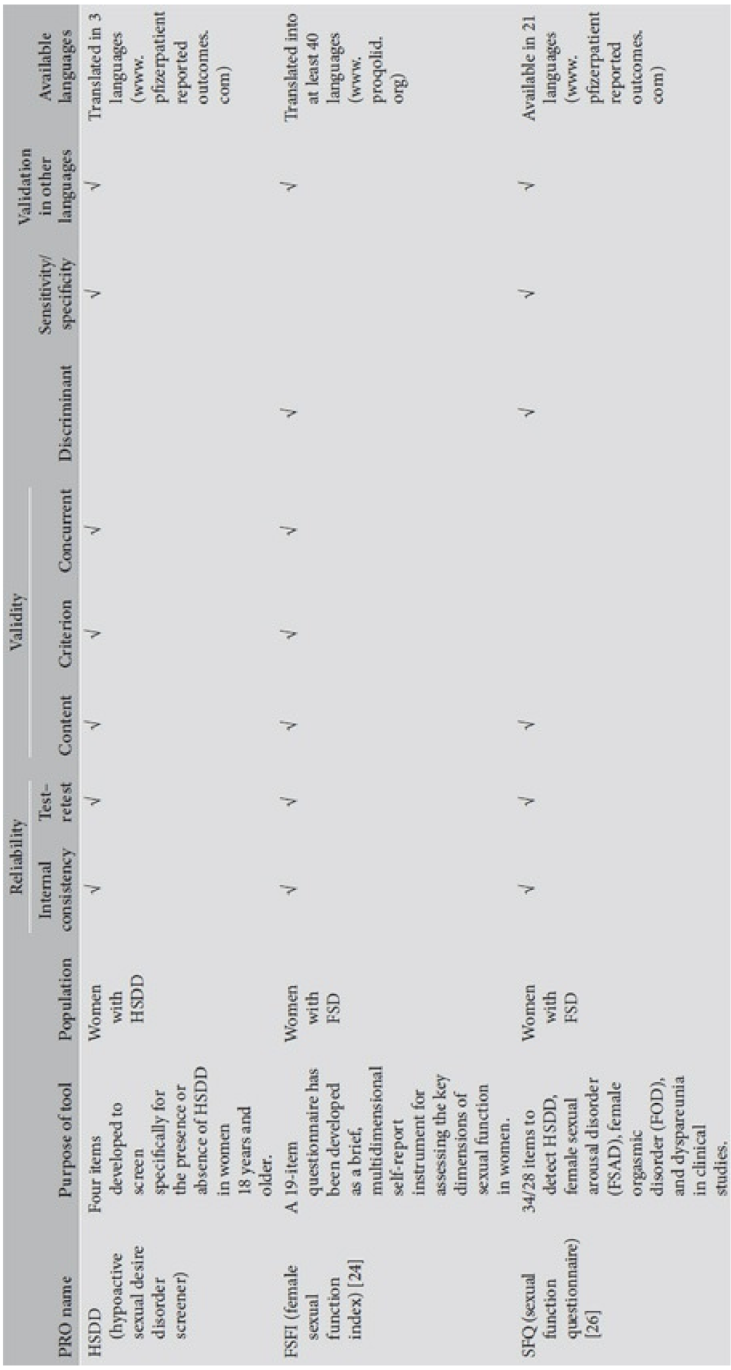
FSAD, FOD, and HSDD [18].

Sexual Function Questionnaire

The Sexual Function Questionnaire (SFQ) developed by Quirk et al. was designed to detect HSDD, FSAD, FOD, and dyspareunia in clinical studies [19]. Further validation of the SFQ was undertaken to determine its usefulness as a screener. The research has demonstrated that the SFQ can distinguish between the presence and absence of specific female sexual dysfunction (FSD) symptoms in a large sample of different clinical populations [20]. The original SFQ consisted of 34 questions in two scales, one on sexual activity and the other on sexual life with a 4-week recall period.

The original questionnaire was shortened to a 28-item SFQ28, which was developed as a screening tool for FSD and also as an efficacy measure in women 18 years and older [27]. The SFQ28 has 6 domains, four of which are specific to the four main types of FSD: FSAD, FOD, HSDD, and pain disorder. The other two domains address “enjoyment” and “partner” issues. The instrument was developed and validated in a broad spectrum of women with FSD. The SFQ is self-administered in approximately 10 minutes and has a 5-point Likert scale and a 4-week recall period.

Table 14.2 Sexual Dysfunction Screeners Overview



PRO name	Purpose of tool	Population	Reliability		Validity						
			Internal consistency	Test-retest	Content	Criterion	Concurrent	Discriminant	Sensitivity/ specificity	Validation in other languages	Available languages
HSDD (hypoactive sexual desire disorder screener)	Four items developed to screen specifically for the presence or absence of HSDD in women 18 years and older.	Women with HSDD	√	√	√	√	√		√	√	Translated in 3 languages (www.pfizerpatientreportedoutcomes.com)
FSFI (female sexual function index) [24]	A 19-item questionnaire has been developed as a brief, multidimensional self-report instrument for assessing the key dimensions of sexual function in women.	Women with FSD	√	√	√	√	√	√		√	Translated into at least 40 languages (www.proqolid.org)
SFQ (sexual function questionnaire) [26]	34/28 items to detect HSDD, female sexual arousal disorder (FSAD), female orgasmic disorder (FOD), and dyspareunia in clinical studies.	Women with FSD	√	√	√			√	√	√	Available in 21 languages (www.pfizerpatientreportedoutcomes.com)

MEASURING PATIENT SATISFACTION AND EXPECTATIONS

Background

Patient satisfaction is the subjective, personal evaluation of treatments, health service, and health-care providers. Although frequently reduced to a single, one-dimensional item in clinical practice “Are you satisfied with your treatment?” satisfaction with medical treatment represents a complicated construct, which includes efficacy, side effects, accessibility/convenience, availability of resources, continuity of care, cost, availability of information on the disease, information giving, and pleasantness of surroundings and quality/competence of health-care providers [21]. At its most basic level, satisfaction is a comprehensive evaluation of several dimensions of health care based on patient expectations and provider and treatment performance.

As an outcome measure, patient satisfaction allows health-care providers to assess the appropriateness of treatment according to patient expectations. Although the importance of patient satisfaction assessment is often ignored, it plays a key role in assessing outcomes. In chronic diseases, where patients must live with treatment, patient satisfaction may be the distinguishing outcome [22]. Evidence suggests that patient satisfaction may be more sensitive to change than the quality of life in clinical trials in chronic diseases [23].

Satisfaction with treatment provides information on treatment effectiveness [24] and is believed to affect clinical outcome [25]. It has been shown that high levels of patient satisfaction with medication correlates with treatment compliance, maintenance of a relationship with a specific provider, and disclosure of important medical information [26]. High levels of satisfaction have also been positively associated with good health status, fewer medical encounters, and shorter hospital stays [27]. In contrast, dissatisfaction with medication may impact a patient's likelihood to register formal complaints about services, engage in legal action against a clinic or provider, or provide unfavorable publicity about a clinic [28]. Preliminary work that suggest satisfaction with pain treatment can influence patient behavior, particularly regarding their intention to continue to take medications [29].

Satisfaction, if measured correctly, differs from other patient-reported, clinician-reported, and objective outcome measures, in that it addresses the influence that expectations can have on satisfaction. For instance, health status instruments measure the outcomes of treatment (whether they be physiological, symptoms, or impact); satisfaction assessments measure the level of satisfaction with these outcomes, given a level of expectations about treatment outcome. The role that expectations play in satisfaction assessments cannot be minimized: a patient with high expectations for treatment outcome may remain dissatisfied even after "successful" treatment because the patient's expectations for treatment benefit were not in alignment with what could be reasonably expected in terms of efficacy. Similarly, a patient with low expectations for treatment benefit can end up extremely satisfied with the treatment regardless of whether or not it worked simply because any treatment benefit, even small, is seen as meeting low expectations. Although the role of expectations in satisfaction assessments cannot be ignored, they can be accounted or controlled for by ensuring that patient expectations are measured at the time a patient initiates treatment.

As in other areas, the use of satisfaction assessments in clinical practice can provide complementary information to other PRO measures and provide information that may be useful in understanding why a patient may or may not remain adherent to treatment.

There are both generic- and condition-specific questionnaires to assess patient satisfaction with urogynecological treatment. There are three generic questionnaires (the Treatment Satisfaction Questionnaire for Medication [TSQM], Benefit, Satisfaction, and Willingness [BSW], and Satisfaction with Medication Questionnaire [SATMED-Q]) and three condition-specific measures (the Global Ratings of Patient Satisfaction and Perceptions of Improvement, the Overactive Bladder Satisfaction with Treatment Questionnaire [OAB-SAT-Q], and the Overactive Bladder Treatment Satisfaction Questionnaire [OAB-S]) that are measures for OAB. Of the three measures, only the OAB-S adequately addresses the role of expectations in satisfaction assessments. Further, the OAB-S examines the tolerability of medications (focused on antimuscarinic treatments) in a more comprehensive manner than the OAB-SAT-Q. Generally, responsiveness cannot be assessed as there is no baseline assessment of patient satisfaction with treatment as no treatment has been given. Here, Table 14.3 presents a summary of generic and disease-specific satisfaction instruments identified in urogynecology and their reliability, validity, and availability.

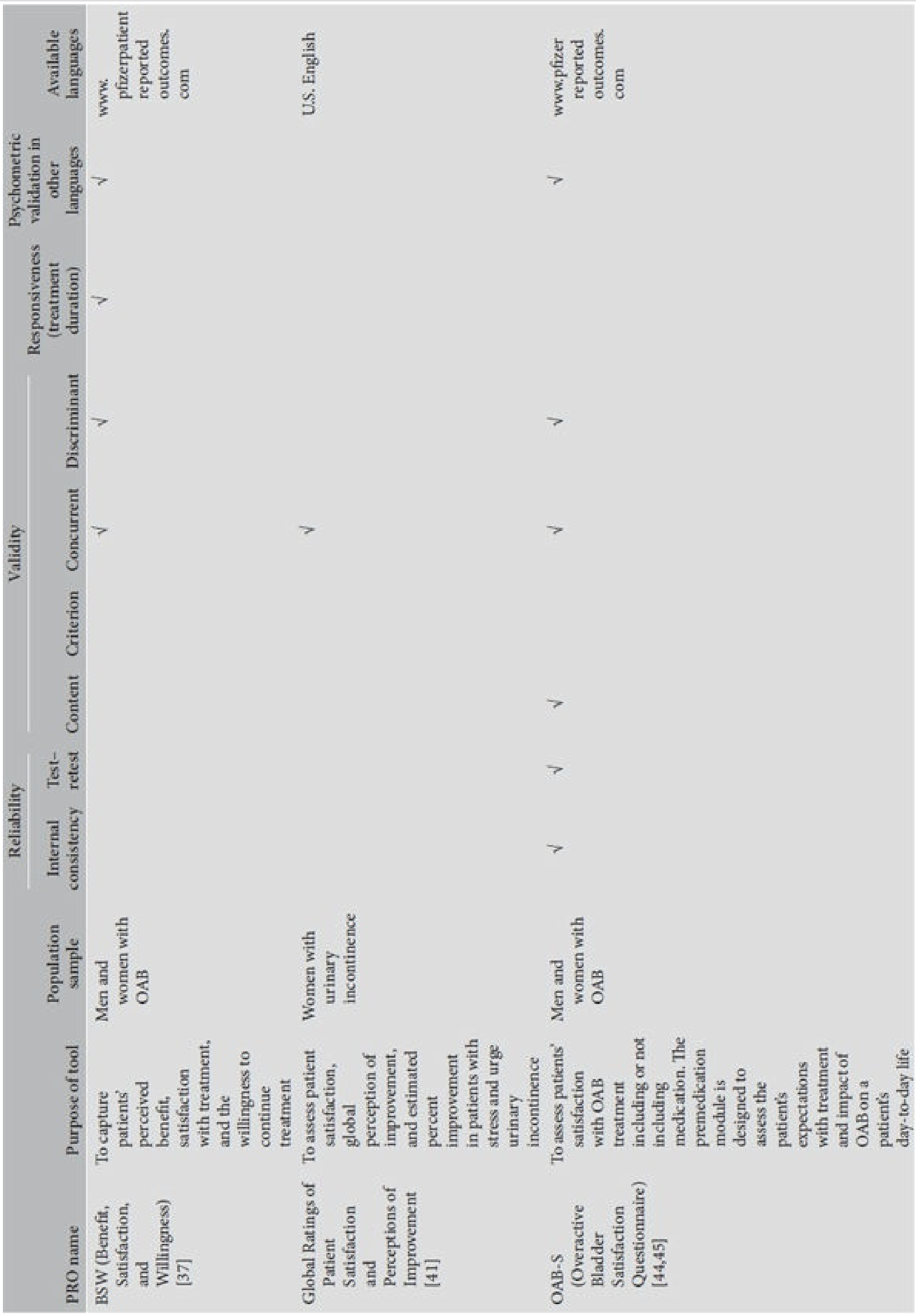
Benefit, Satisfaction, and Willingness Questionnaire

This three-item questionnaire is designed to assess treatment benefit, patient satisfaction with treatment, and patient willingness to continue treatment. The BSW questionnaire was validated using data from three 12-week placebo-controlled trials of tolterodine in patients with OAB [30]. In this validation, study correlations were seen between patient-reported treatment satisfaction and improvements in the OAB-q, KHQ, and micturition variables.

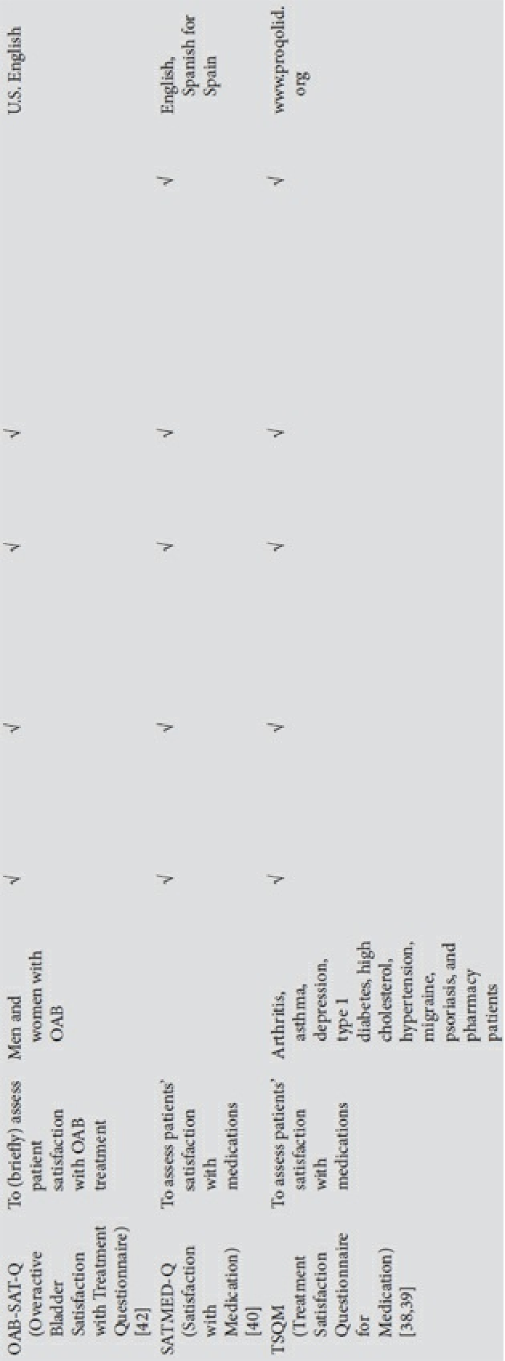
Treatment Satisfaction Questionnaire for Medication

The TSQM is a general measure of treatment satisfaction with medication suitable for use in a wide variety of medication types and illness conditions. Version 1 of the questionnaire contains four scales: side effects (three items), effectiveness (three items), convenience (three items), and global satisfaction (three items). It has been demonstrated to be a psychometrically sound and valid measure of patients' satisfaction with medication [31]. Version 2 of the questionnaire is slightly shorter [32]. Psychometric tests of the two measures have shown that they perform equivalently when predicting measures of concurrent validity.

Table 14.3 Summary of Urogynecological PRO Measures of Patient Satisfaction



PRO name	Purpose of tool	Population sample	Reliability		Validity				Responsiveness (treatment duration)	Psychometric validation in other languages	Available languages
			Internal consistency	Test-retest	Content	Criterion	Concurrent	Discriminant			
BSW (Benefit, Satisfaction, and Willingness) [37]	To capture patients' perceived benefit, satisfaction with treatment, and the willingness to continue treatment	Men and women with OAB					√	√	√	√	www.pfizerpatientreportedoutcomes.com
Global Ratings of Patient Satisfaction and Perceptions of Improvement [41]	To assess patient satisfaction, global perception of improvement, and estimated percent improvement in patients with stress and urge urinary incontinence	Women with urinary incontinence					√				U.S. English
OAB-S (Overactive Bladder Satisfaction Questionnaire) [44,45]	To assess patients' satisfaction with OAB treatment including or not including medication. The premedication module is designed to assess the patient's expectations with treatment and impact of OAB on a patient's day-to-day life	Men and women with OAB	√	√	√		√	√		√	www.pfizerreportedoutcomes.com



OAB-SAT-Q (Overactive Bladder Satisfaction with Treatment Questionnaire) [42]	To (briefly) assess patient satisfaction with OAB treatment	Men and women with OAB	✓	✓	✓	✓		U.S. English
SATMED-Q (Satisfaction with Medication) [40]	To assess patients' satisfaction with medications		✓	✓	✓	✓	✓	English, Spanish for Spain
TSQM (Treatment Satisfaction Questionnaire for Medication) [38,39]	To assess patients' satisfaction with medications	Arthritis, asthma, depression, type 1 diabetes, high cholesterol, hypertension, migraine, psoriasis, and pharmacy patients	✓	✓	✓	✓	✓	www.proqolid.org

Satisfaction with Medication Questionnaire

The SATMED-Q is a 17-item questionnaire with six dimensions: treatment effectiveness, convenience of use, impact on daily activities, medical care, global satisfaction, and undesirable side effects. The SATMED-Q has been demonstrated to be a reliable and valid measure of treatment satisfaction; however, the sensitivity to change has yet to be established [33].

Global Ratings of Patient Satisfaction and Perceptions of Improvement

The Global Ratings of Patient Satisfaction and Perceptions of Improvement questionnaire is a three-item questionnaire that assesses patient satisfaction with treatment, the patient's perception of change, and the patient's estimated percent improvement following an intervention [34]. All questions are global in nature and do not examine particular aspects of changes in health outcomes. The measure has undergone limited psychometric testing and only the concurrent validity of each item compared to the other items has been conducted.

Overactive Bladder Satisfaction with Treatment Questionnaire

The OAB-SAT-Q is a brief 11-item questionnaire, which measures satisfaction, side effects, endorsement (e.g., willingness to use the same treatment), convenience, and preference. Internal consistency reliability were good (Cronbach's alpha 0.84–0.95), Subscale correlations were good and the measure has demonstrated good discriminant validity [35]. The measure has been shown to be responsive and sensitive to treatment differences and changes [36].

Overactive Bladder Treatment Satisfaction Questionnaire

The OAB-S is a five-domain questionnaire, which evaluates control expectations, impact on daily living with OAB, OAB control, fulfillment of OAB medication tolerability, and satisfaction with control. Internal reliability coefficients were good (Cronbach's alpha 0.76–0.96), test–retest reliability has been established (reliability coefficients 0.72–0.87) [37,38], and known groups have been validated. Cultural and linguistic differences were considered early in the development process, and the OAB-S is available in over sixteen languages [39].

GOAL ATTAINMENT SCALING

Background

Goal attainment scaling (GAS) was first introduced in the 1960s by Kiresuk and Sherman [40]. It was created to assess health outcomes in mental health settings, but has in recent years been expanded to other therapeutic areas. This technique is used to measure clinically important change in numerous settings, especially those that require an individualized and multidimensional approach to treatment planning and outcome. Most notably, GAS has been used to assess drug trials for the treatment of Alzheimer's disease [41,42] and has been recently expanded to include evaluations in urogynecology [43,44]. The advantage that GAS offers is that it may be more responsive to change in some instance: GAS has been found to be more responsive to change than the measures commonly used in evaluating effectiveness of specialized intervention [45], but it requires additional investigation in the area of OAB [46]. The validity and reliability of GAS has been demonstrated in the areas of OAB [47], elderly care [48], chronic pain [49], and cognitive rehabilitation [50].

GAS differs from traditional quality of life measures and satisfaction assessments in several ways. First, it represents an individualized approach to measurement that augments information gained from standardized outcome measures. The chief weakness to standardized PRO measures is that it requires that patients answer a fixed set of questions—essentially a "one-size-fits-all" approach to assess quality of life. If the measure is well developed and validated (such as the OAB-q and the OAB-S), it can be assumed that the content is generally relevant to patients; however, even with these measures, there is no adjustment for the individual or a particular situation. Under GAS, the outcome scales are tailored specifically to the individual. Individuals select their own goals for treatment and only rate the symptoms or impacts that they experience: there is no need to rate symptoms or impacts that patients do not care about or never experience. In this sense, GAS represents a patient-centered approach to outcome measurement: only those areas each patient finds important are measured and evaluated.

Second, the role of patient expectations is central to GAS. Under traditional quality of life evaluations, expectations for treatment outcomes are largely ignored. Under satisfaction assessments, the role is made more explicit; however, expectation data in satisfaction assessments are usually only analyzed to determine how much of the change in satisfaction was due to pretreatment expectations vis-à-vis actual treatment efficacy. Under the GAS methodology, the goals or the expectations patients have about treatment benefit are something that is seen to be actively managed. If patients set unrealistic treatment goals and their expectations for treatment benefit can never be achieved, it is up to the health-care provider to separate unrealistic goals from realistic goals and explain to patients what their treatment can actually achieve [51]. In this way, patients are expected to remain adherent to treatment because they understand that some of their goals will never be achieved, while others may be obtained with treatment. For instance, if a patient understands from the outset that their goal of cure is unrealistic, then they may remain happy with a treatment that only alleviates symptoms with few side effects.

The third advantage of GAS is that although it is a very individualized approach to measuring patient-reported outcomes, it may still be employed in clinical trial settings. Although this appears counterintuitive because one patient's goals may differ from another patient's goals both in terms of number of goals and the types of goals, GAS scores may be combined by treatment group into a summary score utilizing standardized z-based scoring. Although GAS should not be used to derive an absolute level of an outcome (a health status score), it can be used to track achievement: at either an individual level or a group level.

GAS involves a multistep approach, which begins with the identification of goals by the patients. Patients are involved in the goal setting and weighting of the importance of goals and communicating the goals to their health-care provider [52]. At the initial assessment, patients list their goals and the importance of each goal to them (for example, 1, fairly important; 2, very important; and 3, extremely important; the score of 0 is not allowed because that would mean that the goal was not important to the patient and therefore not necessary to be included in the list of goal). For the next step, anticipated or expected outcome levels are discussed by patients with their health-care provider: goals that are unrealistic may be eliminated and the health-care provider resets patient expectations for treatment benefit. Finally, a time for the assessment of treatment goal attainment is determined. During this assessment period, goal attainment is rated according to the following: if the goal was achieved as predicted, this is scored 0, achievement above the level predicted is scored at +1 (“somewhat better than expected or predicted”) or +2 (“much better than expected or predicted”), no change or achievement below the expected level is scored as −1, and a worsening of the target function is scored as a −2.

Goal achievement has been used in several studies in the area of urogynecological conditions. The studies are best described as preliminary investigations into how goal setting and attainment play a role in this area. The use of GAS in urogynecological conditions is developing rapidly, and the usefulness, validity, and reliability in these conditions are still being evaluated.

The earliest investigation was by Hullfish et al. [53] In this study, patients were asked to describe 5 personal goals for pelvic floor surgery, which were rated on a 5-point scale. After surgery (3 months, 1 and 3 years), patients assessed their goals and either agreed or disagreed that the goals were met. Agreement was rated as +1 and strong agreement was rated as +2, disagreement was rated as −1, and strong disagreement was rated as −2. The validity of the assessment in pelvic floor surgery was partially established by relating Incontinent Impact Questionnaire and the Urogenital Distress Inventory scores to goal achievement.

Elkadry and others [54] found that women’s goals for reconstructive pelvic surgery are personal and highly subjective and that the decision to undergo surgery is based on specific patient-selected goals. In a follow-up to this work, Mahajan et al. [55] examined goals and satisfaction in an urge incontinence population. Patients were asked to list their goals and at follow-up patients were asked to identify the degree to which each goal was achieved 1 year post surgery (completely to not at all). The study found that failure to meet goals was associated with long-term dissatisfaction with surgery.

In the area of IC/painful bladder syndrome, GAS has been employed to determine whether patients’ treatment goals are unique [56]. This study found over 140 separate goals with a mean number of 4 goals per patient with pain, frequency, and nocturia being the most frequently described goals. Based on these findings, a new GAS instrument is in development in this area.

In the area of drug treatment for urgency and urge incontinence, goal improvement was evaluated in women treated with transdermal oxybutynin or placebo [53]. The most frequently reported goals were in the areas of urgency (“not rushing to the toilet when I hear taps”), nocturia (“not to get up so much at night”), and frequency (“need to go to the toilet less than I do”) [54]. This study found that after 4 weeks of treatment, goal achievement was only slightly higher for transdermal oxybutynin (42%) vs. placebo (32%) with other measures showing only limited convergence with goals [53,54].

In the area of OAB and LUTS, a new measure of GAS has been developed: the Self-Assessment Goal Achievement (SAGA) questionnaire [50]. Due to the fact that early research found that some patients have difficulty formulating goals, interviews with LUTS patients were conducted to identify the most bothersome symptoms. These symptoms were incorporated in the first part of the SAGA tool as a fixed assessment of nine symptom goals. In the second part of SAGA, in line with traditional GAS measures, patients can record any other goals that they have related to their LUTS. At follow-up, patients rate the level of goal achievement on each of the goals they selected. The validity of the measure in clinical practice has recently been demonstrated [57].

CONCLUSION

The accurate and proactive screening for urological conditions should play an increasing role in improving health care. Additionally, the importance of understanding patient expectations, goals, and satisfaction is increasingly recognized as a critical element in judging overall outcomes in urogynecological conditions. The increasing availability of validated PRO screeners that can assist clinicians and researchers with assessing symptoms and conditions has the potential to greatly enhance communication among clinicians and patients, as well as among researchers. Validated tools that assist with assessing expectations, goal setting and achievement, and measurement of satisfaction can be incorporated into clinical and research practice. This is a high-impact area for continued research as clinicians and patients alike seek to improve their understanding of each other's expertise and seek mutually reasonable treatment plans that results in satisfied patients with an improved quality of life. This chapter should facilitate inclusion of appropriate PRO screening and outcomes tools as part of routine assessment in clinical practice. In future urogynecological research, measuring expectations, satisfaction, and goal attainment as primary or coprimary outcomes should be considered as part of a complete assessment of urogynecological treatment.

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15 Questionnaires to Assess Sexual Function

Claudine Domoney and Tara Symonds

Patient-reported outcome (PRO) measures to assess sexual function are perhaps those of most significant value as this sphere of activity is one of the most difficult in which to capture information that is meaningful. These instruments, if designed well, may incorporate the functional aspects of sexuality, the symptom severity, and the impact on quality of life. The WHO has defined sexual health as a state of physical, emotional, mental, and social well-being in relation to sexuality (and), not merely the absence of disease, dysfunction, or infirmity [1], and therefore an important reflector of global well-being. However, there are great differences in the perception of clinicians and patients when discussing sexual outcomes. What is important for the patient may not be easily communicated to the doctor. Monitoring the effect of treatment or interventions on sexual parameters has generally been relatively crude to date. Questions that appear comfortable for doctor and patient to discuss may have little bearing on the true change in sexual activity. The varied urogynecological population, whose sexual backgrounds may be diverse, need determination of the most appropriate method of measuring the desired data. As 11% of women have surgical treatment for pelvic floor dysfunction (PFD) [2], this is the time to properly determine the impact of the disease process and its treatment on sexual function.

WHY USE QUESTIONNAIRES?

Traditionally, gynecologists and urologists have asked questions to their patients pertaining to sex, which are comfortable for both to ask and answer. The enquiry may be directed to areas perceived by clinicians as influenced by the disease or condition and that may reasonably be expected to improve with intervention. These include sexual activity, often phrased as frequency of penetrative vaginal intercourse, and pain or dyspareunia. More qualitative components of sexual function may be more difficult to assess unless posed in a questionnaire format. Asking about orgasm frequency or quality, satisfaction, arousal, and sexual desire may be difficult for both clinicians and patients, particularly if they perceive they have had inadequate training [3,4]. As these factors frequently vary between couples depending on the length and quality of relationship, the age of both partners, and the menopausal or peripartum status, a questionnaire that is sensitive enough to determine these factors may be important if trying to assess the impact of an intervention such as surgery.

It is likely that issues of lesser concern to individuals were previously focused on, and this underestimates the true incidence of sexual difficulties. At present, it appears anatomical vaginal measurements in urogynecological patients do not predict function [5]. Investigations such as urodynamic measures, pelvic blood flow, 4D ultrasound, vaginal plethysmography, and nerve conduction studies may give quantitative values to compare population or study groups, but the evaluation of their relationship to sexual function is in its infancy. Whether they will ever graduate to useful clinical measurements with respect to sexuality is arguable. “The vagina may say yes but the mind says no”—physical measures to assess the state of arousal such as blood flow and lubrication do not reproducibly correlate with subjective sense of arousal in women.

PFD is common with up to one-third of premenopausal and half of postmenopausal women having some form of PFD, which may then lead to a reduction in quality of life, the most important outcome. However, sexual problems are also highly prevalent, with a North American study reporting that up to 43% of women and 31% of men aged between 18 and 59 admitted a problem in the previous year [6]. British studies have indicated that the prevalence of sexual problems in primary care is high with 22% of men and 40% of women being diagnosed with a sexual dysfunction, although this was poorly recognized and documented [7]. However, when the degree of distress or “bother” is considered by clinicians, the proportion with a sexual problem approximately halves in many studies [8]. Clearly, it is important for the pelvic surgeon to be able to evaluate the changes in PFD that prevent sexual activity or reduce satisfaction from those that are common in the general population. Questionnaires that are sensitive enough to detect these differences and the modification that can be expected from urogynecological interventions may help individual patients and studies.

FEMALE SEXUAL FUNCTION

Designing instruments to measure sexuality requires a model to promote the understanding of female (and male) sexuality and its deviations. Over the twentieth century, models of human sexual behavior have been proposed, and its classification of normal and abnormal became clinical measurable entities. However, the norms for function and activity are varied, and at present, there is a debate over how medicalization of human sexual behavior has been propagated by the prospect of pharmaceutical intervention. Yet, there is also a drive from women as expectation of a full and satisfying sexual life has been raised, with over half of one study of 1805 European menopausal women stating it was important [9]. Many other international studies of older populations reinforce these findings [10,11].

The Masters and Johnson human sexual response cycle model from the 1960s details the changes occurring during sexual activity based on observations from laboratory-based sexual encounters [12]. This has been developed into other models over the last 30 years, but more recently, an International Consensus Group on female sexual dysfunction (FSD) has expanded these female sexuality models to include the importance of intimacy and sexual stimuli on innate sexual drive [13,14]. This contrasts to the linear human sexual response model of Masters and Johnson more in keeping with male sexuality, having an inbuilt sexual drive, i.e., libido and desire to be involved in sexual behavior that precedes excitement and arousal. Women, in contrast to men, may only achieve orgasm in 50% of penetrative intercourse and a further 20% with external stimulation.

The International Consensus Group model of female sexuality indicates that a spontaneous sexual drive to be involved in sexual activity does not need to be present for satisfactory relationships to be maintained. The content of sexual activity of women *may* be less goal driven than that of men. Therefore, it is important to understand the other features influencing an individual woman’s ability to be sexual in order to explain why she may be experiencing difficulties. How much urogynecological complaints contribute to this may not be clear to the clinician or patient themselves. Sexuality is modulated by many factors and normal features of life, including life events, reproductive events, health, relationships, and cultural factors. Female sexuality is a complex interplay of physiological, psychological, and cultural factors. A well-developed questionnaire may be able to detect the effect of PFD on sexual function and activity, its effect on quality of life, and the changes in sexual function after interventions.

FEMALE SEXUAL DYSFUNCTION

At present, the most accepted international definitions of FSD have been determined by the International Consensus Conference panel modification of the framework of the International Classification of Diseases-10 and Diagnostic and Statistical Manual of Mental Disorders (DSM-IV and DSM-V) of the American Psychiatric Association. These areas were defined as four separate categories by DSM-IV, but recently, DSM-V has recategorized desire and arousal disorders as one combined disorder and dyspareunia and vaginismus as genitopelvic pain/penetration disorder, with additional disorders such as aversion disorder female sexual orgasmic disorder or female orgasmic disorder (FOD) and noncoital pain disorders. The quantification of these disorders including the identification and qualification of pain can be adapted for clinical and research settings. Specific dysfunctions can be diagnosed if the domains within an instrument are sufficiently sensitive. Not all instruments are diagnostic of dysfunctions, while others are specific to one disorder, e.g., desire disorder. Before choosing an instrument for use, the outcomes sought should be clarified so fitness for purpose can be ensured. Diagnosing FSD or a specific disorder may not be important and global sexual function the most important issue. Questionnaires may be designed to give a composite score that can be broken down into domains to diagnose or screen for a specific dysfunction (e.g., female sexual function index [FSFI]) or a global score for comparison, with nondiagnostic domains (e.g., prolapse and incontinence sexual questionnaire [PISQ]). Many instruments may have a more “user-friendly”short form for use in clinical practice but are likely to be less sensitive.

FSD in Urogynecology

It is clear that the minority of physicians caring for women with PFDs screen for sexual dysfunction at present. Surveys have reported that this is due to lack of time and treatment options, the older age of many of the patient groups, and the perceived lesser importance of this aspect of functioning [3,4]. However, there is objective evidence that pelvic floor problems adversely affect sexual relationships and sexuality, making it important clinicians are aware of change in functioning. Most studies report that 50%–60% of urogynecology research participants are sexually active. Up to 64% may be labeled with FSD [15], but the degree of distress associated with this is pivotal in the diagnosis of true dysfunction. There is a reluctance on the part of patients to seek help that may be mitigated by the doctors' comfort and ability to communicate about such personal matters. It can be easier for both the doctor and patient to use a questionnaire to detect these difficulties. However, this can also be perceived as an avoidance tactic by surgeons with a different agenda. Questionnaires do help to reduce the time constraint of the doctor–patient interaction by having patients complete the questionnaires while waiting for the consultation or before their clinic visit. Furthermore, in the area of sex, reduction of embarrassment may result in more valuable answers. Yet, as all clinicians would agree, these instruments have no replacement for the consultation and should be interpreted and integrated with the patients' complaints.

Up to 50% of women with urinary incontinence complain of coital incontinence with approximately one-third admitting it compromises their sexual health [16]. This has been reported widely as impacting on quality of life [17], yet surgical cure for this complaint is not always reported to improve sexual function [18]. Similar findings have been reported with pelvic organ prolapse procedures although the huge variation in surgical techniques and individual patient anatomy may be potential confounding factors [19]. Validity and reproducibility may depend on the tools used to measure these outcomes and explain the conflicting results from many urogynecological studies with respect to sex [20].

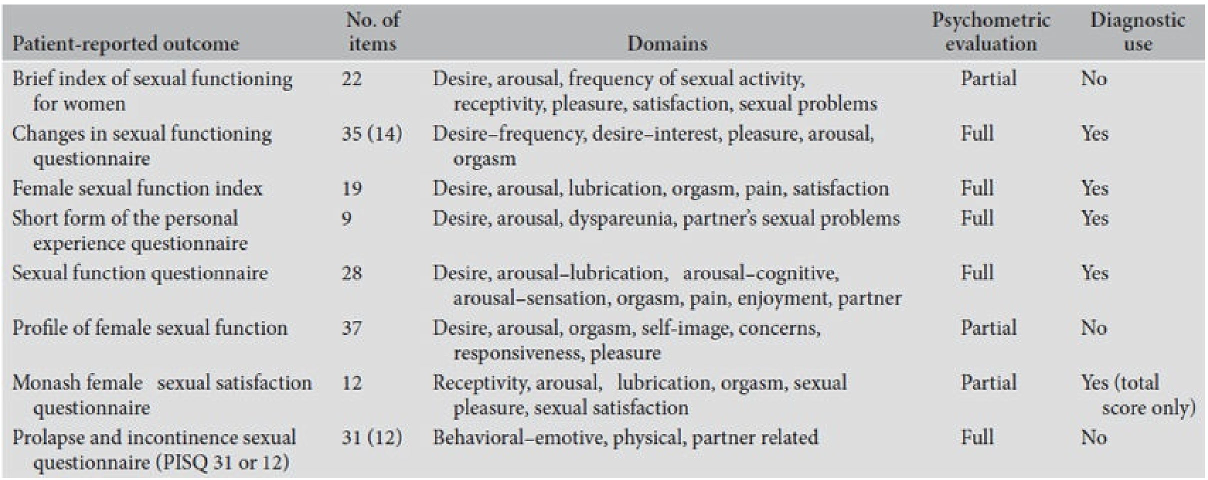
OUTCOME MEASURES

Since the launch of sildenafil in 1998 for the treatment of erectile dysfunction (ED), there has been a significant growth in male and female sexual health research, which has resulted in the development of numerous new assessment measures, both objective and subjective.

Objective Measures

There have been numerous objective measures developed to diagnose and assess erectile function (e.g., Doppler ultrasonography, penile–brachial index [21]), but penile tumescence using Rigiscan has been the most widely used [22]. Diagnosis and assessment of men with premature ejaculation has relied on the use of time (stopwatch assessment) to ejaculation (intravaginal latency time). For women, objective measures have been developed such as vaginal photoplethysmography and Doppler ultrasonography [23]. Objective assessment of sexual function in men with ED shows good agreement with subjective assessments, considered to be because of the obvious biofeedback loop of the rigidity of the penis. However, in women, agreement between the objective and subjective assessments of sexual function has not been easy to demonstrate; this may be due to its being multidimensional compared to the unidimensionality of ED.

Table 15.1 Female Sexual Dysfunction Patient-Reported Outcome Measures



Patient-reported outcome	No. of items	Domains	Psychometric evaluation	Diagnostic use
Brief index of sexual functioning for women	22	Desire, arousal, frequency of sexual activity, receptivity, pleasure, satisfaction, sexual problems	Partial	No
Changes in sexual functioning questionnaire	35 (14)	Desire–frequency, desire–interest, pleasure, arousal, orgasm	Full	Yes
Female sexual function index	19	Desire, arousal, lubrication, orgasm, pain, satisfaction	Full	Yes
Short form of the personal experience questionnaire	9	Desire, arousal, dyspareunia, partner's sexual problems	Full	Yes
Sexual function questionnaire	28	Desire, arousal–lubrication, arousal–cognitive, arousal–sensation, orgasm, pain, enjoyment, partner	Full	Yes
Profile of female sexual function	37	Desire, arousal, orgasm, self-image, concerns, responsiveness, pleasure	Partial	No
Monash female sexual satisfaction questionnaire	12	Receptivity, arousal, lubrication, orgasm, sexual pleasure, sexual satisfaction	Partial	Yes (total score only)
Prolapse and incontinence sexual questionnaire (PISQ 31 or 12)	31 (12)	Behavioral–emotive, physical, partner related	Full	No

Notes: Full, factor analysis for domain structure, internal consistency, test–retest reliability, convergent validity, known-groups validity, and responsiveness. Partial, one or more of the aforementioned were not completed.

Subjective Measures

Subjective measures of sexual health have flourished over the past 10 years. For assessing ED, the gold standard measure is the international index of erectile function [24,25], but for men with premature ejaculation, there is no gold standard equivalent but there are a number of measures to choose from, which were reviewed recently by Althof and Symonds [26]. Assessment of women's sexual health has tended to use sexual inventories, which capture all elements of the DSM-IV female sexual function cycle domains (female sexual arousal disorder [FSAD], FOD, hypoactive sexual desire disorder [HSDD], and pain) (e.g., sexual function questionnaire [SFQ] [27], FSFI [28]; see Table 15.1 for detailed listing of measures).

Clinician Measures

Evaluation of change in sexual function status can be assessed using clinician interview, which benefits from an in-depth discussion of all aspects of the individual's sexual history or problem. However, standardization of an interview is difficult if trying to use this approach in the evaluation of a new treatment and probably has most utility in diagnosis, although even in diagnosis there will be issues with concordance and reliability between clinicians due to the complex diagnostic criteria for FSD. Utian et al. [29] successfully developed a structured diagnostic method for diagnosing FSD, and Derogatis et al. [30] have recently developed a standardized clinician assessment for diagnosing hypoactive sexual desire disorder—women's sexual interest diagnostic interview.

In evaluating the outcome of treatments for both male sexual function and FSD, small lab-based studies have generally relied on an initial clinician diagnosis of sexual dysfunction, followed by an objective assessment. Larger, randomized controlled trials have used similar clinician diagnosis of dysfunction but with subjective measures of outcome due to ease of use.

DIFFICULTIES SPECIFIC TO SEXUAL FUNCTION IN PFD

Neither pelvic floor nor sexual dysfunction is seen as life-threatening disorders and therefore may have been neglected in the past. There is now a priority for assessing patient outcomes rather than that of the clinician attempting to improve health-care provision for these patient groups. Until relatively recently, the only tools available for urogynecologists and urologists to use were generic questionnaires validated in the general population. Prior to the use of these questionnaires that may have previously been considered outside of the remit of surgeons, self-designed items focusing on the clinicians area of interest such as dyspareunia, frequency of penetrative intercourse, and coital incontinence were quantified in the trials. As a result, it is not clear what effect surgical interventions have on sexual functioning as the results are highly variable depending on how and to whom the questions are being asked and over what time frame. The rate of sexual activity and the causes of change needs to include assessment of partner factors, which more often determine sexual activity in a relationship [31]. Pain as an endpoint may be particularly misleading given that it is widely reported by younger women as a significant factor in their sexual problems compared to older women who are more likely to report other physical features of intercourse as problematic. Sixty percent of women in their 30s had intermittent dyspareunia and one-third persistent [32], whereas another study suggested that lubrication was the most important problem for older women [33].

Asking patients about sex is more likely to yield information as sexual difficulties are less often spontaneously reported. However, the use of questionnaires may produce more reproducible answers and less embarrassment. Subjective information can be gathered in an objective manner. If screening is the aim, three simple questions have been shown to be as effective as a detailed interview [34]:

1. Are you sexually active? (Or are you in a sexual relationship?)
2. Are there any problems?
3. Do you have any pain with intercourse?

Pain may be interpreted as physical but be either physical or psychosomatic—for many patients, these are not distinguishable.

A more sophisticated instrument should aim to clarify the presence of symptoms, their severity, and/or frequency. In addition, it should assess how the patient feels and its impact on the activities of daily living and social, psychological, and emotional well-being. Condition-specific questionnaires will further assess the impact of the condition on function. Therefore, general and condition-specific questionnaires seek different endpoints. Generic questionnaires may elucidate the differences in various conditions and allow comparison with control populations without the condition, whereas condition-specific questionnaires will ideally be designed to elucidate the small differences in patients with a condition such as PFD [35]. This may be further distinguished in PFD sufferers such as the comparison between those with urinary incontinence and fecal incontinence, depending on the validation of the instrument. Sexual function measurement with nonvalidated tools leads in inaccurate and inconsistent results.

Questions within other condition-specific quality-of-life measures may be validated but yield limited information about sexual function and activity such as the King’s health questionnaire (KHQ) and the Incontinence Impact Questionnaire (IIQ). If questions regarding global functioning and quality of life are the endpoints of interest and/or more likely to be acceptable to the patient group, this may be more appropriate but the information and conclusions regarding sexual functioning are more limited.

When developing these tools, it is also important to determine how often these questions will be avoided and how easily they can be misinterpreted as with sexual function. This will have a profound impact on the results obtained. During the validation process or in a paid clinical trial, subjects may be more inclined to answer intrusive questions than in general clinical practice. If questions are routinely not answered or if questionnaires are left substantially incomplete (e.g., because the first question asks about penetrative intercourse without stipulating that further questions do not rely on the presence of a partner), the tool will be effectively useless. Additionally, most questionnaires available are only validated in heterosexual relationships.

If the group that are sexually inactive secondary to their pelvic floor problems are excluded, the proportion that will show improvement will not be readily determinable. The recognition of the importance of length of recall regarding the previous sexual intercourse and/or activity when choosing a tool is imperative. One month, three months, or six months are the usual time frames, and some are clearly inappropriate in some settings such as perioperatively. Yet, for those women having sexual intercourse twice a month (the median frequency for British heterosexual couples aged 45–55 years [36]), although the quality may be more important than quantity, the weighting of frequency in the score could potentially wrongly determine FSD.

With respect to urogynecological problems, it is useful to evaluate other confounding factors including age, menopausal status, possibly the length of relationship, and partner functionality. The perception of the partner as reported by the index patient can have a bearing on function as women tend to protect their sexually dysfunctional partners by developing a corresponding dysfunction such as loss of desire to mask their partners’ inability to maintain an erection or ejaculation.

DEVELOPMENT OF SEXUAL FUNCTION MEASURES

Developing useful questionnaires is an involved and expensive process. The initial process of conceptualization requires the input of clinician and patient. The fundamentals of survey questions require item development and evaluation. It can be argued that the only valid perspective is that of the patient, but if the instrument is to be used by surgeons, it needs to incorporate factors of relevance to their practice. A clinician judging the impact of an operation may want to know that a woman has a noncoital pain disorder such as vulvodynia only to be able to counsel that she is unlikely to be cured of this complaint by her prolapse surgery.

The words used in the items need to be appropriate to ask or identify the same aspect of behavior that the clinician is interested in. The shared understanding may need to be tested in focus groups, particularly with respect to sex where both clinicians and patients use surrogate phrases. An example may be the use of the word libido that for many lay people means all aspects of sexual function—desire, arousal, and erection. The words, sentences, and response choices used need to be clear. Simpler, shorter questions with depersonalized answers to sensitive issues are more likely to produce answers that patients are willing to divulge.

Any instrument requires validation and also reliability testing (content/face, construct, and criterion—see Chapter 12 on PRO development). Further validation is recommended in distinct cultural groups since sex/sexual relationship is especially culturally determined.

QUESTIONNAIRES TO ASSESS FEMALE SEXUALITY

Over the years, both generic and condition-specific measures have been developed for assessing sexual (dys)function in men and women; the following text is an overview of some of the generic measures, condition-specific measures for assessing FSD, and disease-specific measures for use in PFD.

Generic

The Derogatis inventory of sexual functioning [37] and the Golombok Rust inventory of sexual satisfaction [38] are earlier measures designed to capture the essence of sexual behavior and sexual dysfunction in both men and women. However, with the surge in research looking to develop suitable pharmacological treatment(s) for FSD, a number of simple PROs have been developed over the past 10–15 years and are summarized in Table 15.1.

The brief index of sexual functioning for women (BISF-W) [39,40], a 22-item measure, was developed for use in large clinical trials and assesses a number of concepts: thoughts/desire, arousal, frequency of sexual activity, receptivity/initiation, pleasure/orgasm, relationship satisfaction, and problems affecting sexual function. It covers a wide range of concepts and assesses the two main sexual dysfunctions—desire and arousal—but validation of the measure is questionable. A follow-up study by Mazer has produced a new scoring algorithm but needs further validation.

The changes in sexual functioning questionnaire (CSFQ) were designed to measure illness and medication effects on sexual functioning [41,42]. There are male and female versions. The female version comprises 35 items, forming five domains: sexual desire/frequency, sexual desire/interest, sexual pleasure, sexual arousal, and sexual orgasm. The CSFQ can assess sexual functioning in both clinical and nonclinical samples, particularly depressed patients, and has shown sensitivity to change [43]. A short form (14 items) was developed and validated to allow easier use in clinical practice [44].

Condition-Specific FSD Measures

The FSFI was developed by an international panel of experts to apply to all types of FSD and was initially validated in an FSAD population [28]. Meston [45] has since shown its validity in women with FOD and HSDD. The FSFI can also be used to classify women with and without sexual dysfunction [46] and, more recently, women with and without HSDD [47]. This was the first measure to show validity across the differing FSD subtypes rather than just in a general dysfunctional group and as such has been used in a number of studies to assess outcome (e.g., Blumel et al. [48]; Bradford and Meston [49]; Ito et al. [50]; Derogatis et al. [51]). It has frequently been used in PFD studies.

The Short Personal Experiences Questionnaire was adapted from the Personal Experiences Questionnaire and was developed to capture the components of female sexual function for menopausal women desire, arousal, dyspareunia, and also an assessment of partner’s sexual problems [51,53]. The measure was subsequently validated in a group of sexually active women, women with a sexual dysfunction, and women attending a psychiatric clinic [52]. However, the number of subjects was small, $n = 115$, $n = 17$, and $n = 16$, respectively, and particularly draws into question the robustness of the cutoff score to indicate sexual dysfunction.

The SFQ was developed using extensive input from women with a sexual dysfunction ($n = 22$) and from those who were sexually functional ($n = 60$). Additionally, the interviews were conducted across seven countries (the United Kingdom, the United States, Australia, the Netherlands, Denmark, France, Italy) to determine whether cultural background affected the way women described their sexual health/function; consistency of reporting was found. Comprehensive validation resulted in 28 items assessing the following concepts: desire, arousal and lubrication, arousal and sensation, orgasm, pain, enjoyment, and partner [27] The SFQ has also been developed to screen for likelihood of sexual dysfunction, across each of the functional domains (desire, arousal and lubrication, arousal and sensation, orgasm, pain) [54,55]. The confirmation of the pain cutoff scores is required because there were few women with sexual pain used in the assessment. An abbreviated 15-item version is also available.

The profile of female sexual dysfunction was developed through patient interviews and focus groups with women from Europe and North America and who were either naturally or surgically postmenopausal and had low desire [56]. The measure was then further evaluated multinationally in surgically menopausal women with HSDD. Item analysis resulted in seven domains (sexual desire, arousal, orgasm, sexual pleasure, sexual concerns, sexual responsiveness, and sexual self-image) across 37 items. The validity and reliability of the profile of female sexual function in naturally menopausal women with HSDD have also been demonstrated [57], although scale structure still needs to be confirmed for this population. A brief seven-item version has also been validated for screening use with HSDD in surgically menopausal women.

The most recently published measure for assessing women’s sexual function is the Monash female sexual satisfaction questionnaire (MFSSQ) and was developed specifically to assess acute therapeutic effects [58]. The 12-item measure was developed from 10 interviews with women, which led to domains of receptivity, arousal, lubrication, sexual pleasure, sexual satisfaction, and orgasm. The validation was conducted in pre- and postmenopausal women who were dissatisfied with their sexual function. The MFSSQ can be used to screen women dissatisfied with their sexual dysfunction, but cutoff scores for the separate domains have yet to be determined. Reliability of the orgasm and receptivity domains were not ideal and should be explored further. Responsiveness of the scale was not reported.

Disease-Specific Questionnaires for Use in Women with PFD

Sexual function measures should seek to evaluate the impact of PFD on sexual function and ultimately the subsequent impact of intervention. The few questions relating to sex in other quality-of-life questionnaires give a score of an overall impact on quality of life (KHQ, IIQ, electronic personal assessment questionnaire [ePAQ]) and are therefore less suitable to examine sexual impact in detail. General questionnaires will analyze function in general populations but may not be sensitive enough to detect subtle changes. Confounders such as age and menopausal status need to be accounted for and could alter the suitability of a particular instrument. For these reasons, disease-specific measures are the gold standard (Table 15.2).

There are two validated condition-specific sexual health measures for PFD available to date: PISQ and the International Consultation on Incontinence Questionnaire—Vaginal Symptoms (ICIQ-VS) [59]. Unfortunately, neither is validated in women with rectal symptoms. The PISQ is currently the most widely used. Both have undergone construct validity and reliability testing. The PISQ has been validated in more languages than the ICIQ-VS and therefore to date may be more suitable for international use.

The PISQ (31 items) has three domains: behavioral–emotive (frequency, orgasm, satisfaction), physical, and partner related (patient perception of). The TISQ has detected an improvement in sexual function in 70% of patients undergoing postsurgical repair of PFD, with an increase in physical and partner-related domains but no significant change in orgasm, desire, or arousal. Many studies using non-disease-specific tools have shown no change, which may be in part due to their lack of sensitivity or could really suggest limited change with surgery. The PISQ results correlate well with established general questionnaires including the FSFI and sexual history form function 12 [60]. It also differentiates depression associated with poor sexual function. Higher scores in the PISQ indicate better function. Normative scores with general population testing established a mean score of 94, maximum being 124. There is a short-form PISQ 12 [61] that correlates well with PISQ 31 scores. The normative score in PISQ 12 in the general population without prolapse or incontinence is 40, maximum score 48. The PISQ 12 scores can be multiplied by 2.58 to equal a PISQ 31 score. Increasing severity of PFD is generally associated with reduced PISQ scores. The PISQ however has its limitations. It cannot diagnose FSD at present, although as stated earlier, global normative values have been determined. It is not suitable for women in same sex relationships. As it excludes all women not engaging in penetrative intercourse and does not screen for other sexual activity, it may underestimate the impact of PFD. The International Urogynecology Association has developed a revision of the PISQ 31 to address issues considered important by an expert panel—the revised PISQ-IR [62].

Table 15.2 Factors to Be Considered When Choosing Sexual Function Assessment Questionnaires for Patients with Pelvic Floor Disorders

Patient factors	**Clinician factors**
Length/number of other questionnaires	Length/number of other questionnaires
Acceptability	Consistency
Validity/reliability	Validity/reliability
Simplicity	Reproducibility
Relevance	Captures outcomes of interest
Cultural validity	Generic/condition specific/disease specific
Language	Self/interviewer administered

The FSFI, a measure to assess FSD (see aforementioned for further details), has also been extensively used in urogynecological studies. One study investigating the effects of vaginal surgery on women with PFD concluded that domain scores changed but overall the scores did not improve [63]. The authors suggest one problem replaces another—altered vaginal anatomy before surgery to dyspareunia postsurgery. This demonstrates the possible unsuitability of general sexual functional scales for the PFD patient groups. Lack of any activity due to the disease process will not be assessed adequately. This has led to the use of the Sexual Distress Scale that measures distress due to the inhibition of sexual function and can be used to measure impact of the disease process on sexuality and benefit of intervention over time, without a need for engagement in sexual activity of any kind [64].

This may be particularly important for women with pain syndromes such as chronic bladder pain syndrome that disproportionately affects younger women and their sex lives. A study using the FSFI detected up to half of women with interstitial cystitis/painful bladder syndrome or recurrent urinary tract infections has a diagnosis of FSD with a deterioration in desire, lubrication, and satisfaction but no difference in arousal or orgasm [65]. Yet, a North American epidemiologically validated questionnaire did not find a significant association between PFD and sexual activity or satisfaction [66]). Overall, the use of nonvalidated and generic questionnaires makes urogynecological studies of sexual function difficult to compare and the results, if contradictory, are inconclusive. Therefore, when determining the right tool to be used, the outcomes of value should be carefully considered to ensure that these are adequately captured.

CLINICAL PRACTICE VS. CLINICAL TRIALS

Ascertaining which measure to use will be based on the setting and research questions under consideration. For instance, if the measure is to be used in clinical practice to monitor patient outcome, then a short instrument would be more realistic to mitigate the time burden for both clinician and patient (e.g., short-form CSFQ). If, however, the aim is to test a new therapeutic agent in a clinical trial, the most relevant measure regardless of length would be the best to ensure all aspects of FSD are captured in the most robust manner possible (e.g., FSFI, SFQ). Alternatively, a clinician may wish to use a measure to help screen for potential sexual function problems and needs a short measure that can also provide guidance on likelihood of FSD or even in relation to a particular FSD domain (e.g., SFQ). The use of a disease-specific tool validated in the appropriate population with a representative recall period (e.g., PISQ-IR) may be most useful to detect global change in sexual activity associated with therapeutic intervention, without the need for diagnosis of specific sexual dysfunctions. Regardless of setting, when choosing a measure, ensuring appropriate information of interest is obtained is essential. Then, an assessment of the measures validity and reliability in the population of interest to the clinician should be evident.

CONCLUSION

The tendency of women to become less interested in sex and men less able to perform with age may be distinguishable with well-designed instruments. It is important to evaluate the engagement in sexual activity and the reasons why it may have ceased or become less satisfying in women with PFD. The distress caused by these difficulties and its alleviation by urogynecological interventions are the information sought by clinicians and that should guide the management of patients. In the area of sexual function, the only reproducible and consistent method of reporting these outcomes is with well-designed, validated questionnaires.

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16 Questionnaires to Assess Bowel Function

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INTRODUCTION

Assessment of bowel function will undoubtedly require a thorough history and clinical examination. However, one needs a qualitative method of assessing not only the type but also the severity of the condition. This requirement is not only needed clinically but also as a research tool in order to compare different groups and monitor the outcome of interventions. As a result of this, questionnaires are widely used in clinical settings for this purpose.

A full appraisal of the use of such tools in the entirety of bowel disease is beyond the scope of this chapter, which will therefore focus on pelvic floor disorders—in particular, fecal incontinence and constipation/evacuatory disorders.

Questionnaire assessment of bowel function is a challenge due to the fact that normal bowel function varies widely not only within an individual but also between individuals. In addition, these ranges overlap between bowel disorders and pelvic floor disorders. As a result, questionnaires lack sensitivity and specificity for particular pelvic floor disorders.

There is the tendency to assess the pelvic floor in a segmental fashion (anterior, middle, and posterior compartments); however, the International Consultation on Incontinence (ICI) was convened in 1998 to develop a modular assessment of pelvic floor function using specific bowel, bladder, sexual, and prolapse assessment tools (www.iciq.net). In particular, emphasis was put on the need to develop tools that assess the severity and quality of life of those patients with incontinence. The committee justified the questionnaires as providing methods for the standardized collection of data from patients relating to incontinence and lower urinary tract symptoms [1]. In addition, the ICI defined principles that underpin the design of questionnaires. Empirical evidence is required to show that a questionnaire is measuring what it was supposed to do and is robust and repeatable (psychometric properties): having therefore validity, reliability, and responsiveness to change [2,3]. The ICI [4] recommended the following schema to assess the quality of questionnaires, and this will be adopted for this chapter:

Grade A—*Highly recommended*: Published evidence confirming robust validity, reliability and responsiveness. “Validity, reliability and responsiveness established with rigour.”

Grade B—*Recommended*: Published evidence confirming two out of the three dimensions (validity, reliability, and responsiveness) usually validity and reliability. “Validity and reliability established with rigour, or validity, reliability, and responsiveness indicated.”

Grade C—*With potential*: Early development—further work required and encouraged.

The ideal assessment tool for bowel dysfunction is yet to be developed. There has been a little guidance from the major gastroenterology or colorectal societies to suggest which bowel-specific questionnaires should be used both for research or clinical practice. This advice is difficult to give, however as there are no highly recommended tools to date with established reliability and validity that are “Grade A” for bowel specific or global pelvic floor function. It is clear that questionnaire assessment of urinary incontinence in particular is far more developed than equivalent tools for bowel-related pelvic floor disorders [5].

QUESTIONNAIRES TO ASSESS SYMPTOMS AND QUALITY OF LIFE IN PATIENTS WITH FECAL INCONTINENCE

The assessment of bowel function has gradually improved as the focus has changed from a physician outcome assessment to a patient-reported outcome. Parks in 1975 was one of the first to stratify fecal incontinence to assess clinical outcome and he divided this into four grades of severity based on the consistency of stool lost (continent, incontinence to flatus, incontinence to liquid, and incontinence to solid stool). He later used this to assess outcome of surgery, namely the postanal repair. It was later appreciated that it was not only the loss of stool that was important to record, but also how frequently this occurred. Subsequently, the frequency of incontinent episodes was included in the Wexner summative score. Events surrounding and leading up to the incontinent episode became added features, to include the degree of fecal urgency and pad usage in the further development by the St. Marks group.

Questionnaires initially focused on symptom severity; however, changes in symptom severity do not always correlate with a clinical change. The focus subsequently and appropriately has moved away from the severity of symptoms but on the impact of these symptoms on lifestyle, and so detailing this, quality of life tools have been introduced.

To date, the most commonly used questionnaires in clinical practice and clinical research are the "Wexner" incontinence score and the generic SF-36 quality of life questionnaire, which has set a precedent. This makes it difficult to introduce newer tools, as comparative studies such as systematic reviews and meta-analysis become more of a challenge to complete.

It is also important to note that the measurement of improvement very much depends upon the perspective of the assessor, i.e., it varies depending upon who is assessing the situation. There can be discordance between the physician and the patient's perspective. For example, the reduction in stool frequency and delay in urgency time can be more important to improve a patient's quality of life than the frequency of incontinence. Frequency of incontinence is, however, a more tangible measurement for a physician to measure. As such, there has been a growing trend toward patient-reported outcomes to reflect the subjective patient experience.

Questionnaires have become more complex over time, incurring some biases, for example, response fatigue. There needs to be a balance between clinical utility and complexity. So, there has been a trend to shorter and validated forms of impact assessment.

Fecal incontinence (FI) is a major healthcare issue that affects 2%–24% of the adult population [6]. The FI can be defined as the recurrent involuntary excretion of feces in inappropriate places or at inappropriate times. It can be either urge incontinence (inability to defer defecation) or passive incontinence (lack of awareness of the passage of feces, gas, or mucus via the anal canal) [7]. The etiology of FI is wide-ranging [8] and rectal evacuation is linked to pelvic floor function [9]. It is therefore necessary to consider assessment of both bowel function and control synchronously. Evacuatory dysfunction may result from a variety of underlying pathologies including outlet obstruction, slow transit or other mechanical, pharmacological, metabolic, endocrine, and neurogenic abnormalities [10].

A large number of questionnaires have been developed to identify the severity of FI and its influence on health-related quality of life (HRQL). Despite the large number, only a few are in regular use in research practice and fewer are used in clinical practice. The quality of psychometric evidence assessing these questionnaires varies widely and their recommendations are graded according to their evidence.

International Consultation on Incontinence Modular Questionnaire Bowel-(Still in Development) ICIQ-B

The ICIQ modular questionnaire remains the gold standard in questionnaire selection in clinical practice and in research [11,12]. It was developed by the ICI and has been robustly validated in relation to urinary incontinence. The ICIQ-B was specifically designed for fecal incontinence (www.iciq.net). This is a 21-point questionnaire that covers bowel pattern, bowel control, and quality of life. The four unscored items included to evaluate important issues from a clinical or patient perspective. Although studies are still ongoing, the ICIQ-B has been recently evaluated [13]. In this study, there was a good to very good reliability and reasonable response to changes in symptom and quality of life status following intervention. The authors concluded that the questionnaire is robust enough to be used in research and clinical practice. Further studies are awaited, but it is likely that this will achieve the highest level of recommendation.

Fecal Incontinence Quality of Life Scale (Grade B)

The Fecal Incontinence Quality of Life Scale developed and tested by Rockwood et al. [14]. It measures impact of anal incontinence over four scales of HRQL; lifestyle (10 items), coping/behavior (9 items), depression self-perception (7 items), and embarrassment (3 items). The purpose of the questionnaire is to measure the effect on quality of life of treatment for individuals with fecal incontinence. A panel of colorectal surgeons and researchers generated the items. 118 patients, and 72 controls took part in the study.

The questionnaire showed good discriminant validity, with significant differences between patients with fecal incontinence and those with other gastrointestinal disorders. Test–retest reliability at a mean interval of 8 days was satisfactory, with correlations for the 4 scales of 0.8–0.96. Internal consistency of the 4 scales was >0.7. Although there was responsiveness data, the questionnaire nevertheless offers a valid and reliable measure of the impact of fecal incontinence on quality of life in men and women with this condition.

Manchester Health Questionnaire Data (Grade B)

This is based on items adapted from the King's Health Questionnaire [15]. Structurally, they have the same features but use a slightly different format. The Manchester health questionnaire data uses a 5-point response scale (rather than the 4-point scale in the KHQ). Items from the HRQL as well as a symptom severity scale are included in the questionnaire. Face validity was assessed by interview with 15 patients with fecal incontinence. Test–retest reliability was measured (Pearson correlation >0.8 in all 9 domains).

The questionnaire was posted to 236 women with fecal incontinence, of which 159 returned completed questionnaires. 121 performed test–retest at a mean interval of 20 days. Cronbach's alpha was >0.7 in all domains tested, indicating adequate internal consistency.

Convergent validity was assessed by comparison with responses in the SF-36, which showed significant correlations between domains of the two instruments.

Birmingham Bowel and Urinary Symptoms Questionnaire (Grade B)

This questionnaire was developed to evaluate both bowel and urinary dysfunction in women. It consists of 22 items that were generated by a panel of experts following a review of the existing literature [16,17]. The questionnaire was evaluated in 141 asymptomatic women and 489 patients. Analysis of the data showed clinically relevant four-factor structure: constipation, evacuatory function anal incontinence, and urinary symptoms, with good distinction between patient groups suggesting good internal structure. Cronbach's alpha showed internal consistency and Kappa values showed good test-retest reliability. Therefore, the authors recommended the questionnaire to be used for both as a research tool and as a clinical measure.

Wexner Score (Grade C)

This is also called the Cleveland Clinic Incontinence Score and was developed in the Cleveland clinic in 1990. It was developed to objectively assess patients with incontinence in order to measure outcome following treatment [18]. It consists of tables for entry of clinical details and a grading system for the type of incontinence ranging from never to always. The scores are then added to generate a figure from 0 (fully continent) to 20 (severely incontinent). This is the most widely used severity index score in Europe and America and its psychometric credentials have been evaluated recently [19,20]. However, the ICI committee has not recommended a higher grade of recommendation due to the lack of more stringent validation.

St. Mark's Incontinence Score (Grade C)

This is a tool designed to assess the severity of fecal incontinence. It has only five questions that address fecal leakage, bowel urgency, the use of pads, medication, and interference with daily activities [21]. Initial validation involved comparing this tool with the Wexner score in a small group of patients [22]. The results were encouraging and showed good inter-instrument correlation and good relationship with a diary card and objective clinical impression. However, another large study of 390 patients that looked at patients with fecal incontinence and compared subjective visual analogue scale score to the St. Mark rescore showed only moderate correlation regardless of the severity of the incontinence [23]. This lack of robust validity leads the ICI panel to state that the tool had potential although more data are required before it can be fully recommended.

Pescatori Incontinence Score (Grade C)

This tool is hardly used in clinical practice. It was developed in 1992 and uses a number to letter system to the type of incontinence (letter A: flatus/mucus; letter B: liquid; letter C: solid; number 1: occasionally; number 2: weekly; number 3: daily) [22]. No comparison has been made with other tools.

Mayo Fecal Incontinence Survey (Grade C)

This is a tool that is used not only for the assessment of fecal incontinence but also its associated symptoms and the risk factors for developing the symptoms [24]. It is a 13-item questionnaire that has been extensively studied [25–27]. It has a good reliability and validity but very little data exist on responsiveness to clinical change.

Elderly Bowel Symptoms Questionnaire (Grade C)

This is another questionnaire developed by the Mayo Clinic group looking at the elderly with bowel symptoms [27]. It was a postal questionnaire with a 77% response rate and test–retest reliability was acceptable.

Fecal Incontinence and Constipation Assessment (Grade C)

This questionnaire is a modification of other existing tools that the Mayo Clinic developed [28]. It is a 98-item questionnaire that assesses the frequency and type of incontinence, number of pads used daily and the severity of urgency. It was validated in an outpatient clinic involving 83 patients. There were 20 of the patients retested 6 months later in order to assess the validity. Although the sample was small, the reproducibility was acceptable.

EQ-5D (Grade B)

This is a generic quality of life tool, applicable across many disease states, translated into most languages. The EQ-5D (developed by the EuroQol group with five dimensions), is a descriptive system that has five dimensions/questions related to mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. In tandem with this addition, there is also a vertical visual analogue scale EQ-VAS, 20 cm (0–100) for self-rated health. It is an HRQL instrument, and one recommended by the National Institute for Health and Care Excellence particularly for the use of health economic analysis in calculations of quality-adjusted life-years (QUALYs). It has been featuring more in clinical trials for fecal incontinence. Its simplicity and ease of analysis is likely to see this gaining popularity over the more complex SF-36 [29].

QUESTIONNAIRES TO ASSESS SYMPTOMS AND QUALITY OF LIFE IN PATIENTS WITH CONSTIPATION/BOWEL EVACUATION DIFFICULTIES

Constipation is a problem that affects a significant proportion of the world's population and is responsible for symptoms and disorders that create discomfort and morbidity, with consequent high social and economic costs for health care systems. Constipation is a subjective symptom that can be related to a multitude of factors, including dietary, psychological, cultural, anatomic, and functional aspects. In addition, constipation is still surrounded by misconceptions and taboos that hamper an objective evaluation and encourage self-medication that is not always innocuous to the patient care.

The absence of firm criteria for the diagnosis of digestive functional disorders includes dietary, psychological, cultural, anatomic, and functional aspects. In addition, ecological and clinical research led a group of experts in the 1980s to create committees for establishing consensus on the criteria used to diagnose these problems [30]. These were known as the Rome criteria. In 1999, the criteria were modified on the basis of new knowledge gained, and they are now referred to as the Rome II criteria [31].

Rome II committee defined functional constipation as occurrence of two or more of the following symptoms for at least 12 weeks, which need not be consecutive, in the preceding 12 months and in the absence of structural and biochemical explanation: Straining during at least 25% of defecations, lumpy or hard stools in at least 25% of defecations, sensation of incomplete evacuation for at least 25% of defecations, sensation of anorectal obstruction/blockage for at least 25% of defecations, manual maneuvers to facilitate at least 25% of defecations (e.g., digital evacuation, support of the pelvic floor), fewer than three defecations per week.

The Rome II criteria for the diagnosis of chronic constipation differ from the Rome I criteria in that they incorporate two new symptoms to identify individuals with obstructed defecation: anal blockage and manual maneuvers to defecate. In addition, the new criteria exclude subjects presenting with loose stool episodes and irritable bowel syndrome. The Rome III criteria (2006) were an update on Rome II and it added the following to the existing criteria: (1) loose stools are rarely present without the use of laxatives and (2) there are insufficient criteria for irritable bowel syndrome. These criteria must be fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis [32].

Patient Assessment of Constipation Quality of Life (Grade B)

The PAC-QOL is a self-reported questionnaire that was used to measure the quality of life of patients [33]. The validated PAC-QOL is composed of 28 items grouped into four subscales: physical discomfort, psychosocial discomfort, worries and concerns, and satisfaction. The first three subscales are used to assess the patient dissatisfaction index, with an overall score ranging from 0 to 96 (where lower scores correspond to better quality of life). The satisfaction subscale includes four items with a global score ranging from 0 to 6, so that each patient's self-reported definitive outcome is defined as either poor [0–4], fairly good [5–8], good [9–12], or excellent [13–16]. This questionnaire has been validated in Europe, North America, and Australia [34]. It, however, focuses less on specific symptoms and their severity.

In order to address severity, some authors have developed it to be used with the symptom severity measure: the constipation symptom assessment instrument (PAC-SYM), another sister questionnaire which has 12 items under 3 subscales assessing: stool symptoms, rectal symptoms and abdominal symptoms [34]. It also has good internal consistency and retest reliability. It was also able to assess responders and nonresponders showing its response to change as discriminant validity.

Wexner Constipation Score (Grade C)

This is the most widely used scoring system in the assessment of constipation [30]. Its aim is to stratify the severity of constipation based on a set of subjective symptomatic complaints. There are eight questions in this score and a global scale of (0–30). Constipation is defined if the score is greater than 15. This score has been widely accepted because it has a good predictive validity but unfortunately does not address quality of life.

The Chinese Constipation Questionnaire (Grade C)

The Chinese Constipation Questionnaire [35] is a six-item self- report measure designed to diagnose functional constipation in Chinese participants. This scale consists of six items with four subscales: bowel function, stool rectal symptoms, laxative use, and abdominal symptoms. A composite score is generated by principal component analysis with a cut-off score of more than 5 being able to discriminate between controls and constipated patients with both a sensitivity and specificity of 91%. This scoring system is a simple validated tool more commonly used in oriental countries in outcome measures.

The Constipation Severity Instrument (Grade C)

Varma et al. [36] developed this tool that consists of 16 questions under 3 subscales: colonic inertia (slow transit), pain (irritable bowel syndrome C symptoms), and obstructive defecation. It has been validated using 191 patients with constipation symptoms and 103 controls. The instrument has good discriminatory validity and good convergent validity when compared with other established questionnaires. This instrument is quickly gaining use in both clinical and research settings, especially when patients present with subtypes of constipation syndromes.

Knowles Eccersley Scott Symptoms Score (Grade C)

The Knowles Eccersley Scott symptoms score is an 11-point tool for the diagnosis of constipation [37]. It has the added advantage of including various subtypes of constipation. However, no definition of constipation has been given and this makes the validity of the test very difficult to assess.

Gastrointestinal Quality of Life Index (Grade C)

The gastrointestinal quality of life (QoL) questionnaire [38] was designed to address all gastrointestinal symptoms and therefore is not specific for constipation. It includes 36 items with 5 possible answers, and it has a maximum possible score of 180.

Another statistically validated QoL questionnaire, the Constipation-Related Quality of Life [39], has been developed. This includes four domains: social impact (11 items), distress (11 items), usual diet (11 items), and defecation features (4 items). It appears to be an invaluable tool for assessing the effects of constipation on the quality of life.

Obstructive Defecation Syndrome Score (Grade C)

Obstructed defecation syndrome (ODS) is an emerging and challenging clinical problem described by normal desire to defecate with impaired ability to evacuate contents from the rectum. This new entity has been a subject of debate with gastroenterologists and colorectal surgeons during the last few years. The mainstay of treatment for this condition is conservative, with measures involving dietary manipulation and biofeedback techniques using different modalities. Surgical interventions such as Rectopexy and Stapled Transanal Rectal Resection (STARR) are reserved for those who fail on the above measures.

A new scoring system was developed by Longo et al., who also devised the STARR procedure for the treatment of ODS to correlate the symptoms with objective physiological findings and to allow uniformity in assessment of its severity [40–42]. The original Longo score (0–40) is an 8-point scale (defecation frequency, straining, sensation of incomplete evacuation, recto/perineal pain/discomfort, activity reduction per week, laxatives, enemas, and digitations). A modified Longo score is now in use [42] and a lifestyle change parameter has been added to the seven symptom-based parameters. Currently, Modified ODS Longo score is the most commonly used scoring system to decide treatment strategy for ODS patients as well as an outcome measure. It has no quality of life items and is still to be validated.

Measure Yourself Medical Outcome Profile (Grade C)

This is a bespoke questionnaire and is evolving as one of the evolving self-reported tools with potential clinical impact. Patients are asked for their top two troublesome symptoms and the impact of these on their activities of daily living and on general well-being, with both being scored using a 7-point [43] Likert scale. It is simple to use and will apply to all bowel disorders. As it involves generic questions, it allows the patient to self-report symptoms that are important to them. These types of self-reported scoring systems are particularly useful in the follow up assessment of patients and are more sensitive to change than the SF-36. This questionnaire is individualized, thus making it difficult to compare different patients, thus making it less of a research tool, and more of a clinical tool for individual outcome.

CONCLUSION

A wide range of questionnaires and scoring systems are in existence in order to evaluate bowel function. The mere fact of the bewildering array of different tools is an indication of the generally low quality of the tools. Very few of the questionnaires have been rigorously assessed despite their widespread use. Organizations such as the ICI and the Rome Criteria have recognized this problem and one hopes that in the future international consensus will be achieved in order to improve the quality of the tools that are available to assess bowel function currently.

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17 International Consultation on Incontinence Modular Questionnaire

Nikki Cotterill and Paul Abrams

WHAT IS ICIQ?

The first International Consultation on Incontinence was held in 1998 to provide evidence-based recommendations regarding all aspects of incontinence care and research. Committees of experts were convened to encompass all the relevant subject areas. These individuals were from multidisciplinary backgrounds and represented the worldwide scientific community and the range of specialities involved. Each committee was tasked with performing a systematic review of the relevant medical literature in order to make recommendations for clinical practice and research. One such committee responsible for the review of symptom and quality of life assessment identified numerous published questionnaires for the assessment of urinary incontinence (UI). Grades of recommendation regarding their use were applied based on their degree of validation in the published literature [1]. The use of questionnaires with the highest levels of validation was encouraged in clinical practice and research to enable robust evaluation of symptoms and their impact on quality of life and to facilitate the comparison of results across studies. It was also suggested that there was a need for a universally applicable, brief, and simple UI questionnaire to be developed and used widely across the population in clinical practice and research—the International Consultation on Incontinence Modular Questionnaire (ICIQ)-UI Short Form [2]. Such an instrument would facilitate comparisons between findings in different settings and studies and was supported by the ICI Scientific Committee [3].

An advisory board was convened to steer development of this questionnaire, and while not included in the review at the first consultation, the lack of questionnaires available for bowel symptoms and incontinence, and vaginal symptoms such as prolapse, was recognized. The decision was taken to expand the project to enable the recommendation and development of, where required, high-quality, fully validated questionnaires for all lower pelvic dysfunction related to incontinence. The ICIQ project was then established to include a wider spectrum of urinary, bowel, and vaginal symptoms and their impact on quality of life.

AIMS AND OBJECTIVES

The ICIQ's objectives are to provide consensus on the use of published questionnaires for the assessment of lower pelvic symptoms and their impact on quality of life. Three aims underpin the ICIQ in order to achieve clarity over questionnaire use:

1. To recommend high-quality self-completion questionnaires according to evidence of validation
2. To promote wider use of questionnaires to standardize assessment of lower pelvic dysfunction and its impact on quality of life
3. To facilitate communication in different patient settings and different patient groups

HOW IS THE ICIQ DEVELOPED?

Development of the ICIQ is achieved in two ways:

1. Inclusion of existing high-quality questionnaires with the author's permission
2. Production of new questionnaires

Inclusion into the ICIQ is based on a principal factor: evidence of a questionnaire's robust validation. Psychometric testing of questionnaires for use in clinical practice and research is considered essential to afford confidence in the results obtained [4]. This is of particular importance where decisions regarding treatment or research outcomes are made. There are three main components to standard psychometric evaluation:

1. Validity—indicates that the instrument is a valid measure of the concept in question
2. Reliability—indicates that the instrument can measure the concept in a reproducible and consistent manner
3. Sensitivity to change—indicates that the instrument is able to detect real change in the concept under evaluation [4–9]

To achieve these standards requires considerable time and effort. Production of a new questionnaire therefore is only undertaken when there is a specific requirement for the new instrument and when available instruments are inadequate.

METHODS OF ICIQ DEVELOPMENT

ICIQ questionnaire production follows a standard protocol incorporating mixed methodology.

Qualitative studies are undertaken to achieve the aims of both patients and clinical relevance dependent on the nature of the questionnaire. Potential respondents, symptomatic patients, for example, are particularly well placed to provide insight regarding the lived experience of their symptoms and describe the impact on their quality of life [10]. Issues required for clinical evaluation may be more readily identified by clinical experts particularly where specific clinical manifestations are required to infer diagnosis, for example, urinary urgency and frequency are symptoms characteristic of overactive bladder (OAB) [11]. There is inevitably overlap between these groups however. This process ensures that the most pertinent issues for evaluation are identified. The value of conducting qualitative enquiry is also in establishing the most appropriate phraseology and terminology for self-report questionnaires [12]. This approach is considered essential in producing a credible patient-reported tool [13] and provides a sound evidence base for questionnaires to go on and be evaluated using rigorous quantitative methods.

Parallel studies are conducted to evaluate different aspects of validity, reliability, and sensitivity to change in subgroups of potential respondents (e.g., outcome following conservative and surgical treatments). These substudies provide larger datasets on which to conduct numerous statistical analyses in order to make decisions regarding the most robust measurement question items to retain in the final version of the questionnaire. Further consultations with clinicians and potential respondents are conducted to ensure the final version of the questionnaire reflects clinical and patient relevance while displaying the most robust psychometric properties.

The ICIQ’s international nature requires that translations are available, which is also conducted according to an established protocol involving structured translation and back translation to ensure the original meaning of the questionnaire is retained. Over 40 language versions are now provided across available ICIQ modules.

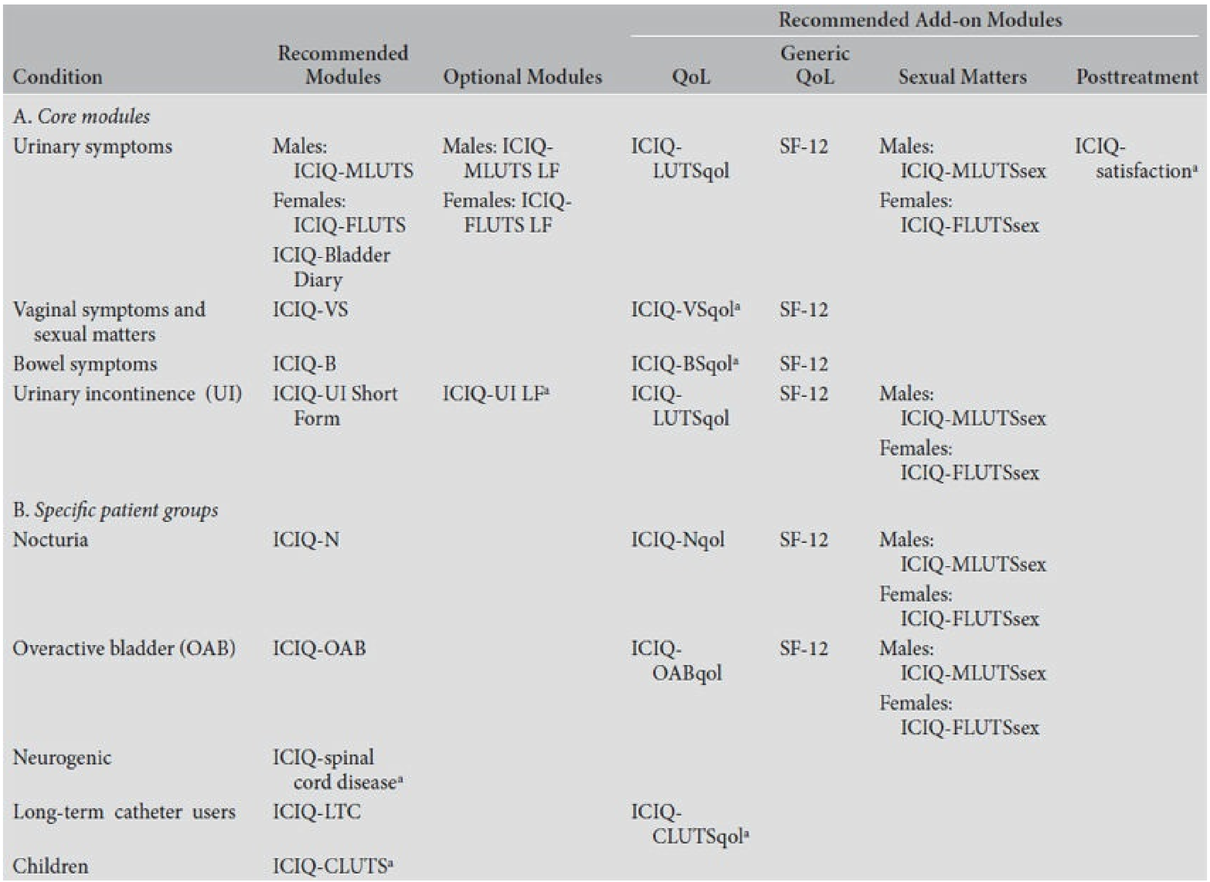
HOW TO USE THE ICIQ

Sixteen ICIQ modules/questionnaires are currently available for use, which includes two recently finalized tools—the ICIQ-Bladder Diary and ICIQ-LTCqol for the evaluation of quality of life associated with long-term catheterization (discussed in detail in the following texts). Clinicians or researchers are able to select modules to compile a tailored questionnaire set that meets their study/clinical practice requirements to achieve complete evaluation.

In order to simplify this, modules have been categorized to aid selection (Table 17.1).

The ICIQ recommends the use of a “core” or “symptom-specific” module and an “add-on” quality of life measure in all patient evaluations for both clinical practice and research. Symptom alleviation may not indicate a difference in impact on quality of life and so the evaluation of both is recommended to encompass all relevant aspects to the individual [14,15]. This approach can also target treatment to the most bothersome component of a symptom complex. The features of each module are summarized in the following texts to inform decisions regarding questionnaire selection.

Table 17.1 International Consultation on Incontinence Modular Questionnaire Modular Structure



			Recommended Add-on Modules			
Condition	Recommended Modules	Optional Modules	QoL	Generic QoL	Sexual Matters	Posttreatment
A. *Core modules*						
Urinary symptoms	Males: ICIQ-MLUTS Females: ICIQ-FLUTS ICIQ-Bladder Diary	Males: ICIQ-MLUTS LF Females: ICIQ-FLUTS LF	ICIQ-LUTSqol	SF-12	Males: ICIQ-MLUTSsex Females: ICIQ-FLUTSsex	ICIQ-satisfaction[a]
Vaginal symptoms and sexual matters	ICIQ-VS		ICIQ-VSqol[a]	SF-12		
Bowel symptoms	ICIQ-B		ICIQ-BSqol[a]	SF-12		
Urinary incontinence (UI)	ICIQ-UI Short Form	ICIQ-UI LF[a]	ICIQ-LUTSqol	SF-12	Males: ICIQ-MLUTSsex Females: ICIQ-FLUTSsex	
B. *Specific patient groups*						
Nocturia	ICIQ-N		ICIQ-Nqol	SF-12	Males: ICIQ-MLUTSsex Females: ICIQ-FLUTSsex	
Overactive bladder (OAB)	ICIQ-OAB		ICIQ-OABqol	SF-12	Males: ICIQ-MLUTSsex Females: ICIQ-FLUTSsex	
Neurogenic	ICIQ-spinal cord disease[a]					
Long-term catheter users	ICIQ-LTC		ICIQ-CLUTSqol[a]			
Children	ICIQ-CLUTS[a]					

[a] In development

Recommended Modules

Core Modules

The questionnaire modules provide assessment of core symptoms of lower pelvic dysfunction:

- Lower urinary tract symptoms (LUTSs) (male and female specific versions): ICIQ-MLUTS/ICIQ-FLUTS
- Diary of urinary events: ICIQ-Bladder Diary
- Vaginal symptoms (female version only): ICIQ-VS
- Bowel symptoms focusing on anal incontinence (male and female applicable version): ICIQ-B
- UI (male and female applicable version): ICIQ-UI Short Form

Each questionnaire provides a comprehensive yet brief instrument for measurement of the stated symptoms and associated “bother.” The bother items attached to individual symptoms enable the individual to indicate areas causing the most impact on quality of life, as perceived by them. This can be a more sensitive indicator of treatment outcome than frequency of symptoms alone (Figure 17.1).

The bladder diary provides the first validated diary for the collection of bladder-related events. Qualitative studies were conducted to derive the parameters for inclusion followed by quantitative studies to evaluate the robustness of the tool.

The characteristics of the core ICIQ modules are summarized in Table 17.2.

Specific Patient Groups

This group of questionnaires provides assessment of some specific conditions or symptom complexes such as nocturia and OAB. This category also includes specific patient groups (e.g., children, individuals with long-term catheters). These instruments contain only question items associated with the symptom complex or have been developed specifically for use in a specific group. These questionnaires therefore are only utilizable in the stated populations and would need further evaluation for use in other groups:

- Nocturia (male and female applicable version): ICIQ-N
- OAB (male and female applicable version): ICIQ-OAB
- Patients with spinal cord disease: ICIQ-spinal cord disease
- Patients using long-term catheters: ICIQ-LTCqol
- LUTSs in children: ICIQ-CLUTS

Bother items are included for all except the children's questionnaire.

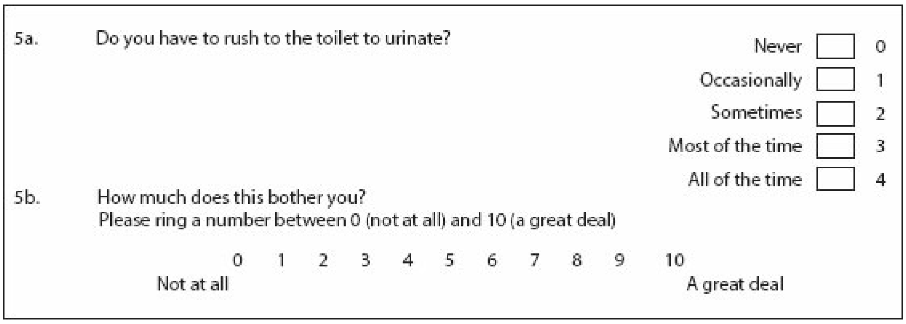
The characteristics and developmental progress of the ICIQ modules for use in specific patient groups are summarized in Tables 17.3 and 17.4.

Recommended Add-On Modules

Core Modules

This group of questionnaires incorporates quality of life and sexual matters modules. They are recommended to be completed as stand-alone questionnaires or alongside core or specific symptom evaluations. The core symptom modules described earlier contain bother items indicating impact on quality of life directly related to symptoms. Quality of life questionnaires cover more specific issues that are a consequence of symptoms (e.g., limiting activities and affecting relationships). The combination of symptom assessment with associated bother and a quality of life assessment provides a more complete evaluation of the patient's experience [15,22]. In addition, given the nature of lower pelvic dysfunction, sexual matters can also be affected and questionnaires are available for this further evaluation where appropriate:

- Quality of life associated with LUTSs (male and female applicable version): ICIQ-LUTSqol.
- Quality of life associated with vaginal symptoms (female version only): ICIQ-VSqol.
- Quality of life associated with bowel symptoms (male and female applicable version): ICIQ-BSqol.
- Sexual matters associated with LUTSs (male and female specific versions): ICIQ-MLUTSsex/ICIQ-FLUTSsex.
- Sexual matters associated with vaginal symptoms are included in the symptom questionnaire (ICIQ-VS) as the issues were considered too intrinsically linked to separate for evaluation.
- Sexual matters associated with bowel symptoms are included in the symptom and quality of life questionnaire (ICIQ-B) as the issues were considered too intrinsically linked to separate for evaluation.



5a. Do you have to rush to the toilet to urinate?

Never ☐ 0
Occasionally ☐ 1
Sometimes ☐ 2
Most of the time ☐ 3
All of the time ☐ 4

5b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 10
Not at all A great deal

Figure 17.1 Example of an International Consultation on Incontinence Modular Questionnaire question item.

Table 17.2 Core Modules Available for Use

1. ICIQ-MLUTS	
Purpose	Comprehensive assessment of male lower urinary tract symptoms and associated bother
Availability	Available for use Published evidence of validity, reliability, and sensitivity to change [16,17]
Domains/items	Voiding

	Incontinence Individual items evaluating frequency and nocturia
Number of items	13
Available translations	26
Scoring system	0–20 voiding symptoms subscale 0–24 incontinence symptoms subscale Bother scales are not incorporated in the overall score but indicate impact of individual symptoms for the patient
Derived from	ICS*male*SF [16]
2. ICIQ-FLUTS	
Purpose	Comprehensive assessment of female lower urinary tract symptoms and associated bother
Availability	Available for use Published evidence of validity, reliability, and sensitivity to change [18]
Domains/items	Filling Voiding Incontinence
Number of items	12
Available translations	19
Scoring system	0–15 filling symptoms subscale 0–12 voiding symptoms subscale 0–20 incontinence symptoms subscale Bother scales are not incorporated in the overall score but indicate impact of individual symptoms for the patient
Derived from	Bristol Female Lower Urinary Tract Symptoms Questionnaire-Short Form (BFLUTS-SF) [18]
3. ICIQ-Bladder Diary	
Purpose	Comprehensive tool to enable robust recording of bladder-related events
Availability	Available for use Published evidence of validity and reliability, sensitivity to change implied but requires more extensive evaluation
Items	Fluid intake, urine output, bladder sensation, incontinence events
Duration	24 hour recordings for 3 days
Available translations	Initial translations in progress
Derived from	Newly developed module [19,20]
4. ICIQ-VS	
Purpose	Comprehensive assessment of vaginal symptoms and associated bother
Availability	Available for use Published evidence of validity, reliability, and sensitivity to change [21]
Domains/items	Vaginal symptoms Sexual matters Quality of life
Number of items	14
Available translations	2
Scoring system	0–53 vaginal symptoms subscale 0–58 sexual matters subscale 0–10 overall impact on quality of life subscale Bother scales are not incorporated in the overall score but indicate impact of individual symptoms for the patient
Derived from	Newly developed module
5. ICIQ-B	
Purpose	Comprehensive assessment of male/female bowel symptoms, predominantly anal incontinence, and associated impact on quality of life

Availability	Available for use Evidence to suggest validity, reliability, and sensitivity to change awaiting publication
Domains/items	Bowel pattern Bowel control Quality of life
Number of items	21
Available translations	2 in production
Scoring system	1–21 bowel pattern subscale 0–28 bowel control subscale 0–26 impact on quality of life subscale Bother scales are not incorporated in the overall score but indicate impact of individual symptoms for the patient
Derived from	Newly developed module
6. ICIQ-UI Short Form	
Purpose	Comprehensive assessment of male/female UI
Availability	Available for use Published evidence of validity, reliability, and sensitivity to change [2].
Domains/items	UI including items on frequency and amount of leakage along with overall interference A self-diagnostic item invites respondents to indicate the cause of incontinence
Number of items	4
Available translations	32
Scoring system	0–21 UI score Self-diagnostic item not scored
Derived from	Newly developed module

Bother associated with impact items is included as this can be very personal and quite unrelated to the frequency of the issue alone.

The characteristics and developmental progress of the ICIQ recommended add-on modules for use alongside the core questionnaires are summarized in Tables 17.5 and 17.6.

Specific Patient Groups

In the same manner as the symptom modules, quality of life modules are available for specific symptom complexes.

- Quality of life associated with nocturia (male and female applicable version): ICIQ-Nqol.
- Quality of life associated with OAB (male and female applicable version): ICIQ-OABqol.

The characteristics of the ICIQ recommended add-on modules for use in specific patient groups are summarized in Table 17.7.

Table 17.3 Specific Patient Group Modules Available for Use

1. ICIQ-N	
Purpose	Comprehensive assessment of symptoms of nocturia and associated bother
Availability	Available for use Evidence of validity, reliability, and sensitivity to change [16–18]
Domains/items	Frequency Nocturia
Number of items	2
Available translations	30
Scoring system	0–8 total score of both items Bother scales are not incorporated in the overall score but indicate impact of individual symptoms for the patient

Derived from	ICS*male*SF/BFLUTS-SF [16,18]
2. ICIQ-OAB	
Purpose	Comprehensive assessment of symptoms of OAB and associated bother
Availability	Available for use Evidence of validity, reliability, and sensitivity to change [16–18]
Domains/items	Frequency Nocturia Urgency Urge incontinence
Number of items	4
Available translations	22
Scoring system	0–16 total score of all items Bother scales are not incorporated in the overall score but indicate impact of individual symptoms for the patient
Derived from	ICS*male*SF/BFLUTS-SF [16,18]
3. ICIQ-LTCqol	
Purpose	Assessment of urinary symptoms and impact on quality of life associated with long-term urethral catheterization and related bother
Availability	Available for use Evidence of validity and reliability. Requires evaluation of sensitivity to change
Domains/items	Catheter function and concern Lifestyle impact
Number of items	17
Available translations	Nil
Scoring system	0–42 catheter function and concern subscale 3–15 lifestyle impact subscale
Derived from	Newly developed module (submitted for publication)

Table 17.4 Specific Patient Group Modules in Development

1. ICIQ-Spinal Cord Disease	
Purpose	Assessment of urinary symptoms and impact on quality of life associated with specific management devices and related bother
Current status	Draft instrument prepared Content validity testing and full psychometric validation to be commenced
Development methodology	Items generated by clinical experts and patients managing urinary symptoms with varying devices
Domains/items	Bladder function Issues associated with specific management devices Sexual matters Quality of life
Derived from	Newly developed module
2. ICIQ-CLUTS	
Purpose	Assessment of urinary symptoms in children
Current status	Draft instrument prepared and has undergone content validity testing Further validity testing underway in the United Kingdom, Italy, and Germany Reliability and sensitivity to change evaluation to be commenced
Development methodology	Items generated by clinical experts Criterion validity evaluated by comparison with gold standard clinical parameters
Domains/items	Urinary symptoms and incontinence
Derived from	Newly developed module

Optional Modules

This category includes lengthier questionnaires for more exploratory evaluation of the core symptoms of lower pelvic dysfunction. While these questionnaires are suitable for use in clinical practice, they have not been shortened for clinical efficiency and are therefore more widely used in research studies where exploration of a broader range of symptoms may be desired and more feasible:

- ICIQ-MLUTS Long Form/ICIQ-FLUTS Long Form
- ICIQ-UI Long Form

The characteristics of the ICIQ optional modules, availability for use and progress of one module in development are summarized in Tables 17.8 and 17.9.

Posttreatment Module

The issue of posttreatment satisfaction evaluation is being explored from various perspectives. To date, a fully validated questionnaire for generic use among individuals undergoing varied treatments for all lower pelvic dysfunction has not been fully validated. The feasibility of an ICIQ module for this purpose is undergoing exploration to establish if satisfaction following treatment can be characterized by a set of common question items applicable to all treatments. An alternative suggestion is that satisfaction may be simply assumed by alleviation of symptoms or improvement in quality of life. Ongoing studies will provide further evidence on which to make suggestions regarding posttreatment evaluation.

Table 17.5 Add-On Modules Available for Use

1. ICIQ-LUTSqol	
Purpose	Detailed assessment of quality of life issues associated with urinary symptoms and related bother
Availability	Available for use Published evidence of validity, reliability, and sensitivity to change [23].
Domains/items	Life restrictions Emotional aspects Preventive measures
Number of items	22
Available translations	45
Scoring system	0–76 total score of all items 0–10 overall impact on everyday life subscale Bother scales are not incorporated in the overall score but indicate impact of individual quality of life aspects for the patient
Derived from	King's Health Questionnaire [23]
2. ICIQ-MLUTSsex	
Purpose	Assessment of male sexual matters associated with urinary symptoms and related bother
Availability	Available for use Published evidence of validity, reliability, and sensitivity to change [17,24]
Domains/items	Erection and ejaculation issues Overall interference
Number of items	4
Available translations	24
Scoring system	0–12 total score of all items 0–10 overall impact on sexual matters subscale Bother scales are not incorporated in the overall score but indicate impact of individual symptoms for the patient
Derived from	ICS*male*SF [16,17,24]
3. ICIQ-FLUTSsex	

Purpose	Assessment of female sexual matters associated with urinary symptoms and related bother
Availability	Available for use Published evidence of validity, reliability, and sensitivity to change [25]
Domains/items	Pain and leakage with sexual intercourse Overall interference
Number of items	4
Available translations	18
Scoring system	0–14 total score of all items Bother scales are not incorporated in the overall score but indicate impact of individual symptoms for the patient
Derived from	BFLUTS [25]

Table 17.6 Add-On Modules in Development

1. ICIQ-VSqol	
Purpose	Detailed assessment of quality of life issues associated with vaginal symptoms and related bother
Current status	Draft instrument prepared and has undergone content validity testing Data collection ongoing
Development methodology	Items generated by clinical experts and patients with vaginal symptoms Content validity testing with potential respondents and clinical experts Multicenter postal administration to potential respondents for validity, reliability, and sensitivity to change data collection
Domain/items	Life restrictions Emotional aspects
Derived from	Newly developed module
2. ICIQ-BSqol	
Purpose	Detailed assessment of quality of life issues associated with bowel symptoms and related bother
Current status	Data collection complete and final analysis underway Evidence to suggest validity, reliability, and sensitivity to change
Development methodology	Items generated by clinical experts and patients with anal incontinence [12] Extensive content validity testing with potential respondents and clinical experts Multicenter postal administration to potential respondents for validity, reliability, and sensitivity to change data collection
Domains/items	Life restrictions Emotional aspects Preventative measures/coping strategies
Derived from	Newly developed module

Adaptation of the ICIQ

Studies have been conducted to evaluate the acceptability and equivalence of the psychometric robustness of electronic versions of the ICIQ. Qualitative studies were undertaken to evaluate the acceptability to the population of interest and to identify modifications required to enable the ICIQ to be completed in an electronic format. Quantitative studies were also undertaken to evaluate the comparability of findings between the different formats to ensure at least equivalence of the measurement properties, which is considered standard methodology for the conversion of paper questionnaires for electronic completion [28]. This will increase the versatility of the ICIQ at a time where technology is advancing at a pace.

Table 17.7 Specific Patient Group Add-On Modules Available for Use

1. ICIQ-Nqol	
Purpose	Detailed assessment of quality of life issues associated with nocturia
Availability	Available for use Published evidence of validity, reliability, and sensitivity to change [26]
Domain/items	Issues associated with sleep disturbance

	Preventive measures
Number of items	13
Available translations	27
Scoring system	0–48 total score of all items or 0–24 sleep/energy subscale 0–24 bother/concern subscale 0–10 overall interference caused by nocturia subscale
Derived from	N-QoL [26]
2. ICIQ-OABqol	
Purpose	Detailed assessment of quality of life issues associated with OAB
Availability	Available for use Published evidence of validity, reliability, and sensitivity to change [27]
Domains/items	Life restrictions Emotional aspects Measure to accommodate OAB
Number of items	26
Available translations	33
Scoring system	0–150 total score of all items 0–10 overall impact on everyday life subscale
Derived from	OAB-q [27]

Table 17.8 Optional Modules Available for Use

1. ICIQ-MLUTS Long Form	
Purpose	Detailed assessment of male lower urinary tract symptoms and associated bother
Availability	Available for use Published evidence of validity, reliability, and sensitivity to change [16,24]
Domains/items	Varied lower urinary tract symptoms
Number of items	23 (including the 13 items within the ICIQ-MLUTS)
Available translations	29
Scoring system	1–84 total score of all items Bother scales are not incorporated in the overall score but indicate impact of individual symptoms for the patient
Derived from	ICS*male* [17,24]
2. ICIQ-FLUTS Long Form	
Purpose	Detailed assessment of female lower urinary tract symptoms and associated bother
Availability	Available for use Published evidence of validity, reliability, and sensitivity to change [18,25]
Domains/items	Varied lower urinary tract symptoms
Number of items	18 (including the 12 items within the ICIQ-FLUTS)
Available translations	7
Scoring system	0–69 total score of all items Bother scales are not incorporated in the overall score but indicate impact of individual symptoms for the patient
Derived from	BFLUTS [25]

Table 17.9 Optional Module in Development

ICIQ-UI Long Form	
Purpose	Detailed assessment of perceived causes of UI
Current status	Draft instrument prepared and has undergone content validity testing Data collection ongoing
Development methodology	Items generated by clinical experts and patients with UI Extensive content validity testing with potential respondents and clinical experts

	Postal administration to potential respondents for validity, reliability and sensitivity to change data collection
Domains/items	For each perceived cause of incontinence (for example, physical activity), the frequency, amount, and degree of bother are evaluated
Derived from	Newly developed module

UPTAKE OF THE ICIQ

Use of the ICIQ in clinical practice and research has been encouraging in achieving the aims of standardized, high-quality assessment for symptoms of lower pelvic dysfunction and their impact on quality of life. More than 1200 requests for use of the various modules have been recorded and over 200 related publications have been identified. The most widely applied module is the ICIQ-UI Short Form (ICIQ), which is closely followed by the ICIQ-FLUTS reflecting the fact that most applications relate to the evaluation of female urinary symptoms. The ICIQ has most commonly been applied to clinical and general practice settings, alongside its considerable uptake in the research setting.

CONCLUSION

The ICIQ modular questionnaire project provides an expanding series of standardized questionnaires for the assessment of lower pelvic dysfunction and its impact on quality of life. The ICIQ provides clarity over which questionnaires to use by recommending only those with evidence of high quality and robust psychometric validation data. This assurance provides the user with confidence in the results obtained. This is particularly important in clinical practice and research where treatment decisions or trial outcomes increasingly rely on this source of evidence. Increasing awareness of the ICIQ aims to promote increased usage of standardized questionnaires thereby facilitating communication and more widespread comparisons between different treatments and in different patient groups worldwide.

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18 Electronic Personal Assessment Questionnaire Pelvic Floor

Stephen Radley and Deepa Gopinath

BACKGROUND

Interest in questionnaire use in healthcare has largely been driven by the need for reliable and valid instruments for outcomes research. More recently, however, their use has now become a desirable, if not essential element in routine clinical practice [1]. This chapter explores the concept, development, and introduction of electronic assessment in urogynecology, aiming to bridge the divide between research use and day-to-day patient care.

Whereas electronic systems now provide integral elements in industries such as retail, finance, travel and communication; healthcare generally lags behind. Large-scale capital projects such as the National Health Service (NHS) National Programme for IT (now *Connecting for Health*) have proven to be long, complex, and expensive [2]. Paper-based recording systems are however increasingly recognized as being outdated, and change in this sector is gathering pace.

There is a growing enthusiasm for reducing the resource burden of questionnaire-based assessments using IT. Electronic data collection compares favorably with paper-based systems in terms of reliability and validity, with lower levels of missing data. Patients have found them relatively easy and even enjoyable to complete, offering efficiency advantages for large surveys [3,4]. When collecting sensitive data, computer-assisted interviewing results in greater openness and disclosure than paper-based questionnaires or face-to-face interviews [5–7]. These findings have implications for questionnaire use in urogynecology, both in research and clinical practice. Web-based and paper versions of the Pelvic Floor Distress Inventory-20 (PFDI-20), Pelvic Floor Impact Questionnaire-7 (PFIQ-7), and Pelvic Organ Prolapse/Urinary Incontinence Sexual Function Questionnaire (PISQ-12) have been compared and found to be reliable and with high correlations between the different formats [8,9]. The sample sizes in these studies were relatively small (n = 52), and although correlations were strong, differences were observed between different formats and not all patients were willing or able to use the electronic questionnaire. In the select sample of those who did use both formats, the majority expressed a preference for web-based completion.

PELVIC FLOOR QUESTIONNAIRES

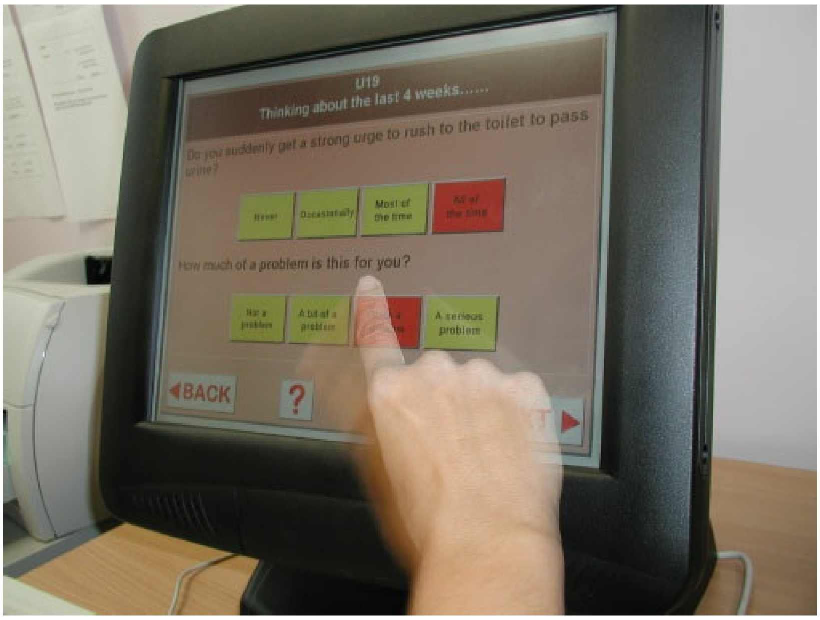
A range of questionnaires have been developed to measure and record symptomatology, conditions, health, and health-related quality of life in urogynecology. Such instruments have often been designed for a specific purpose or setting, the better established patient-reported outcome measures (PROMs) having been developed for research. Using questionnaires in direct clinical care presents substantially different challenges [10]. In order for a questionnaire to be clinically useful, it must be accessible, meaningful, and easy-to-use (both for patients *and* clinicians) as well as possessing demonstrable reliability, validity, and responsiveness. In order to inform clinical assessment, a questionnaire should ideally be completed *prior to* clinical consultation, although most condition-specific questionnaires are too narrow in their scope to be used in this way. Women with pelvic floor disorders commonly have interrelated problems, for example, bowel *and* urinary incontinence, incontinence prolapse, and prolapse *and* sexual dysfunction. This has driven the development of more generic urogynecology/pelvic floor questionnaires, covering a range of disorders. For these broader instruments, there is then a tension between the burden of providing sufficient detail and the lack of depth afforded by brevity.

DEVELOPMENT OF ELECTRONIC PERSONAL ASSESSMENT QUESTIONNAIRE: PELVIC FLOOR

The original concept for electronic Personal Assessment Questionnaire (ePAQ) arose from a desire to harness the accuracy and reliability of well-designed questionnaires in clinical practice, enhance communication, and provide in-depth, objective understanding of the patients' conditions. The aim was to utilize computer technology to provide an efficient, interactive, single instrument, addressing issues of feasibility faced with the use of paper questionnaires such as compliance, burden, and cost associated with entering, processing, and storing large volumes of clinical data (Figure 18.1) [11].

ePAQ was initially created as a web-based software application, using Microsoft Access® combined with Structured Query Language (SQL) server and dot Net programming to produce an interactive system for use on touch-screen computer terminals. The purpose-built Microsoft Access® "Q-Builder" software incorporated all the technical elements: physical layout and display (e.g., colors, buttons, and font sizes), item content, and response data. Active Server Pages provide dynamic and interactive elements, supporting a database interface with via SQL server that allowed data management on a single database. The system is forward-compatible with electronic data management software systems, allowing integration with other modalities such as new electronic results reporting and electronic patient records.

The initial prototype for electronic Personal Assessment Questionnaire: Pelvic Floor (ePAQ-PF) was based on existing paper-based questionnaires; Birmingham Bowel and Urinary Symptoms and Sheffield prolapse symptoms questionnaires were adapted and combined in a single instrument. Consultation with specialists in urology, gynecology, colorectal surgery, and sexual medicine identified additional items, whose format was unified to achieve consistency throughout. Subquestions on impact (as used in the ICS-Male and Bristol Female Lower Urinary Tract Symptoms Questionnaires) were included. Paper and electronic versions were reviewed by the local maternity user group who provided critical structured feedback. Psychometric testing was carried out in 432 patients in primary and secondary care [12]. Test–retest indicated good stability over time and patient acceptability was high. This was evaluated in terms of value and burden using a 10-item questionnaire (QQ-10), specifically designed for this purpose, and administered to patients immediately following their clinical episode [13]. ePAQ showed high value and low burden; most women find it relevant, valuable, and easy-to-use. Secondary factor analysis was carried out in a further 247 patients, confirmed the item content and 19-domain structure of the instrument now in clinical use, which was subsequently found to be responsive to change in women undergoing surgical intervention for incontinence and prolapse [14,15].



U19

Thinking about the last 4 weeks......

Do you suddenly get a strong urge to rush to the toilet to pass urine?

How much of a problem is this for you?

Figure 18.1 Touch-screen PC used in gynecology outpatient department. ePAQ was initially deployed in outpatient clinics using touch-screen terminals. The majority of patients now complete the questionnaire via the Internet. Women who are unable to complete online are invited to attend early in order to do complete the questionnaire using a touch-screen terminal, prior to their clinical consultation. This takes approximately 20 minutes.

QUESTIONNAIRE STRUCTURE AND CONTENT

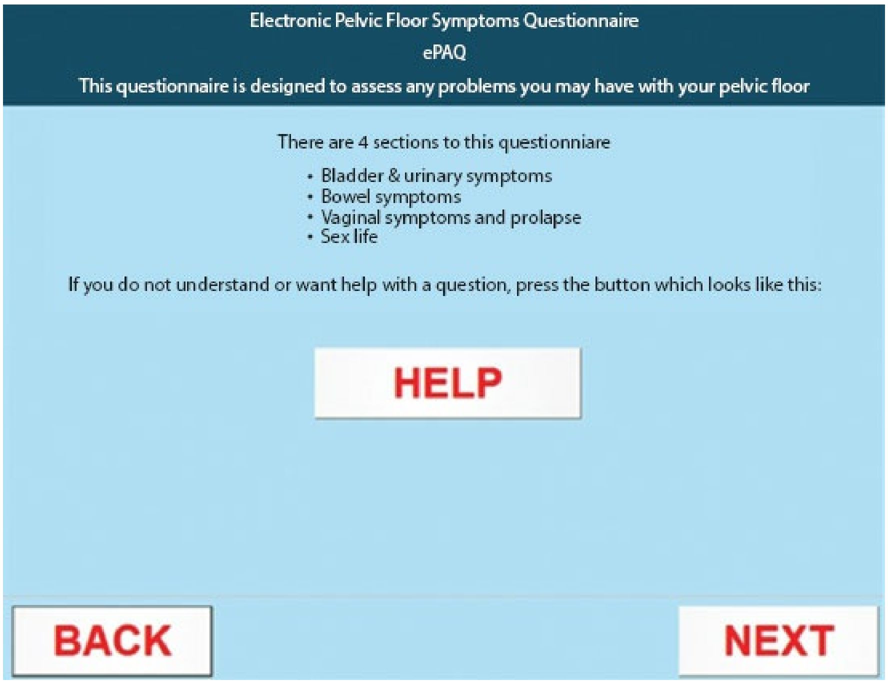
The main questionnaire section of ePAQ is preceded by introductory pages, which provide information about the system and instructions for unsupervised completion. The standard format presents one question per page, each of which includes its own “Help Page.”

Navigation through the questionnaire uses “Next” and “Back” buttons, with a “Skip” button allowing subjects not to answer a question, thereby eliminating accidental nonresponse—a fundamental problem with paper-based instruments (Figures 18.2 and 18.3).

The questionnaire automatically adapts responses to screening questions enabling skipping of nonrelevant items or sections, while more probing questions are presented when appropriate. Responses to key screening questions determine whether or not subsequent items are skipped, thereby minimizing burden (Figure 18.4). When subjects are asymptomatic, the number of questions is reduced, minimizing respondent burden. Conversely, symptomatic individuals undergo more detailed and relevant assessment.

The full questionnaire comprises 129 items, distributed across 4 dimensions: (1) urinary, (2) bowel, (3) vaginal, and (4) sexual (Figure 18.5). Within each dimension are four to five scored domains (19 in total), each comprising of three to seven items (questions). All items included in these domains are scored between 0 and 3. Domains themselves are scored by dividing the sum total of item response values by the maximum possible score and transforming this value onto a scale of 0 to 100 (0 indicating “Best” and 100 “Worst” health status). The 19 domains of ePAQ and a summary of their constituent items are shown in Table 18.1.

ePAQ is interactive on a number of levels. The standard item format includes a question on how often a symptom occurs (symptom frequency) and a subquestion on how much of a problem this is (symptom impact). These subquestions are also hidden if subjects are asymptomatic (screen negative).



Electronic Pelvic Floor Symptoms Questionnaire

ePAQ

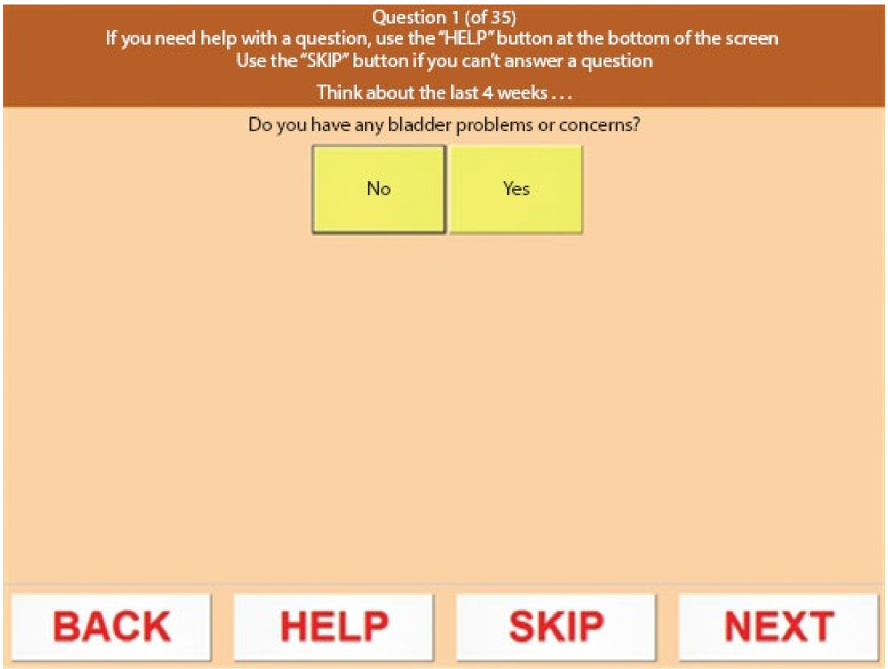
This questionnaire is designed to assess any problems you may have with your pelvic floor

There are 4 sections to this questionnaire

- Bladder & urinary symptoms
- Bowel symptoms
- Vaginal symptoms and prolapse
- Sex life

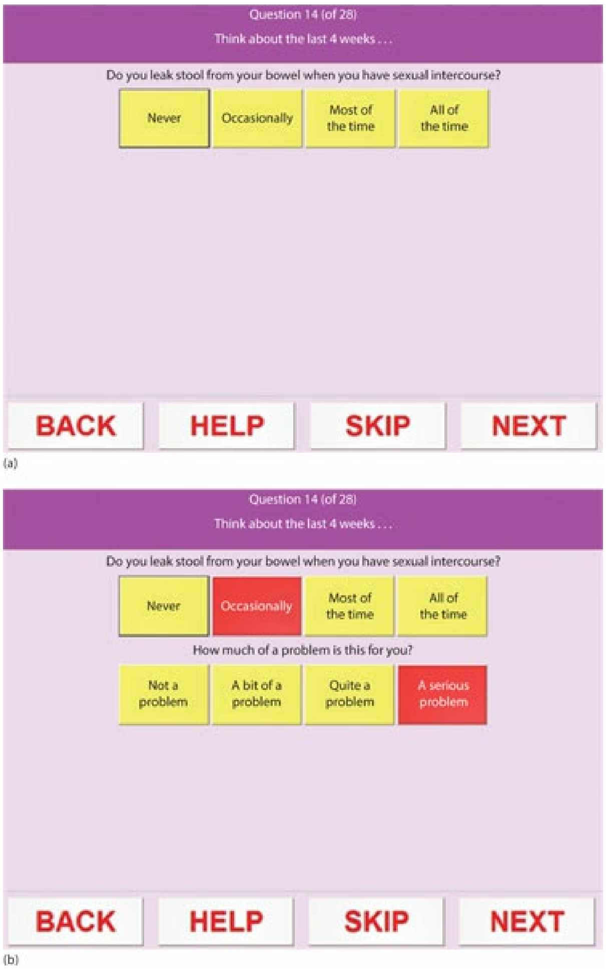
If you do not understand or want help with a question, press the button which looks like this:

Figure 18.2 Introductory page of ePAQ introduces subjects to the questionnaire and the use of “Back,” “Next,” and “Help” buttons to navigate through the questionnaire.


Question 1 (of 35)
If you need help with a question, use the "HELP" button at the bottom of the screen
Use the "SKIP" button if you can't answer a question
Think about the last 4 weeks . . .

Do you have any bladder problems or concerns?

Figure 18.3 ePAQ screening item with navigation buttons "Back, Help, Skip, and Next." Screening items such as this contribute to inbuilt skipping rules, reducing respondent burden, while allowing the questionnaire to probe symptomatic areas or concerns.


Question 14 (of 28)
Think about the last 4 weeks . . .

Do you leak stool from your bowel when you have sexual intercourse?

Question 14 (of 28)
Think about the last 4 weeks . . .

Do you leak stool from your bowel when you have sexual intercourse?

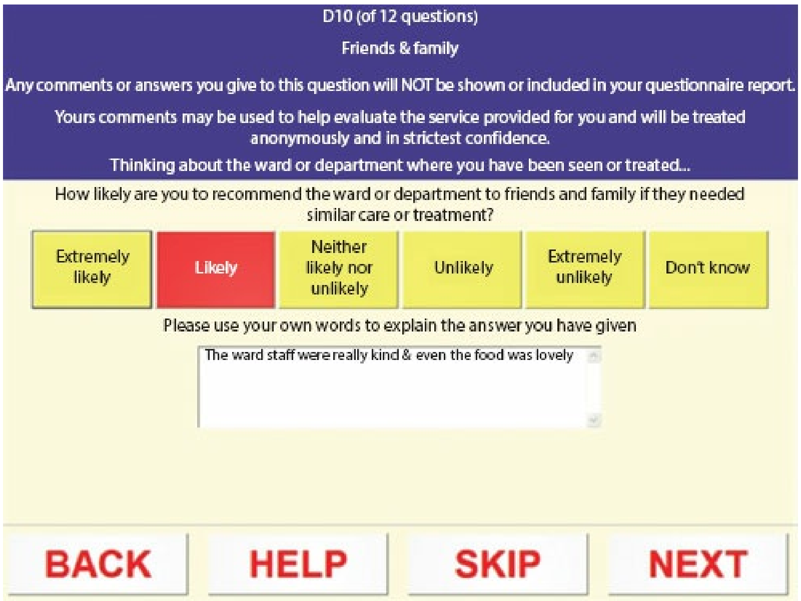
How much of a problem is this for you?

Figure 18.4 (a) Example of ePAQ item, illustrating its simple 4-point scale with standard question and response formats. (b) The questionnaire is interactive on a number of levels; when subjects report symptoms, a sub-question on impact “How much of a problem is this for you?” is shown.

The “friends and family test” has recently been incorporated, giving patients the opportunity to provide feedback on the care that they have received (Figure 18.5). The final item records patients’ willingness for their data to be used for nonclinical purposes, such as service evaluation and audit; 95% of patients agree to this (Figure 18.6).

REPORTS AND PROGRESS REPORTS

On completion, a summary ePAQ report is available, which can be viewed on screen or printed as a PDF. This presents summary data and 19 domain scores on one page, as well as a detailed report that includes responses to individual items, with a further page for each dimension. The clock face icons adjacent to the domain scores provide a visual measure of the *maximum* impact associated with any one of the constituent items of that domain: an empty circle; ○ = “Not a problem,” one-third of a full circle; ◔ = “A bit of a problem” two-thirds fill; ◕ = “Quite a problem” and a solid circle;●= “A serious problem” (Figure 18.7).



D10 (of 12 questions)

Friends & family

Any comments or answers you give to this question will NOT be shown or included in your questionnaire report.

Yours comments may be used to help evaluate the service provided for you and will be treated anonymously and in strictest confidence.

Thinking about the ward or department where you have been seen or treated...

How likely are you to recommend the ward or department to friends and family if they needed similar care or treatment?

Likely

Please use your own words to explain the answer you have given

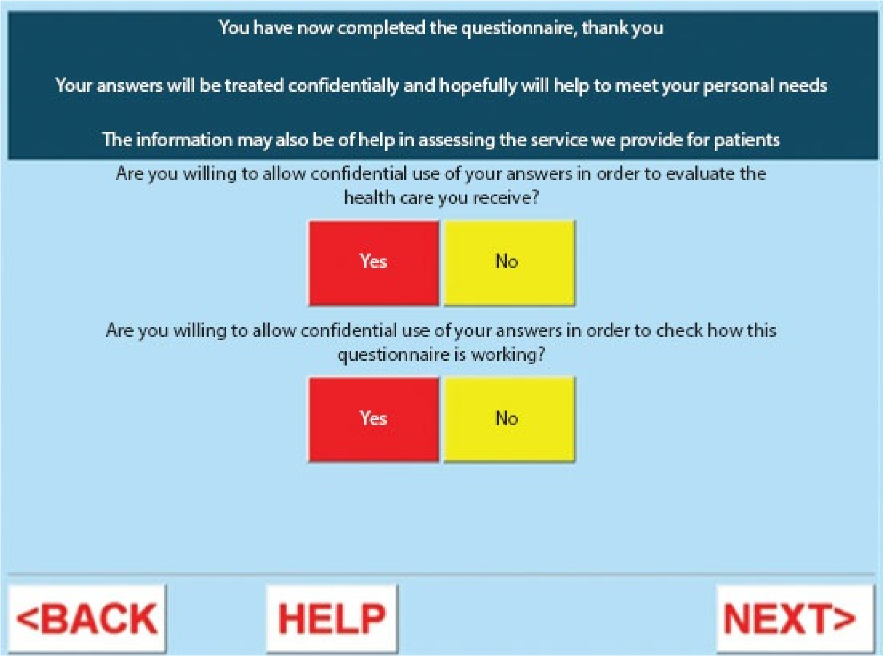
The ward staff were really kind & even the food was lovely

Figure 18.5 NHS friends and family test. Data from this item are not shown in the ePAQ report but are stored on the database, thereby facilitating collection of information that may be of value in service evaluation, appraisal, and revalidation.

Table 18.1 Domains of ePAQ

Domains	**Summary of Individual Items**
Urinary	
Pain	Bladder pain, burns with void, void relieves pain, reduced sensation
Voiding	Difficult voiding/void incomplete/strains to void/reduced stream/digitation to void
Overactive bladder	Urgency/urgency incontinence/hand wash incontinence/key in the door incontinence
Stress incontinence	Cough incontinence/sneeze/exercise/movement/walk
Quality of life	Impact on overall enjoyment of life/physical activities/social activities
Bowel	
IBS	Stool variability/regularity/pain pre-defecation/mucus or slime/bloating
Constipation	Stool hard/frequency/laxative use
Evacuation	Incomplete evacuation/straining/painful evacuation/duration of evacuation/perineal splinting/anal

	digitation/unable to evacuate
Continence	Incontinence liquid stool/flatus/solid stool/incontinence without warning/urgency/incontinence with urgency/ability to defer
Quality of life	Impact on overall enjoyment of life/physical activities/social activities
Vaginal	
Pain and sensation	Dryness, soreness/reduced sensation/dragging pain
Capacity	Tight entrance/tight inside/shortness
Prolapse	Something coming down/laxity/awareness of lump/complete prolapse
Quality of life	Impact on overall enjoyment of life/physical activities/social activities
Sexual	
Urinary	Incontinence during sex, avoids sex c/o bladder, partner avoids c/o bladder, bladder worries and sex, overall impact on sex
Bowel	Incontinence during sex, avoids sex c/o bowel, partner avoids c/o bowel, bowel worries and sex, overall impact on sex
Vaginal	Pain/discomfort and sex, avoids sex c/o vagina, partner avoids c/o vagina, vaginal worries and sex, overall impact on sex
Dyspareunia	Dryness/lack of sensation/discomfort and pain/tightness/obstruction
General sex life	Overall problems/loss of libido/satisfied overall/own health and sex/partner health and sex



You have now completed the questionnaire, thank you

Your answers will be treated confidentially and hopefully will help to meet your personal needs

The information may also be of help in assessing the service we provide for patients

Are you willing to allow confidential use of your answers in order to evaluate the health care you receive?

Yes No

Are you willing to allow confidential use of your answers in order to check how this questionnaire is working?

Yes No

Figure 18.6 Consent item—95% of patients agree to their data being used for nonclinical purposes, thereby enabling an ethical approach to activities such as audit and service evaluation.

When patients repeat ePAQ following intervention, consecutive questionnaires can be presented in a single *progress report*. The patient’s response to a *global rating of change* item is also highlighted at the top of this report. These data facilitate real-time outcomes monitoring for individual patients and are a key element in “Virtual Clinics” where ePAQ is combined with telephone consultation, for example, following incontinence or prolapse surgery or for women undergoing intravesical botulinum treatment for overactive bladder and again, if and when symptoms recur over time (Figure 18.8).

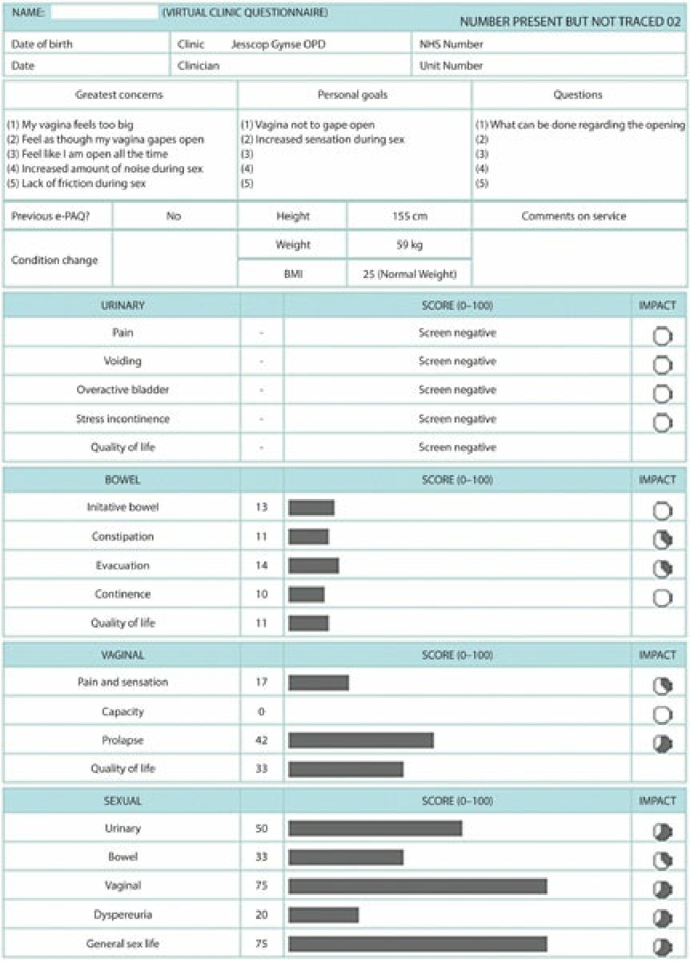
INTERNET COMPLETION

When originally introduced, ePAQ was exclusively used on touch-screen computer terminals used in clinics, substitute for keyboard and mouse. However, the majority of ePAQ users now complete the questionnaire via the Internet, linked to individual Trust-based installations on the NHS-N3 network.

All online data are collected anonymously and transferred to the NHS-N3 ePAQ database, where data are personalized and stored. Access to patient data is only possible for NHS registered users, each with their own username and password. Vouchers for online completion of ePAQ are issued by clerical, admin, or clinical staff, all of whom have personal logins. The system generates a unique voucher code for each patient, embedded in a preformatted letter, which can be printed, posted, or emailed. The voucher letter provides information about ePAQ and how to use it and can be modified to suit individual clinics or settings (Figure 18.9). Vouchers are issued to postoperative patients at the time of discharge from the ward, with instructions to complete the questionnaire via the Internet (http://www.epaq-voucher.co.uk) in advance of their next appointment. Most women, who have given the option of attending outpatients or the virtual clinic, choose the latter.

DEPLOYMENT

The feasibility of questionnaire use involves an understanding of the resources required to effectively deploy the instrument in a specific setting, achieving acceptable levels of compliance, value, and burden for patients and clinicians [17]. Ease of administration and interpretation is the key element in this, as well as overall cost, which should include societal and personal costs, and environmental issues such as travel. Generally though, Trusts are the most interested in institutional costs. With large-scale deployment, electronic questionnaires may offer economic advantages compared with facsimile and scanning scoring methods [4]. Costs include the supply and maintenance of hardware such as touch-screen terminals, labor costs, and software licensing and support. Current research is examining the health economic impact of ePAQ in different clinical settings, virtual clinics, and long-term follow-up of patients following surgery (Figure 18.10).



NAME: (VIRTUAL CLINIC QUESTIONNAIRE)

NUMBER PRESENT BUT NOT TRACED 02

Date of birth	Clinic Jesscop Gynse OPD	NHS Number
Date	Clinician	Unit Number

Greatest concerns	Personal goals	Questions
(1) My vagina feels too big (2) Feel as though my vagina gapes open (3) Feel like I am open all the time (4) Increased amount of noise during sex (5) Lack of friction during sex	(1) Vagina not to gape open (2) Increased sensation during sex (3) (4) (5)	(1) What can be done regarding the opening (2) (3) (4) (5)

Previous e-PAQ?	No	Height	155 cm	Comments on service
Condition change		Weight	59 kg	
		BMI	25 (Normal Weight)	

URINARY		SCORE (0–100)	IMPACT
Pain	-	Screen negative	○
Voiding	-	Screen negative	○
Overactive bladder	-	Screen negative	○
Stress incontinence	-	Screen negative	○
Quality of life	-	Screen negative	

BOWEL		SCORE (0–100)	IMPACT
Initative bowel	13		○
Constipation	11		◔
Evacuation	14		◔
Continence	10		○
Quality of life	11		

VAGINAL		SCORE (0–100)	IMPACT
Pain and sensation	17		◔
Capacity	0		○
Prolapse	42		◑
Quality of life	33		

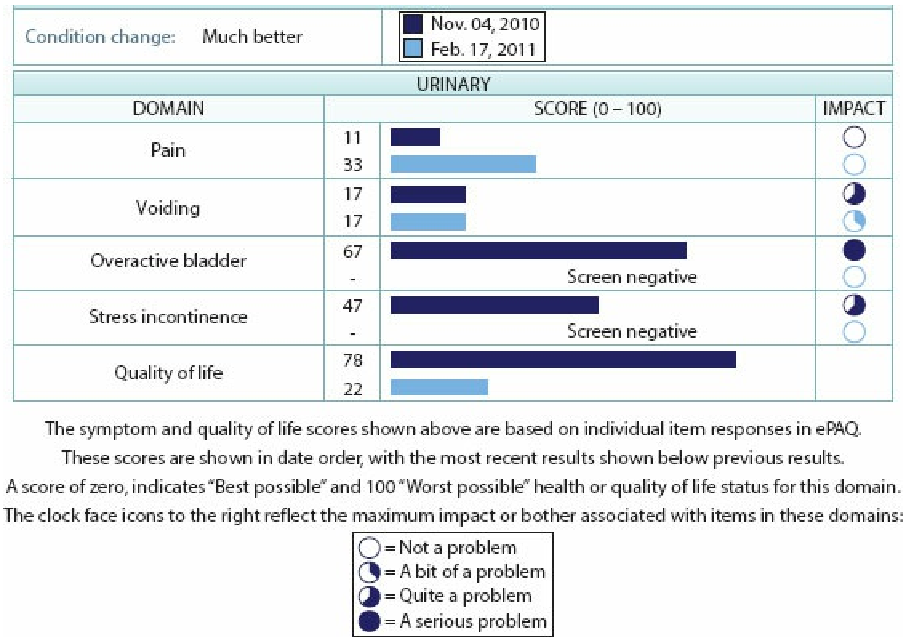
SEXUAL		SCORE (0–100)	IMPACT
Urinary	50		◑
Bowel	33		◔
Vaginal	75		◑
Dyspereuria	20		◑
General sex life	75		◑

Figure 18.7 Summary report.

CLINICAL DECISION-MAKING

The ePAQ report serves as an adjunct to clinical evaluation—recording, processing, and relaying sensitive information relating to patients' own views of their condition. The consultation may be better informed, more efficient and effective as a result. Surveys of patients' views commonly find that patients find the questionnaire that allows them to focus on problems that concern them, often in areas that are difficult to discuss openly, such as fecal incontinence and sexual dysfunction. The inclusion of free text items relating to patients' personal goals enables the collection of qualitative data and a degree of self-expression beyond the scope of closed multiple choice questions. ePAQ reports are used alongside other information, such as frequency volume chart data, urodynamic findings, and clinical correspondence, to inform consultation, discussion, and decision-making (Figure 18.11).

The questionnaire helps to differentiate and measure related conditions such as constipation and obstructed defecation, dyspareunia and prolapse, and stress and urge incontinence. This has proved particularly valuable in deciding whether or not urodynamic investigation is required prior to incontinence surgery. An overview of global pelvic floor health helps in managing expectations in patients with multiple conditions, for example, informing discussion regarding outcomes for overactive bladder symptoms in women undergoing stress incontinence surgery.



Condition change: Much better

■ Nov. 04, 2010
■ Feb. 17, 2011

URINARY

DOMAIN	SCORE (0 – 100)		IMPACT
Pain	11 33		○ ○
Voiding	17 17		◑ ◔
Overactive bladder	67 -	Screen negative	● ○
Stress incontinence	47 -	Screen negative	◑ ○
Quality of life	78 22		

The symptom and quality of life scores shown above are based on individual item responses in ePAQ.
These scores are shown in date order, with the most recent results shown below previous results.
A score of zero, indicates "Best possible" and 100 "Worst possible" health or quality of life status for this domain.
The clock face icons to the right reflect the maximum impact or bother associated with items in these domains:

○ = Not a problem
◔ = A bit of a problem
◑ = Quite a problem
● = A serious problem

Figure 18.8 Progress report used to assess following intravesical botox in overactive bladder.

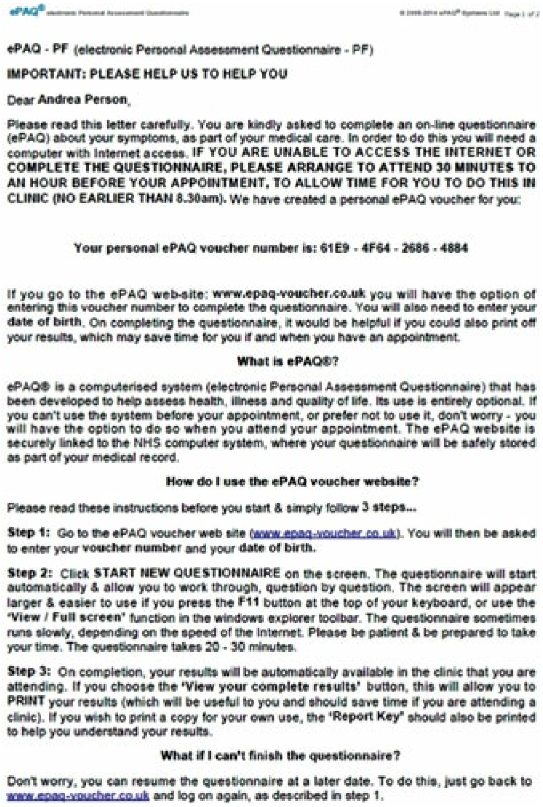
Pressures on clinical time can result in important issues such as fecal incontinence being overlooked in women with urinary incontinence, dyspareunia, and vaginal dryness not being considered in women with prolapse. The impact of symptoms shown alongside domain scores assists in prioritizing key areas from the patient's perspective; for example, some women with prolapse may be relatively asymptomatic or unbothered by prolapse-related symptoms and not requiring treatment. Women with dyspareunia and sexual dysfunction may be more appropriately prescribed Hormone Replacement Therapy than prolapse surgery. In relation to functional bowel problems, differentiating between obstructive defecation and constipation is important in women with rectocele. Measuring these parameters routinely, before and following intervention in larger cohorts of patients can provide greater insight into the impact that surgery for prolapse and incontinence has on wider aspects of pelvic floor function [16–19].

CLINICAL PATHWAYS

Ultimately, the use of this technology is likely to lead to increasing devolvement of patient care from secondary to primary care. Well-informed and targeted referrals for patients not responding to conservative measures enable the initiation of appropriate treatment via streamlined pathways. When used earlier in the care pathway, this may help with triage to appropriate services, for example, to physiotherapy for women with stress incontinence or to joint colorectal—urogynecology service for women with urinary and fecal incontinence. Greater use in primary care may support initial evidence-based management by GPs and other primary care clinicians, while facilitating and supporting integrated care with a single assessment tool throughout primary, secondary, and tertiary care, as well as across specialties such as urology, colorectal surgery, and urogynecology. When implementing new treatment modalities, such as percutaneous tibial nerve stimulation, having a PROM embedded in routine clinical care facilitates service evaluation in different areas using standard outcome measure [20]. Similarly, the routine collection of outcomes data is now mandatory for a number of urogynecological procedures and the British Society of Urogynaecology (BSUG) database now includes the option of entering ePAQ data in this context [21].

MULTIDISCIPLINARY TEAM WORKING

In women with recurrent or complex presentations (for example, coexistent urinary, colorectal, vaginal, and sexual problems), an objective and valid measure of all aspects of pelvic floor symptoms and their impact are extremely valuable. This may be particularly relevant in multidisciplinary case discussions, in related correspondence, and when coordinating and prioritizing a multidisciplinary approach. ePAQ enables a patient-focused approach to multidisciplinary team discussions, providing a comprehensive profile of symptoms and health-related quality of life for reference among other measures of health such as urodynamics, history, and physical findings.



ePAQ - PF (electronic Personal Assessment Questionnaire - PF)

IMPORTANT: PLEASE HELP US TO HELP YOU

Dear **Andrea Person**,

Please read this letter carefully. You are kindly asked to complete an on-line questionnaire (ePAQ) about your symptoms, as part of your medical care. In order to do this you will need a computer with Internet access. **IF YOU ARE UNABLE TO ACCESS THE INTERNET OR COMPLETE THE QUESTIONNAIRE, PLEASE ARRANGE TO ATTEND 30 MINUTES TO AN HOUR BEFORE YOUR APPOINTMENT, TO ALLOW TIME FOR YOU TO DO THIS IN CLINIC (NO EARLIER THAN 8.30am).** We have created a personal ePAQ voucher for you:

Your personal ePAQ voucher number is: 61E9 - 4F64 - 2686 - 4884

If you go to the ePAQ web-site: **www.epaq-voucher.co.uk** you will have the option of entering this voucher number to complete the questionnaire. You will also need to enter your **date of birth**. On completing the questionnaire, it would be helpful if you could also print off your results, which may save time for you if and when you have an appointment.

What is ePAQ®?

ePAQ® is a computerised system (electronic Personal Assessment Questionnaire) that has been developed to help assess health, illness and quality of life. Its use is entirely optional. If you can't use the system before your appointment, or prefer not to use it, don't worry - you will have the option to do so when you attend your appointment. The ePAQ website is securely linked to the NHS computer system, where your questionnaire will be safely stored as part of your medical record.

How do I use the ePAQ voucher website?

Please read these instructions before you start & simply follow **3 steps...**

Step 1: Go to the ePAQ voucher web site (www.epaq-voucher.co.uk). You will then be asked to enter your **voucher number** and your **date of birth.**

Step 2: Click **START NEW QUESTIONNAIRE** on the screen. The questionnaire will start automatically & allow you to work through, question by question. The screen will appear larger & easier to use if you press the **F11** button at the top of your keyboard, or use the **'View / Full screen'** function in the windows explorer toolbar. The questionnaire sometimes runs slowly, depending on the speed of the Internet. Please be patient & be prepared to take your time. The questionnaire takes 20 - 30 minutes.

Step 3: On completion, your results will be automatically available in the clinic that you are attending. If you choose the **'View your complete results'** button, this will allow you to **PRINT** your results (which will be useful to you and should save time if you are attending a clinic). If you wish to print a copy for your own use, the **'Report Key'** should also be printed to help you understand your results.

What if I can't finish the questionnaire?

Don't worry, you can resume the questionnaire at a later date. To do this, just go back to www.epaq-voucher.co.uk and log on again, as described in step 1.

Figure 18.9 ePAQ voucher, embedded in automatically generated letter, which can be edited to suit the specific requirements of the clinic. These voucher letters are issued by clerical staff and sent or given to patients along with their appointment details.

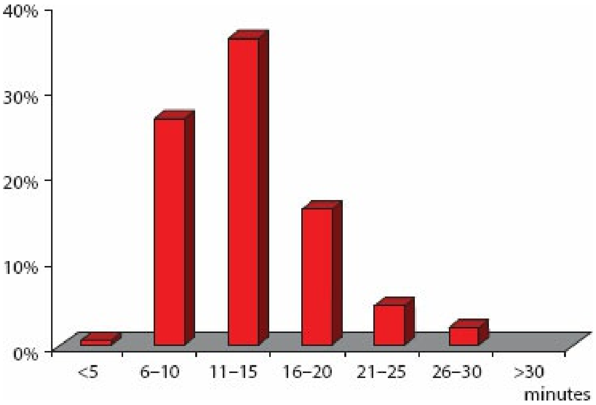


Figure 18.10 Completion times for ePAQ using touch-screen terminals in gynecology outpatients. Although the median completion time was 15 minutes, many patients take considerably longer than this and some require assistance from clinical staff or carers, which is recorded in the questionnaire.

VIRTUAL CLINICS

The Virtual Urogynaecology Clinic (VUC) combines electronic interviewing using ePAQ-PF with telephone consultation. Initial evaluation of VUC has shown high-patient satisfaction and acceptability, particularly in relation to communication and access. Early experience indicates the potential for improved efficiency as well as quality of care, particularly for follow-up patients. Patients generally find the system easy and rewarding to use. Women, given the option of attending the outpatient clinic or virtual clinic following prolapse surgery, most commonly choose the latter.

Surveys of ePAQ users in a number of units have identified the need to provide local administrative support, staff training justification of costs, and adequate patient completion time for those who are unable or unwilling to complete the questionnaire online. Informing patients of the value and importance of questionnaire completion, both before and following, was felt to be important, as was the need for adequate resources and staff education in achieving this. Qualitative evaluation of patient experience of ePAQ suggested that women felt that the questionnaire improved their understanding of their condition; improved communication with clinicians and preparedness for clinical consultation appeared to support improved focus and insight, which in turn contributed to the setting of realistic expectations [22].

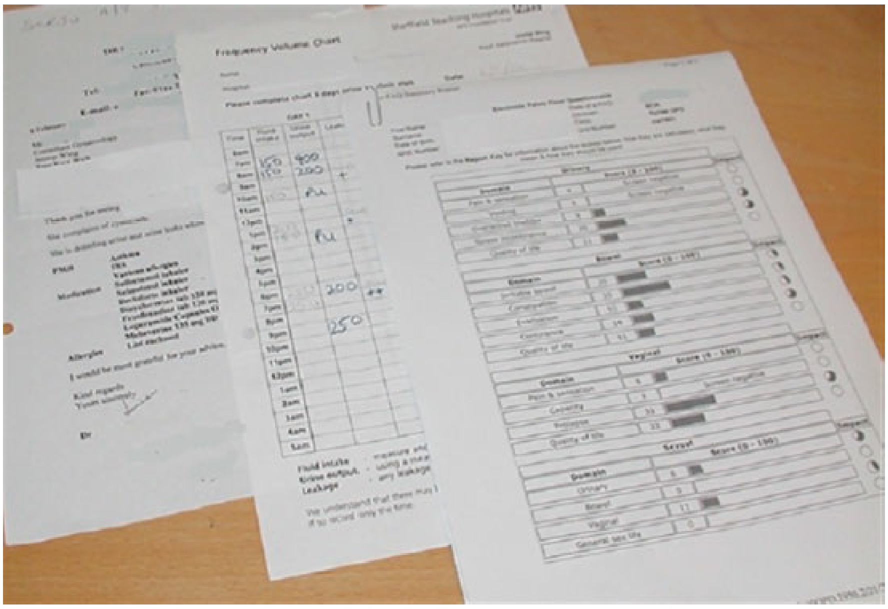


Figure 18.11 New patients in urogynecology usually precomplete ePAQ and frequency volume charts prior to consultations. When combined with referral letters, these elements provide significant insight into the

patient's condition, enabling a focussed and effective consultation.

Multisite survey data have shown that between 72% and 85% of women attending urogynecology clinics had internet access and 60%–80% of women will complete ePAQ online when posted a voucher letter accompanying their first clinic appointment. Attempts to improve response rates include the use of reminders and explanatory letters, using higher font size (12) and the use of colored, headed paper for correspondence. Emphasizing the value to patients themselves and encouraging active participation and engagement (rather than passive acceptance) in their own health and healthcare may have additional benefits, for both patients and providers. Although levels of connectivity and computer literacy have increased substantially in recent years, increasing age and low socioeconomic status remain important barriers, though being female is a consistent positive predictor of eHealth use [23]. Women may seek the help of family members or close friends, though this may impact on the accuracy of data provided.

OTHER INSTRUMENTS

ePAQ® is currently being used in 15 units in the United Kingdom. There is an interest in developing questionnaires for other clinical areas and conditions; a generic platform questionnaire builder now supports the development of instruments in a variety of fields. A number of additional prototype questionnaires such as preoperative assessment (ePAQ-PO), menstrual, pain, and hormonal (ePAQ-MPH), and ePAQ-Vulva have been created and are currently being evaluated to establish their clinical utility, validity, and reliability.

CONCLUSIONS

The primary goals of interventions for pelvic floor disorders are the relief of symptoms, restoration of function, and improvement in quality of life. A responsive patient-based measure of health as well as symptom severity and impact is a valuable addition in this context, providing initial assessment and patient-based measure of outcome, presented in a meaningful way. There is evidence that for sensitive issues, computer-assisted interviewing can enhance disclosure and openness. In recent years, IT literacy and access to and sophistication of electronic systems have advanced substantially, now making electronic interviewing in healthcare an increasingly realistic option, with a shift toward greater use of eHealth and online assessments. Long-term follow-up using this technology is currently being evaluated. Addressing issues of access and compliance, particularly for patients with low socioeconomic status and advancing age is an important challenge. The overall impact on provider costs, patient experience, the quality of healthcare provision, and subsequent outcomes is demanding of further research.

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19

Questionnaires to Assess Pelvic Organ Prolapse

Alex Digesu

EPIDEMIOLOGY

Pelvic organ prolapse (POP) is a common finding especially in parous women who have delivered vaginally. It has been calculated that up to 50% of parous women have some degree of POP, but only 10%–20% seek help for their condition [1]. The prevalence of POP is not well known as the data reported vary significantly according to the criteria utilized in various studies, ranging from 3% to 50%. In fact, POP when defined by symptoms has a prevalence of 3%–6%, and it rises up to 50% when based upon vaginal examination [2].

The risk of developing POP increases significantly with age and parity [3,4]. It has been estimated that up to 40% of women more than 50 years of age are affected by POP [5]. Considering that the women life expectancy is increasing, the prevalence of POP will increase significantly in the future years. By 2050, the number of women suffering from symptomatic POP in the United States is expected to increase by a minimum of 46% [6].

It has been calculated that surgery for POP is performed twice as commonly as continence surgery with a lifetime risk of undergoing prolapse repair of about 11% [7]. The prevalence of POP surgery varies from 6% to 18%, and the incidence ranges from 1.5 to 1.8 per 1000 women [1].

Bladder, bowel, and sexual symptoms are often associated with POP. Ellerkmann et al. found that in 237 women with POP, 73% had urinary incontinence (UI), 86% urgency and/or frequency, 34%–62% voiding difficulties, and 31% fecal incontinence. In view of the high prevalence of these associated symptoms, it is essential to fully evaluate the bladder, bowel, and sexual function while assessing women with POP [8].

Although POP and its associated symptoms are not life threatening, they may have a significant impact on quality of life (QoL) causing physical, social, psychological, role, domestic, personal, and/or sexual limitations [9,10].

Therefore, in recent years more attention has been paid to the complex relationships between POP and its often coexisting symptoms as well as on the impact of POP on women's QoL. It has been reported that there is a significantly weak to moderate correlation between the degree of POP, poor QoL, and severity of bladder, bowel, and sexual symptoms. However, the data reported in the literature are still controversial [2,8,11–15]. Finally, the postoperative QoL and patient's satisfaction with prolapse surgery are not correlated with a postoperative anatomical success alone but improve significantly only if the symptoms disappear and/or improve [16].

QUESTIONNAIRES

The evaluation of women with POP entails a complete assessment of all pelvic floor dysfunctions. The only valid way of measuring the severity of symptoms and their impact on QoL is through the use of psychometrically robust self-completed questionnaires [10,17–21].

Therefore, in the last decade, the evaluation of QoL in women with POP using validated self-completed questionnaires has become more popular in both clinical and research settings as the most important treatment goal for women has been shown to be the relief of symptoms and the improvement of their QoL [2,16]. It has also been suggested that QoL should be considered as an end point in all clinical trials [22].

Several validated and reliable generic as well as condition-specific health-related QoL (HRQoL) questionnaires have been described to assess POP to date [10,17–24]. Their use in clinical practice has also been recommended in the recent joint report of the International Continence Society (ICS) and International Urogynecological Association (IUGA) (grade C) [23,24].

In 2005, the Symptom and Quality of Life Committee of the International Consultation on

Incontinence (ICI) performed a systematic review of questionnaires related to urinary/anal incontinence, vaginal, and pelvic floor problems and concluded that "although considerable advances have been made in the assessment of urinary incontinence with 18 questionnaires now achieving the highest level (grade A) of scientific rigor, the development of questionnaires in the area of anal incontinence, vaginal and pelvic floor problems was at a much earlier stage." None of those could be considered as highly recommended (grade A); only two questionnaires were considered of established validity and reliability and consequently included in the grade B area; five of them were considered in the early stages of development and considered as grade C [25]. A summary of the questionnaires used to assess women with POP is shown in Table 19.1.

Pelvic Floor Distress Inventory and Pelvic Floor Impact Questionnaire

The *Pelvic Floor Distress Inventory* (PFDI) and *Pelvic Floor Impact Questionnaire* (PFIQ) were developed in 2001 by Barber et al. [17,18]. These questionnaires evolved from two questionnaires designed to evaluate the impact of UI on QoL: the *Urogenital Distress Inventory* (UDI) and the *Incontinence Impact Questionnaire* (IIQ) [26,27].

The PFDI was designed to evaluate the symptom distress or bother in women with pelvic floor dysfunction. It includes all of the items of the original UDI questionnaire and has additional questions related to POP and colorectal dysfunction. The PFDI contains 46 items divided into three domains: (1) UDI (28 items), (2) Colorectal–Anal Distress Inventory (CRADI) (17 items), and (3) POP Distress Inventory (POPDI) (16 items).

Table 19.1 Summary of the Questionnaires used to Assess Women with POP

Questionnaire	Purpose	No. of items	Domains	Scoring system
PFDI	To measure degree of bother and distress caused by pelvic floor dysfunction	46	3 scales Urogenital Distress Inventory Colorectal–Anal Distress Inventory	Each scale: 0 (least distress) to 100 (greatest distress)
PFDI-20 (short form)		20	POP Distress Inventory	
PFIQ	To assess the impact of the pelvic floor disorders on women's life	93	3 scales Urinary Impact Questionnaire POP Impact Questionnaire	Each scale: 0 (least impact) to 100 (greatest impact)
PFIQ-7 (short form)		7	Colorectal–Anal Impact Questionnaire	
P-QoL	1. To assess POP symptoms severity 2. To evaluate QoL of women with POP 3. To better identify those women needing treatment 4. To assess the treatment outcome of women with POP	20	General health perceptions Prolapse impact Role limitations Physical limitations Social limitations Personal relationships Emotions Sleep/energy Severity measures	Each item: four-point Likert Scale—"none/not at all," "slightly/a little," "moderately," and "a lot" Scoring system each domain score: 0–100 Higher scores: poor QoL

ICIQ-VS	ICI module to assess the severity of POP symptoms (vaginal and sexual), to measure their impact on QoL, and to evaluate the treatment outcome	27	Vaginal symptoms	0–53 vaginal symptoms subscale
Sexual matters	0–58 sexual matters subscale			
Final version		14	Impact of vaginal symptoms on QoL 2 additional introductive filter questions	0–10 overall impact on quality of life subscale Higher scores: poor QoL
POP-SS	To measure primary outcome of POP treatments	7	Feeling of something coming down from the vagina? Vaginal pain worse when standing? Heaviness in lower abdomen? Heaviness in lower back? Need to strain to empty your bladder? Bladder voiding incomplete? Bowel voiding incomplete?	Five-point Likert scale Total score (range 0–28) calculated by summing the seven individual scores
PFDQ	To compare symptoms related to pelvic floor dysfunctions with the location and severity of the coexisting POP	65	8 domains UI Irritative urinary symptoms Voiding dysfunction POP Fecal incontinence Defecatory dysfunction Pelvic pain Sexual dysfunction	Likert scale to quantify the severity (none, 0; minimally, 1; moderately, 2; severely, 3), the duration of symptoms (never, 0; <25% of time, 1; <50% of time, 2; <75% of time, 3; 100% of time, 4), and the impact on QoL

Abbreviations:PFDI, Pelvic Floor Distress Inventory; PFIQ, Pelvic Floor Impact Questionnaire; P-QoL, Prolapse Quality of Life; ICIQ-VS, International Consultation on Incontinence—Vaginal Symptoms; POP-SS, Pelvic Organ

Prolapse–Symptom Score; PFDQ, Pelvic Floor Dysfunction Questionnaire; DPQ, Danish Prolapse Questionnaire; PISQ, Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire; ePAQ-PF, electronic Personal Assessment—Pelvic Floor; APFQ, Australian Pelvic Floor Questionnaire; VAS, visual analog scale; PGI-I, Patient Global Impression of Improvement.

The PFIQ was designed to assess the impact of the pelvic floor disorders on women's life. Similar to PFDI, it contains all the items included in the original IIQ and has additional items related to other pelvic floor dysfunction. In all, the PFIQ has 93 items divided into three domains: (1) Urinary Impact Questionnaire, (2) POP Impact Questionnaire, and (3) Colorectal–Anal Impact Questionnaire.

PFDI and PFIQ have shown good validity and reliability (both content and construct). Despite the strengths of these two complementary questionnaires, their comprehensive nature and relative length (23 minutes to be completed) may be inefficient and impractical in the clinical practice. Therefore, the same authors developed and validated the shorter versions 4 years later [7]. The PFDI-20, which contained 20 items instead of 46, and the PFIQ-7, which included 7 items instead of 93, are short forms that maintained their excellent correlation with the PFDI and PFIQ long forms and have proved to be reliable and responsive to change. They have a 3-month recall period of symptom, thus being helpful instruments to use particularly when evaluating the outcomes of conservative therapy that may require some time to show any clinical benefit [17,18].

These instruments have been considered of great help in the evaluation of the largest spectrum of pelvic floor dysfunctions, ranging from POP to bladder and bowel disorders, which usually coexist. To date, these questionnaires have been translated into Korean, Spanish, Greek, Danish, Turkish, Swedish, and French [28–36].

Prolapse Quality of Life

The prolapse QoL (P-QoL) questionnaire was developed in 2004 by Digesu et al. in response to the necessity for a shorter and easier questionnaire able to investigate the severity of POP symptoms and their impact on women's QoL, which was missing in the PFDI and PFIQ [10].

P-QoL contains 20 questions divided into nine domains: general health (1 item), prolapse impact (1 item), role limitations (2 items), physical limitations (2 items), social limitations (3 items), personal relationships (2 items), emotional limitations (3 items), sleep/energy disturbance (2 items), and severity measurement (4 items). The structure is similar to the King's Health Questionnaire. The answers are categorized using a four-point Likert scale: "none/not at all," "slightly/a little," "moderately," and "a lot." A score is calculated for each domain ranging from 0 to 100. A higher score indicates a greater impairment of QoL or poor QoL.

In addition to the QoL items, the P-QoL also includes 18 symptom questions: 11 urogenital (bladder, sexual) and 7 bowel. The responses for those 18 questions are categorized using a five-point Likert scale: the same four options used for QoL items plus a "not applicable" option if the women do not have the symptom. These symptom questions do not compose any dimension or a score.

The P-QoL has been shown to be a valid, reliable self-completed questionnaire that is easy to understand and to complete. P-QoL domain scores have also been demonstrated to be significantly different between symptomatic and asymptomatic women, thus showing a good content reliability as well as being significantly higher (poor QoL) in women with more advanced/severe POP stages thus demonstrating a good construct reliability.

To date, the P-QoL has been cross-culturally translated and validated into several languages including English, Italian, Dutch, Thai, Slovakian, Portuguese, German, Turkish, Persian, Japanese, Spanish, and French and used in clinical as well as research practice. It is a useful tool: (1) to assess POP symptoms severity, (2) to evaluate QoL of women with POP, (3) to better identify those women needing treatment, and (4) to assess the treatment outcome of women with POP [10,37–45].

Pelvic Floor Dysfunction Questionnaire

The Pelvic Floor Dysfunction Questionnaire (PFDQ) was designed by Ellerkmann et al. [8] in 2001 to compare symptoms related to pelvic floor dysfunctions with the location and severity of the coexisting POP. This is a symptom-specific Likert scale questionnaire that included 65 questions that were assembled from commonly used validated instruments. The PFDQ is divided into eight domains, each related to a specific dysfunction. These domains include UI, irritative urinary symptoms, voiding dysfunction, POP symptoms, fecal incontinence, defecatory dysfunction, pelvic pain, and sexual dysfunction. A Likert scale is used both to quantify the severity (none, 0; minimally, 1; moderately, 2; severely, 3), the duration of symptoms (never, 0; <25% of time, 1; <50% of time, 2; <75% of time, 3; 100% of time, 4), and the impact on QoL. The authors tested this questionnaire on 237 women and concluded that (1) POP symptoms do not necessarily correlate with compartment-specific defects and (2) increasing severity of POP is weakly to moderately associated with urinary, defecatory, and sexual dysfunction [8]. The psychometric properties (validity and reliability) of this questionnaire have never been tested.

Danish Prolapse Questionnaire

The Danish Prolapse Questionnaire was developed and validated by Mouritsen and Larsen in 2003 to evaluate the symptom distress in women with POP [46].

It is a symptom-bother questionnaire that contains 34 questions divided into four domains: (1) mechanical symptoms, (2) lower urinary tract symptoms, (3) bowel symptoms, and (4) sexual symptoms. The severity of each symptom is graded according to frequency (1, never or less than once/month; 2, less than once/week; 3, once or more/week; 4. daily).

An additional four-point bother score was included to assess how each symptom affected QoL. The questionnaire was tested on 110 women with POP and symptom’s severity was compared to the POP stage.

Despite the frequency of bladder bowel and sexual dysfunctions in patients with POP and the related QoL impairment, this study failed to show any specific correlation between coexisting symptoms and POP location and severity.

The psychometric properties (validity and reliability) of this questionnaire have never been tested.

International Consultation on Incontinence Questionnaire: Vaginal Symptoms Questionnaire

The International Consultation on Incontinence Questionnaire–Vaginal Symptoms (ICIQ-VS) questionnaire was developed and validated by Price et al. [20] in 2006. It is a self-completed questionnaire designed as an ICI module to assess the severity of POP symptoms (vaginal and sexual), to measure their impact on QoL, and to evaluate the treatment outcome.

The ICIQ-VS questionnaire was originally structured into three domains including 14 items related to vaginal symptoms, 10 items related to sexual matters, a single question to evaluate the impact of vaginal symptoms on QoL, and 2 introductive filter questions. The scores range from 0 to 53 (vaginal symptom score), 0 to 58 (sexual matter score), and 0 to 10 (QoL score). A high score indicates greater impairment/poor QoL, while a low score indicates a good QoL. In view of the redundancy and overlapping of some items, the final version of the ICIQ-VS questionnaire was restricted to 14 items. It has been demonstrated to be a simple, reliable, valid, and widely applicable self-completed questionnaire able to measure the severity of vaginal and sexual symptoms in women with POP and to evaluate their impact on QoL. It has shown a high internal consistency (Cronbach’s alpha 0.70 and 0.84 for vaginal and sexual symptoms, respectively) and a good sensitivity to change.

Australian Pelvic Floor Questionnaire

The Australian Pelvic Floor Questionnaire can be used as a self- and/or interviewer-completed questionnaire. Both versions have been proved to be simple, easy to complete, valid, reliable, and sensitive to change [21,47]. They can be used in both clinical and research practice to evaluate all pelvic floor symptoms such as bladder, bowel, and sexual function, prolapse symptoms, symptom severity, impact on QoL, and symptoms bother. The self-completed version is preferred when evaluating the treatment outcome independently of health-care providers. The questions are grouped in four domains: bladder function (15 items), bowel function (12 items), prolapse symptoms (5 items), and sexual function (10 items). A four-point scoring system is used to assess the frequency, severity, and bothersomeness of pelvic floor symptoms for the majority of the items. Frequency of defecation, bowel consistency, lubrication, and sexual abstinence are excluded from the score.

The score for each of the four domains ranges between 0 and 10. The maximum total pelvic floor dysfunction score is 40 or 30 if a woman is not sexually active.

POP/UI Sexual Questionnaire

The POP/UI Sexual Questionnaire (PISQ) is a condition-specific, reliable, valid, and self-completed questionnaire designed and developed by Rogers et al. [48] in 2001 to assess sexual function in women with POP and/or UI. The PISQ contains 31 items categorized in three domains (subscales): (1) behavioral/emotive (15 items), (2) physical (10 items), (3) partner related (6 items). Responses are graded on a five-point Likert scale from “never” to “always.” The validation of the PISQ was a two-phase process including 83 and 99 women respectively. In phase 1, the PISQ scores were correlated with the IIQ-7 scores. In phase 2, the PISQ was compared with the Sexual History Form-12 (SHF-12). In view of the high correlation between domain scores of PISQ and IIQ-7 and SHF-12 scores, the authors concluded that PISQ is a valid, reliable, and useful instrument for the assessment of women with POP.

Two years later, Rogers et al. developed and validated the short form of the PISQ. The PISQ-12, which includes 12 items, revealed good to excellent correlation with PISQ-31 scores, good reliability, and reproducibility [49].

Electronic Personal Assessment Questionnaire: Pelvic Floor

The idea of an electronic Personal Assessment Questionnaire (ePAQ) by using a computer interview process started in 2008. The ePAQ–pelvic floor (ePAQ-PF) questionnaire was developed from the Birmingham Bowel and Urinary Symptoms Questionnaire (BBUSQ-22) [50], the Sheffield Prolapse Symptoms Questionnaire (SPSQ) [51], and the Female Sexual Function Index (FSFI) questionnaire [52].

The BBUSQ-22 is a 22-item questionnaire developed to assess patients with functional bowel and urinary symptoms.

The SPSQ specifically assesses symptom severity in women with anatomical and functional pelvic floor disorders. It is divided into four domains: (1) lump and pain, (2) bladder function, (3) bowel function, and (4) sexual function. It also includes a final evaluation of the impact of POP symptoms on women’s QoL.

The FSFI, a validated 19-item questionnaire, is developed as a multidimensional tool to evaluate female sexual function. It provides scores on six domains of sexual function (desire, arousal, lubrication, orgasm, satisfaction, and pain) as well as a total score.

The ePAQ-PF questionnaire was developed as a valid instrument to evaluate the impact of urinary, bowel, vaginal, and sexual symptoms on QoL. It also includes additional domains on dyspareunia and general sex life. ePAQ-PF includes four dimensions (urinary, bowel, vaginal, and sexual [each consisting of 35, 33, 22, and 28 items, respectively]) and 19 scored domains. All items score between 0 and 3 (0 indicating best and 3 indicating worst health status). These domain scores are calculated, by dividing the sum of all items in the domain by the total possible item score and multiplying this by 100, to produce a scale 0–100. A higher score indicates the worst possible health status. The “bothersomeness” of a symptom is scored using a four-point scale (0, not a problem; 1, a bit of a problem; 2, quite a problem; and 3, a serious problem).

A cross-sectional study was performed to assess the validity and reliability of the ePAQ-PF. A total of 599 women with pelvic floor disorders were studied. Internal reliability, levels of missing data, secondary factor analysis, floor and ceiling effects, descriptive statistics, item-to-total correlation scores, item discriminant, and convergent validity were measured. All 19 domains were internally reliable with Cronbach’s alpha scores ranging from 0.71 to 0.93. Missing response rates ranged from 0.2% to 1.3%. All items were found to be most highly correlated with their own corrected scale. Therefore, the authors concluded that the ePAQ-PF is a valid and reliable instrument to assess (1) the severity and bother of pelvic floor disorders, (2) the impact of pelvic floor disorders on women’s QoL, and (3) the treatment outcome [53,54].

The advantages of this computerized instrument are the reduction of missing data and the high satisfaction ratings, probably due to the greater privacy setting. Furthermore, ePAQ allows direct input of the data collected into a database, while paper-based questionnaires need to be entered manually onto the computer database.

Nevertheless, the cost of technology and the necessity of patient technological skills might be a limitation for the wide spread of the ePAQ-PF, especially considering that the majority of women with POP are elderly.

OTHER INSTRUMENTS TO ASSESS POP

Visual Analog Scale

A visual analog scale (VAS) is a highly repeatable method that was originally developed for the evaluation of pain. It has been recently adapted by urogynecologists as an easy method to use in the routine clinical practice to assess the severity of pelvic floor disorders, degree of bother, and the treatment outcome and satisfaction. Responders are asked to indicate the severity of their disease on a 10 cm VAS; 0 indicates no complaints, whereas 10 indicates unbearable symptoms. Although it cannot be compared to more complex validated questionnaires that investigate a wide range of symptoms, VAS score has shown to be a reliable tool to assess subjective impact of POP symptoms on QoL. In a recent study, Ulrich et al. [55] used a VAS to assess the degree of bother of POP. The authors studied 636 women with POP. VAS bother scores for POP symptoms were significantly associated with both clinical and ultrasound measures of pelvic organ descent. Therefore, the authors concluded that VAS is a valid, repeatable, and a simple tool to measure the POP bother in the clinical practice [55].

POP Symptom Score

The POP–Symptom Score (POP-SS) was designed and validated in 2008 by Hagen et al. to assess POP symptoms before and after treatment. It includes a set of key questions covering the symptoms caused or worsened by POP that could be used as outcome measures for randomized trials to compare different treatments of POP [56].

The POP-SS consists of seven items, each with a five-point Likert response set (0, never; 1, occasionally; 2, sometimes; 3, most of the time; and 4, all of the time). A total score (range 0–28) is calculated by summing the seven responses. An additional question to identify the symptoms that cause most bother is also included. The POP-SS has showed a good internal consistency (Cronbach's alpha 0.723–0.823), has showed good construct reliability, and is sensitive to change. To test its validity, the POP-SS was evaluated in three studies based on three different patient clusters: postpartum women, patients treated with pelvic floor muscle training (PFMT), and patients undergoing surgical repair of POP. Those studies demonstrated that POP-SS is a very useful instrument to measure treatment effectiveness [57].

Patient Global Impression of Improvement

The Patient Global Impression of Improvement (PGI-I) [58], originally described in 1976 (Clinical Global Impression), is a seven-point scale that may be used to rate the response of a condition to a therapy. PGI-I is a simple, direct, easy-to-use scale. It is a single-question, self-completed questionnaire that can be used in both clinical and research practice. The PGI-I measures the patient impression of improvement after treatment. It is rated as (1) very much improved, (2) much improved, (3) minimally improved, (4) no change, (5) minimally worse, (6) much worse, or (7) very much worse.

The PGI-I have been widely used in psychiatry and several other fields in medicine. Its validity and reliability has also been tested on women with stress UI. In 2009, Srikrishna et al. validated the PGI-I in women with POP and showed that it is a valid, reliable, and sensitive to change tool to assess in a simple manner the outcome of POP surgery [59].

POP Questionnaires in Clinical and Research Practice

QoL questionnaires have provided important insights for a better understanding of (1) impact of POP on daily life, (2) relationship between anatomical defects and coexisting symptoms, and (3) outcomes of various therapeutic modalities available to women with POP. A summary of the data reported in the literature is described in the following text.

POP Questionnaires and Pessary Usage

It has been demonstrated that the stage of POP does not determine the success of pessaries and therefore should not influence the clinical decision when choosing candidates for pessary use [60]. QoL questionnaires have been used in the past to evaluate the short- and long-term outcomes in women with POP managed with pessaries. Those studies have shown the following: 1. high treatment satisfaction (70%–92%) [61,62], 2. improvement of sexual function (both frequency and satisfaction) demonstrating that sexual activity should not be considered a contraindication to pessary use [63,64], and 3. improvement in bladder and prolapse symptoms [62,65–68].

Few studies have compared QoL outcomes between surgery and pessary use in women with POP, and the data are controversial. Abdool et al. [63] reported similar improvements in both groups while Barber et al. [69] found that surgery is associated with greater QoL improvements when compared to pessary use.

POP Questionnaires and Physiotherapy

POP questionnaires have also been used to evaluate the outcomes of physiotherapy, showing a significant improvement of POP symptoms and QoL in women with POP [70,71].

Brækken et al. [72] studied women with POP quantification (POP-Q) < IV stage, with no previous surgery, and who were able to contract pelvic floor muscles. This was a randomized controlled trial using a four-point scale questionnaire to assess the frequency and bother of POP symptoms before and after PFMT. Those women were randomized to an intervention group (weekly physiotherapy visits for 3 months followed by fortnightly visits for 3 months) or to a control group with no intervention. The authors reported a significant greater improvement of POP-Q stages as well as severity and bother of POP symptoms in the PFMT group compared to the control group.

In another interesting randomized controlled trial, Barber et al. used PISQ-12 and incontinence QoL (I-QoL) before and after PFMT in women with POP undergoing surgery. The authors concluded that in women who had preoperative PFMT sexual function, vaginal examination findings, and QoL improved significantly compared to those who had surgery alone [73].

POP Questionnaires and Surgery

Several studies looked at the effect of POP surgery on women's QoL. Although sometimes data reported have been controversial, overall the majority of the studies confirmed that POP symptoms (bladder, bowel, vaginal), sexual function, and QoL improve significantly after POP surgery (i.e., vaginal hysterectomy, pelvic floor repair, sacrocolpopexy [abdominal, laparoscopic, and robotic], sacrospinous ligament fixation (SSLF), mesh repair, and colpocleisis) [74–83].

These data have also been confirmed by a recent meta-analysis that demonstrated that POP surgery improves women's QoL [84].

An interesting study from Fayyad et al. showed that POP surgery improved also POP symptoms. Increased urinary frequency, urgency, poor urinary stream, and incomplete bladder emptying improved significantly after anterior and posterior repair. Urge incontinence improved with anterior repair but did not improve with posterior repair. Stress UI did not improve after anterior or posterior repair. Bowel symptoms improved after posterior repair, and vaginal symptoms improved with any type of correction [85].

Few studies have reported a new onset of dyspareunia and worsening sexual function scores following SSLF and mesh repair [86,87].

Therefore, additional longitudinal larger studies are needed to further evaluate the outcomes of these procedures.

Colpocleisis is known as an obliterative procedure that may affect the sexual life and woman's QoL. Surprisingly, Fitzgerald et al. [88] studied 152 women before and after colpocleisis using PFDI and PFIQ and reported that 95% of those were either "very satisfied" or "satisfied" with the surgical outcome at 1-year follow up. Interestingly, 87% reported no change and 10% an improvement in sexual function. Similar results were confirmed by Barber et al. [89] who looked at QoL before and after colpocleisis and reported that such obliterative surgery has similar improvements in QoL with no increase in depressive symptoms compared to other pelvic reconstructive surgery.

CONCLUSIONS

POP is a common condition affecting women's QoL. Vaginal, urinary, bowel, and sexual dysfunctions are coexisting symptoms that may or may not be related to the descending pelvic organs but do affect the patient's daily life causing physical limitations, social limitations, personal limitations, depression, and low self-esteem.

Defining the "success" of POP treatment is not as simple as it seems. Historically, the majority of authors focused exclusively on anatomical success ignoring other important areas such as presence, absence, and severity of associated symptoms, sexual function, QoL, and patient's satisfaction. Considering that for a patient the most important outcome is the relief of her symptoms and improvement of her QoL [16], all the earlier findings should not be discounted. Therefore, the assessment and management of women with POP should not merely be determined by vaginal examination findings (defined as *clinician-reported outcomes* [CRO]) but more importantly be focused on the evaluation of the coexisting symptoms (defined as *patient-reported outcomes* [PRO]) using valid and reliable instruments able to measure their severity and burden as recommended by the Food and Drug Administration [90].

The use of questionnaires to assess subjective (PRO) and objective (CRO) outcomes by measuring the severity of associated symptoms (presence, burden, and severity), QoL, and treatment satisfaction in women with POP has been recently advocated in a joint report from the ICS and IUGA [24]. Their use in both clinical and research practice has been also recommended and encouraged by other organizations such as the National Institutes of Health (NIH) and World Health Organization's ICI [91].

Those questionnaires can be divided into four categories: (1) symptom-specific questionnaires (i.e., VAS), (2) HRQoL questionnaires, (3) sexual function questionnaires, and (4) Global Impression of Improvement.

HRQoL questionnaires are instruments able to assess the physical, emotional, social, sexual, and occupational limitation on a patient's QoL.

They can be classified into two types: generic and condition-specific questionnaires. Generic instruments can be used for different conditions but may lack sensitivity [18]. The two generic HRQoL instruments that have been used most frequently in women with POP are the SF-36 and the European QoL.

The condition-specific HRQoL questionnaires are designed to measure the impact on QoL of a specific health condition, providing a deeper assessment of the targeted disease, hence being more responsive to change than generic questionnaires. The use of ePAQ has been advocated and has several advantages compared to the paper-based questionnaires. However, the cost of technology and patient technological know-how should also be taken into account.

Long forms questionnaires may be desirable for research studies where detail is needed while short forms may have wider applicability in clinical practice, which is important to minimize respondent burden and cost. It is generally desirable to use a validated, simple, self-completed, psychometrically robust, easy-to-understand, and complete questionnaire that is widely accepted and has been used in the targeted population [91].

Only a few questionnaires are available for POP compared to UI. The majority of those have been assessed for validity and reliability, are fairly lengthy, cover a range of symptoms, and include a number of subscales related to urinary and bowel disorders. However, their ability to detect changes can vary [91].

Several studies have demonstrated that POP questionnaires are useful tools in clinical as well as research practice: (1) to evaluate the severity of symptoms, (2) to assess the symptoms' impact on QoL, (3) to screen and to identify those women who would benefit from treatment, and (4) to detect posttreatment changes.

Due to the amount of validated POP questionnaires developed in recent years, the clinician's choice should be guided by the desired outcome they would like to measure as well as based on the instrument they are more familiar with.

It is important to remember that administering too many questionnaires to a patient may be unhelpful since they can lead to patient's fatigue and possibly erroneous answers.

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20 Economic Aspects of Urinary Incontinence

Kate H. Moore

INTRODUCTION

Since the publication of this chapter, concerning the economics of incontinence, in the previous edition of this book, the global financial crisis of 2008 has impacted upon health-care budgets in many countries. Now, more than ever, patients and health-care providers are seeking "value for money." In the current economic climate, we all need to be aware of the costs of the treatments that we recommend and be able to judge whether a new treatment is truly cost-effective.

Although health economics is sometimes considered a rather "dry" subject, this chapter is written from the clinician's perspective in an attempt to make the concept "come alive" for those working "at the coalface." We are all struggling to fight for enough money to care for our patients properly. As the population becomes more aged, the prevalence of urinary incontinence (UI) will rise, but our health-care budget will probably not keep pace with the demand for continence services. Most countries in the developed world have "controlled" budgets for health. As we all know, the prevalence of lethal conditions such as cardiovascular disease and stroke is also rising with the aging population. Because incontinence is not generally lethal, we must be able to compete with clinicians in other fields of medicine for increasingly precious health-care resources.

The recent controversy surrounding the use of medicated stents for coronary artery disease is a good example. A decade ago, the evidence appeared to show that inserting a medicated stent was a good way to avoid coronary artery bypass graft (CABG) surgery, resulting in large savings to the health economy. The need for long-term clopidogrel therapy, with its associated hemorrhagic risks if the patients needed urgent surgery for another condition, was considered a "necessary evil" to allow this cost saving. However, in the last few years, it was found that, in the long term, these medicated stents were still likely to occlude, so the patient was no better off. Now with the passage of time, the pendulum is swinging back to CABG surgery, because it is more cost-effective over the long term. Thus, although CABG surgery is very expensive, it has now been functionally "validated" from an economic perspective (although formal economic studies have not been concluded for all aspects of the aforementioned changes).

In our field, the transition from open Burch colposuspension, moving to laparoscopic colposuspension to allow early discharge with cost savings, then onto the tension-free vaginal tape (TVT) with its reusable instruments but equivalent if not better efficacy and cost savings, is analogous. In actual fact, a head-to-head cost comparison of laparoscopic colposuspension versus TVT has not been conducted. Nevertheless, with the advent of the TVT and transobturator procedures, it would seem that we have achieved the same cost savings but with a more robust cure rate, at least in the first 11–12 years of the TVT. Attempts to further "minimalize" bladder neck surgery with the recent "mini" procedures will certainly need long-term cost and efficacy data before their true value can be judged.

One of the major issues faced by the urogynecologists is the fact that the very companies who create and manufacture new surgical devices are the people we look to for funding of clinical trials of these products. Certainly, such companies are seriously interested in efficacy data (witness the withdrawal of the minimalistic" TVT secure device by Gynecare). However, surgical supply companies are not likely to conduct economic analyses for general publication. As business entrepreneurs, they must conduct market analysis and calculate what the market will bear, to thus determine whether they can realistically introduce a new product and still make an appropriate degree of profit. Similar practical constraints limit the ability of pharmaceutical companies to embark upon economic studies when introducing new drugs for incontinence. Nevertheless, government purchasing agents in many countries are now demanding some economic information in order to place new pharmacotherapies onto the government subsidy list (see later discussion regarding Markov models in this chapter [Figure 20.4]).

In order to make sense of what is going on economically, as each new product is introduced to the market (and some are discarded), the continence clinician needs to have a basic understanding of economic analysis in our field. This chapter will deal only with UI in women, in keeping with the subject of this textbook, and also because economic data about fecal incontinence and prolapse are very limited.

Also, because a formal survey of the economics of incontinence has recently been undertaken by a team of health economists and continence clinicians for the International Consultation of Incontinence [1], the present chapter gives a more clinically based summary of economic matters. The chapter is divided into two parts. Part One describes how to interpret an economic study, and Part Two outlines how to conduct an economic analysis. Throughout each part, important examples will be given from the literature, followed by a summary of important economic analyses from our field in the last decade.

PART ONE: HOW TO INTERPRET AN ECONOMIC STUDY IN THE CONTINENCE FIELD

Problem of Perspective

The perspective taken by any author in writing an economic analysis is fundamental to interpreting their analysis. For example, pharmaceutical companies often undertake *willingness to pay (WTP)* studies (see later for details of this method). They are most interested in knowing what patients will pay "out of pocket" for a new medication, which provides a certain theoretical degree of symptom relief. But *WTP* studies only consider the patients' perspective and their out-of-pocket expenses, with no calculation for the government subsidy provided for many drugs in many countries (see later for further discussion).

Surgical authors often look at the costs of a new procedure versus the old standard procedure, but if one looks at these reports critically, they often have a very short-term perspective, i.e., 6–12 months. We only have to remember the "honeymoon" success of the Stamey/Gittes/Raz procedures in the late 1980s, which soon gave way to large failure rates, to be reminded of this important axiom. One cannot stress strongly enough that at least 2 years and preferably 5 years of outcome and economic data should be looked at, before concluding that a new treatment is superior to the old one.

The final note of caution concerns economic models, such as the decision tree and the Markov model. Clinical (nonacademic) urogynecologists probably don't realize that an economist can design a Markov model to include whatever input parameters, success rates, procedural costs, etc., they wish. Now of course most economists would "fill in" the data in their model with published outcomes from the literature. The problem comes when there are no data to use!!! Economists may then make estimates for cure rates, complication rates, etc., and try to "plug in the numbers" into their model. This can have unfortunate consequences (see Section "Markov Models").

Different Types of Economic Studies Available: Cost of Illness versus "Economic Analysis" Studies

When reading an economic study, to start with, we need to consider whether one is looking at a cost of illness (COI) study or an analysis of the benefit of one treatment compared with another (hereafter called an economic analysis).

A COI study just simply tabulates all the costs of the incontinence being studied. Usually, these studies have three parts. First, they consider the *direct costs* of incontinence, which comprise the personal and treatment costs of the condition. The patient's perspective is usually taken first, for personal costs of incontinence products, laundry, barrier creams, etc. Then, the "payer" perspective is usually taken, for the costs of investigations and treatments. The payer is often a government body, except in the United States where a combination of Medicare/Medicaid and private insurance payers will be considered. Often, investigations and treatments involve some out-of-pocket "co-payment" from the patient (see Table 20.1 and Dowell et al. [2] for more detail).

Table 20.1 Direct Costs of Incontinence

Personal costs	Incontinence pads, disposable or reusable laundry costs for reusable products + urine-stained clothes/sheets Dry-cleaning of urine-stained clothes Replacement of urine-stained clothes Cleaning/replacing uriniferous carpets/furniture

	Barrier creams, Zinc ointment to prevent urine excoriation of the skin
	Bed pads, disposable or reusable
Treatment costs	Specialist visits (urogynecologists, urologist, geriatrician)
	Urodynamic tests, renal/postvoid ultrasounds
	Midstream urine cultures, other laboratory tests
	Pharmacotherapy costs
	Physiotherapy/NCA treatments
	Catheters for CISC
	Vaginal devices, e.g., dish pessaries and contiform
Surgical costs	Anesthetic costs/preop workup
	Surgeons' fees
	Theater fees
	Inpatient bed stay fees
	Post-op follow-up, treatment of complications

As can be seen in Table 20.1, the "payer" for this broad range of direct costs varies considerably, especially in the treatment section. For example, patients in a public hospital in most Commonwealth/European countries would seldom have any notion of operating theater fees, as the hospital budget is derived from the taxpayer revenue. However, most Americans would have a very clear notion of just how costly operating theater fees can be.

Another aspect of the *direct costs* of incontinence, which is not always considered, is the cost of the consequences of being incontinent. Part of the reason that these costs may be missed is that they are controversial. For example, the literature now contains several reports that incontinent people are 26% more likely to fall, and 34% more likely to sustain a fracture, than nonincontinent people [3]. This may occur because they are rushing to the toilet with urgency [4] or because they slip over when the urine renders the floor wet. However, this subject was initially quite controversial.

Even more controversial is the issue of whether incontinence can precipitate admission to a nursing home. The paper by Thom et al. [5] is frequently quoted to show that the risk of admission to a nursing home for an incontinent women age >65 is twice that of a nonincontinent woman, which of course has huge cost of implications. However, the actual study focused upon women who had either Parkinsonism, dementia, stroke, depression, or congestive heart failure, *with or without incontinence*. This would accord with clinical experience, i.e., UI in an otherwise *nonfrail* elderly woman who does not usually provoke nursing home admission, and it is the incontinence on top of the comorbidities that may provide the "final insult."

The top-down versus bottom-up approach to COI: Readers should be aware that many COI studies (and also economic models that are discussed in the next section) can compile their cost data in two ways. The *top-down* approach uses large national databases for costs (such as the Diagnostic-Related Groups [DRGs] in the United States/Australia or the Healthcare Resource Groups [HRGs] in the United Kingdom) combined with national prevalence data, to give an overall estimate of national expenditure for a particular condition. This is also known as *gross costing*. For example, see Hu et al. [6]. The alternative approach is to conduct individual, face-to-face enquiries about costs and utilization of resources in a sample of, say, 100 typical patients. This is known as the *bottom-up* approach, which is of course more accurate, but much more costly as a researcher has to actually interview all these patients about their incontinence costs in a systematic fashion (*for example, see* [7]). This method is also known as *microcosting*.

Second, the *indirect costs* of the condition are considered. These comprise costs arising from the individual losing productivity, e.g., time off work (and the cost implications for society). In the late 1990s, preliminary data began appearing regarding the impact of incontinence upon working women [8] including teachers and soldiers [9]. Between 21% and 33% of such working women suffered from incontinence. The effects upon their productivity included the loss of concentration, interference with job performance, need to take time from work for frequency of micturition, and the tendency to fluid restrict on the job. Nocturia with sleep disturbance leading to impaired daytime performance was also noted.

These results agree with large postal questionnaires from 2326 employed American women, [10] in which 37% had leaked urine generally in the past month. Severity (on Sandvik index) was slight 52%, moderate 40%, and severe 8%. The impact of incontinence upon ability to concentrate, performance of physical activities, self-confidence, and ability to complete tasks without interruption worsened with the severity of the leak (affecting nearly 75% of all those with severe leak status). Wu et al. [11] focused upon the work loss burden of women with overactive bladder (OAB). Absenteeism was 15% higher among 3077 OAB employees compared to 6154 controls. Multivariate analysis showed that OAB subjects had 4.4 more days off work than that of non-OAB subjects, yielding an excess cost of $1220 per OAB employee per annum.

Very recently, a specialized Work Productivity and Activity Questionnaire (WPAI) has been used in this type of research, which is broken down into sections about general health impact (WPAI-GH) and specific health disorders impact (WPAI-SH). Coyne et al. [12] studied 2323 adults with OAB symptoms versus 3472 adults with no or minimal OAB symptoms in 2012, using an Internet questionnaire format, with weighting of the respondents to reflect the general population. They found a highly significant impairment of work function in patients with OAB symptoms (see Figure 20.1). The rate of unemployment was doubled in men with OAB symptoms (not seen in women), and health-related unemployment was similar to that for asthma and rheumatoid arthritis.

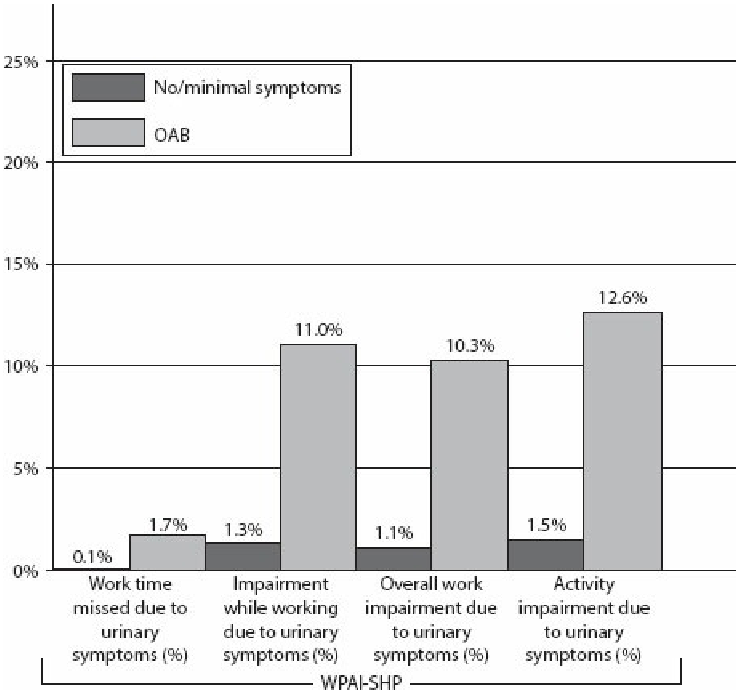

Figure 20.1 Percentage work impairment of overactive bladder patients WPAI-SHP, for women. (Reproduced with permission from Coyne KS et al., *Urology*, 80, 97, 2012.)

A further *indirect cost* of incontinence that is poorly measured to date is the cost of care provided by spouses and informal caregivers. Langa et al. [13] analyzed a large American dataset and estimated the yearly cost of informal continence care by relatives at US$ 6 billion (1998 dollars) or about $2000–$4000 per annum for women and men whose incontinence was severe enough to warrant using pads.

Third, a COI study should consider the *intangible costs* of the condition such as pain from urine excoriation or depression from the psychological impact of long-standing unpredictable incontinence. Urge incontinence is known to have a strong association with depressive symptoms [14] that occurs in 60% of those with idiopathic urge incontinence compared to 14% of those with pure stress incontinence, but the economic/cost–utility impact of this has not been studied.

Many COI studies have now been published regarding UI for most European and Commonwealth countries, for example, Sweden [15], Italy [16], France [17], the United States [18], and Australia [19].

COI studies are now considered somewhat “passé” within the field of health economics. Nevertheless, urogynecologists should be mindful that few COI studies have been published for prolapse treatments (see [1]). For a full description of the recent COI studies and economic analysis in the subject of fecal incontinence, see Moore et al. [1].

However, recently there have been two important COI studies published, which focus upon particular aspects of UI. Goren et al. evaluated the direct and indirect costs of patients with urge incontinence [20], to study the relative costs of patients who were undergoing treatments, (n = 481) compared with those who were untreated with prescription meds (n = 709). The authors used data from the 2011 U.S. National Health and Wellness Survey, which were an Internet-based questionnaire of a national sample of adults (total n = 75,000). The stratified random sample was checked to ensure that it was the representative of the corresponding adult U.S. population. Health-care utilization costs (e.g., doctor visits, emergency room visits) were precisely *costed*. Work productivity was assessed in employed subjects by a validated 6-item questionnaire that also noted activity impairment (the percentage of impairment in daily activities because of one's health in the last 7 days). Treatment users had *significantly* lower activity impairment (41% vs. 47%) but higher total direct costs ($27,290 vs. $21,490) (see Figure 20.2). Indirect costs did not differ between groups. The study was funded by Pfizer Inc.

Tapia et al. performed a meta-analysis of the literature [21] regarding the economic burden of UI in patients with neuropathic detrusor overactivity (DO), arising from multiple sclerosis (4 articles), spinal cord injury (4 studies), Parkinson's disease (2 articles), stroke (5 studies), and spina bifida (2 articles). They pointed out that neuropathic DO can result in severe uncontrolled urge incontinence, but the impact of this condition upon quality of life (QOL) and economic burden has not been well studied. The authors found that in all these neuropathic disorders, those who were incontinent had highly significant increased impairment of QOL than those who were not incontinent, but suffered from the same neurological disease. The economic burden of incontinence pad usage, diagnostic procedures, office visits, surgical procedures, urinary tract infection (UTI) costs, and fractures was several hundred dollars more per annum per patient with incontinence, compared to those with the neuropathic condition alone. The study was funded by Allergan.

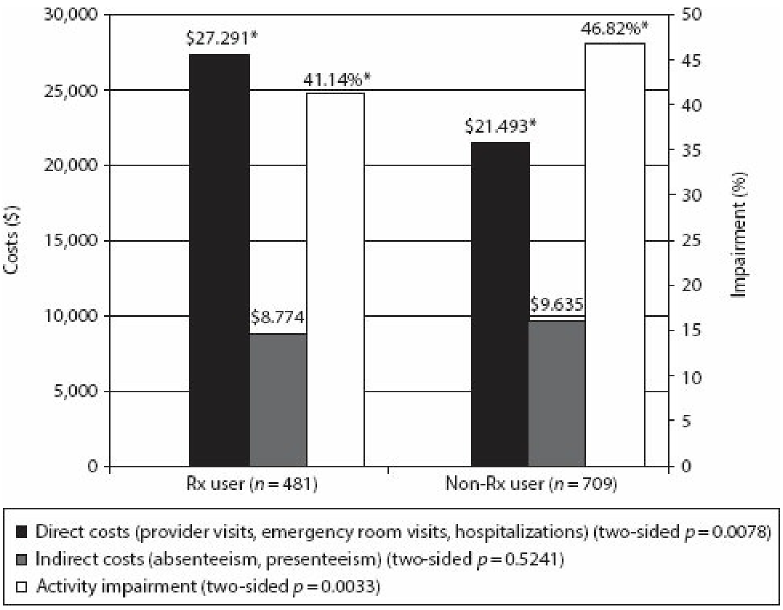

Figure 20.2 Direct and indirect costs of patient with urge incontinence, in the treatment users and treatment nonusers, with employed status*. Two-sided p-value < 0.05, for difference between treated and nontreated patients. (Reproduced with permission from Goren A et al., *Int J Clin Pract*, 68, 336, 2014.)

Formal Economic Analyses

As described, COI studies are not formal economic analyses because they simply summate the costs of the condition for a given population. Because the COI study does not measure the "value" of the treatments under study, it does not help clinicians decide how to allocate precious funds. In the following paragraphs, an overview of true economic analyses is given, with focus on the most desirable type, which is a cost-utility analysis (CUA). See Drummond et al. [22] for full review.

1. *Cost-minimization analysis* (*CMA*): In a CMA study, the costs of alternative health-care

strategies are compared, but we assume at the beginning of the study that the benefits of the two options are likely to be equivalent. When the two treatments actually prove to be equivalent in their outcomes, complications, and patient satisfaction, then a CMA is sufficient; the cheapest intervention is to be desired.

For example, our group undertook a randomized controlled trial (RCT) of the urogynecologists versus the nurse continence advisor (NCA), in the performance of conservative continence therapy for any mild to moderate incontinence. Nurses were able to give relevant prescriptions for anticholinergic drugs that the urogynecologists had written at the enrollment visit. We hypothesized that the outcomes for each clinician would be similar, which proved true. As might be expected, the nurses were a great deal cheaper despite the same result [23]. CMA studies are actually not that common in the literature.

2. *Cost–consequence analysis* (*CCA*): The CCA is a variation on CMA. It tests the hypothesis that a new treatment may result in a greater decrease in health-care utilization than a standard treatment. Unfortunately, whether the new treatment gives any benefit in outcome is not assessed, so CCA is not recommended.
3. *Cost–effectiveness analysis* (*CEA*): The term CEA covers a broad type of economic analyses wherein the effectiveness is measured by a general health outcome. One can perform a CEA with a narrow outcome such as a pad test, but you will miss other important effects. Therefore, we generally prefer the use of quality-adjusted life-years (QALYs) as the best health outcome measure for CEA. Once you include QALYs in your analysis, the study becomes known as a CUA. Other utility measures are also available, such as time trade-off or standard gamble (see the next section).
4. *CUA*: The CUA study is a type of CEA, wherein QALYs are generally used as the outcome measure, to compare two different treatments for the same condition. CUA is now considered to be the gold standard. QALYs capture all potential benefits of an intervention and allow comparisons with other health conditions, which is vitally important. The “bottom line” of both the CEA and the CUA are represented by the incremental cost–effectiveness ratio (ICER). The ICER represents the average cost of the intervention group minus the average cost of the control group. This amount is then divided by the average utility (QALY) of the intervention group minus the average utility (QALY) of the control group (see Section “Part Two: How to Conduct an Economic Analysis,” for full formula).
5. *Cost–benefit analysis* (*CBA*): Involves measuring the benefits in dollars (or other currency). When everything is measured in dollars, optimal choice can be found by addition and subtraction. However, it is difficult to measure the benefits in dollars, and many researchers, policymakers, and clinicians avoid placing a dollar value on life. CBA often uses a technique called WTP. This method involves giving a group of patients a questionnaire about how much money they would be willing to pay, from their own income, to achieve a given reduction in incontinence. For example, see [24].

> Imagine that a new drug, free of side-effects, against incontinence becomes available, that is not paid for by the state. This new drug reduces the number of times per day you need to go to the bathroom and number of urinary leakages per day by one quarter (25%); this means that if you, for instance, at present need to go to the bathroom 12 times per day and you have four urinary leakages per day, this will be reduced to nine bathroom visits and three urinary leakages per day. Would you choose to take this new drug if you, out of your income, have to pay 9 pounds per month [or 100 Swedish krona]?

The price can be varied up or down, and the leakage reduction is usually then varied up to 50% benefit.

The authors [24] found that the median amount patients were willing to pay ranged from 240 krona for 25% reduction to 470 krona for 50% reduction in symptoms. However, the authors noted that measuring WTP in the Swedish population is difficult, because health-care costs and the cost of pads are paid for by the state in Sweden, so patients will not have figured in these costs in their willingness to spend disposable income. Indeed, economists dislike WTP because such questionnaires survey people about their preferences and intents but do not observe actual behavior. WTP is similar to the standard gamble technique, which suffers from similar problems [25]. Thus, the preferred economic evaluation method remains the use of QALYs in CUA (using tests described later).

Test Instruments Suitable for Measuring Quality-Adjusted Life-Years

Instead of using theoretical questionnaires such as WTP, time trade-off, or standard gamble, there are several dedicated utility preference scores designed to measure QALYs, by directly questioning patients, before and after a given treatment. A utility score is a measure of patient preference for a given health state. The utility score is a standardized QOL test that summarizes the morbidity of a condition on a scale from 0 (death) to 1 (optimum health). Some scales allow patients to be so severely affected by the condition that they can give a score worse than death. Utility scores are combined with life expectancy to calculate QALYs, which can be used to quantify the benefits of any given treatment (or intervention).

EuroQol-5D: www.euroqol.org

The EQ-5D was developed by the EuroQol team from seven European countries [26,27]. It has 5 items measuring mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The upper boundary is 1.00, and the lower boundary is −0.59. This has become a popular instrument in clinical trials because it has been used in many languages and is very brief (five items).

For example, Tincello et al. [27] tested the relationship between stress incontinence and QOL, on the EQ-5D. The stress urinary incontinence (SUI) treatment study, a 12-month, prospective, observational, multicenter study in four European countries, evaluated the association of SUI symptoms with the EQ-5D among 3762 women seeking treatment. The EQ-5D scores were significantly and independently influenced by the comorbidities and by the total number of stress and urge incontinence episodes.

Assessment of Quality of Life AQoL

The AQoL comprises 15 items, 12 of which are used to compute the utility score. It includes 5 dimensions: illness (not used in utility calculations)-independent living, social relationships, physical senses, and psychological well-being [28]. The upper boundary is 1.00, and the lower boundary is −0.04.

15D

The 15D, created in Finland, has 15 items measuring mobility, vision, hearing, breathing, sleeping, eating, speech, elimination, usual activities, mental function, discomfort and symptoms, depression, distress, vitality, and sexual function [29]. The upper boundary is 1.00, and lower boundary is +0.11 (so a state worse than death is not allowed).

The 15D is a self-administered test of health-related quality of life (HRQOL) [29]. The single index score (15D score) on a 0–1 scale represents the overall HRQOL and is calculated based on population-based preference or utility weights. The 15D scores are shown to be highly reliable, sensitive, and responsive to change and valid for deriving QALYs. The 15D score is sensitive to UI in cross-sectional studies [30] and to change in incontinence severity following therapy [31].

Health Utility Index Mark 3: www.healthutilities.com

The health utility index (HUI) uses 12 items that measure 8 domains (vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain). The upper boundary is 1.00, and the lower boundary is −0.36. Harvie et al. have shown that the HUI Mark 3 (HUI-3) correlates well with other tests such as EQ-5D and the SF6-D [32].

SF-6D: www.qualitymetric.com

Whenever SF-36 raw scores are available, SF-6D utilities can be computed [33]. The SF-6D measures physical functioning, bodily pain, mental health, physical role, emotional role, social functioning, and vitality. The endpoints for the SF-6D are 1.00 and 0.30 for the worst possible health. Recently, the disease-specific King’s Health Questionnaire has been used for computation of QALYs also [34].

Decision Analysis: Economic Modeling

The aforementioned methods of economic analysis generally involve “real data,” e.g., that taken from a RCT or even a prospective observational study of one treatment versus the costs of “no intervention.” However, there are other forms of economic analysis that involve the construction of a theoretical model, that is then filled in with, or “populated”, from samples of data taken from the previous literature.

The two most common of these are the decision analysis, which involves making a decision tree, and a broader-based (more all-encompassing) Markov model. In both cases, the first step in the analysis is to identify the structure of the clinical problem, i.e., make a list of all the likely decision alternatives, all the clinical outcomes, and a sequence of events. Then, one assigns a mathematical probability to all chance events (e.g., 80% likelihood of cure, 2% likelihood of death). In step three, one assigns an outcome measure such as a QALY to all outcomes. In the fourth step, one performs the mathematical calculation of the expected utility for each strategy; this may reveal the preferred strategy. Finally, one has to test how “robust” the model is (how sensitive the outcomes would be to changes in the input parameters) by performing sensitivity analyses. A range of different inputs such as cure rates are changed, e.g., from 80% to 95%, to see if the model still holds true.

The *decision tree* is easy to understand. A group of patients with a certain type of incontinence enter into theoretical pathway along which they will undergo treatments and have a variety of outcomes. As they pass along the tree, various limbs of the tree branch off—each of these branches is called a “node.” A “decision node” is a branching off where the patient or the doctor makes a decision about what kind of treatment to have/administer. A “chance node” is a fork in the tree where a range of chance events occur that the patient or doctor may have little control over, such as “cure,” “partial response,” “nonresponse,” or complete failure (or they may encounter a complication, such as death, nursing home admission). The final event on the end of the branches of the tree is called the “terminal nodes.”

A recent example of a decision tree analysis in the field of UI was conducted in 2012. The authors constructed a decision tree model to compare medical costs and QOL associated with improved incontinence arising from treatment with percutaneous tibial nerve stimulation (PTNS) (12 sessions over 12 weeks) versus tolterodine extended-release (ER) tablets [35]. Figure 20.3 shows the decision node (square box) where patients have either PTNS or tolterodine for 3 months. Moving along to the right on the diagram, the first chance node yields options of “response” or “no response.” The next chance node concerns side effects, which may or may not cause the patient to stop the treatment. Final options are improvement or persistent symptoms.

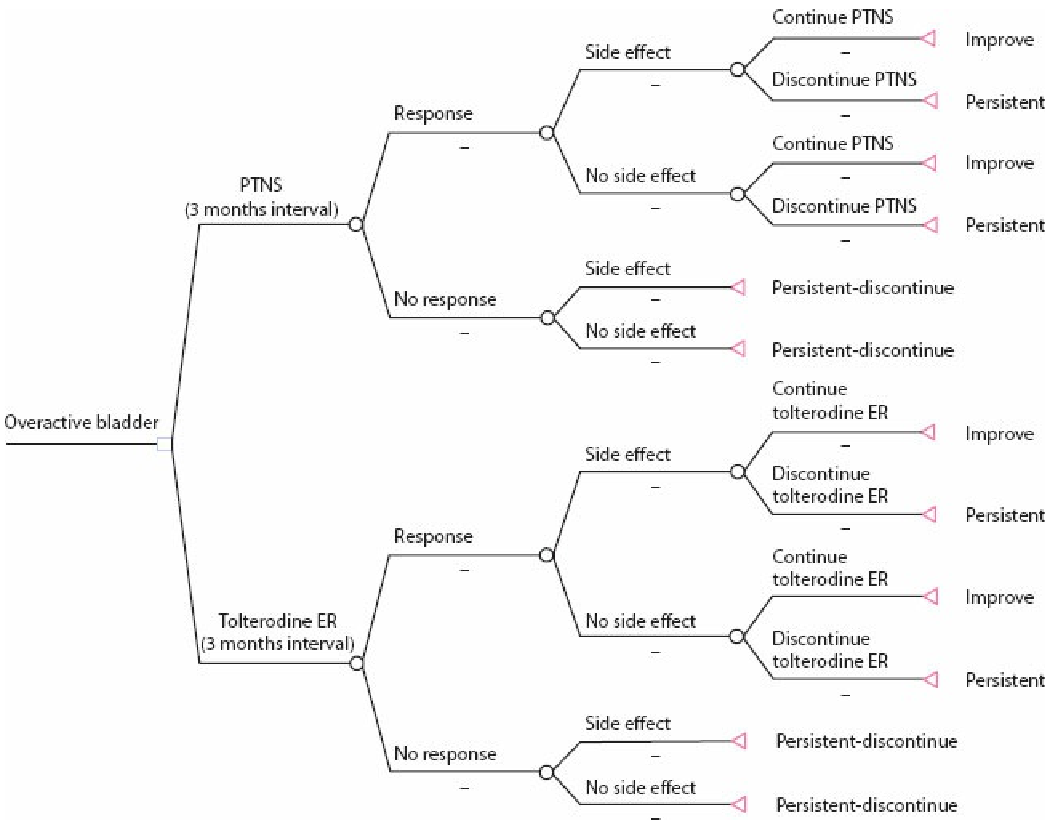

Figure 20.3 Decision tree analysis comparing percutaneous tibial nerve stimulation versus tolterodine

extended-release model runs over a 3-month interval (analyzed over 12 months, 4 cycles). (Reproduced with permission from Chen HW et al., *J Urol*, 187, 178, 2012.)

In the model, the likelihood of symptom improvement was 79% for PTNS at 3 months and 56% for tolterodine, based on a published RCT [36]. The likelihood that patients would continue therapy was 75% and 63%, respectively, from the literature. Side effect probability was 21% and 31%, respectively, although PTNS side effects were estimated (actual published side effects of PTNS are 3%–16%).

The cost analysis was from a societal perspective, based on direct medical costs (no indirect or intangible costs). The 1-year cost of PTNS was $43,754 per patient, versus $13,400 for tolterodine, taken from U.S. Medicare codes. The PTNS cost per session was $203, which seems a high cost. The tolterodine cost was $150 per month, clearly based on the costs in the United States and not applicable to Europe, the United Kingdom, or Australasia. Personal incontinence costs were taken from Subak et al. [37].

The QALY value for improved UI was 0.92 versus 0.73 for persistent incontinence. These values were taken from the time trade-off questionnaire [38], in which 40 women with a variety of OAB symptoms were asked to evaluate a range of clinical scenarios. Thus, the QALY scores were estimated from a study of patients who had not undergone either of these treatments.

A *Markov model* is slightly superior to a decision tree because it allows the dimension of time to come into the analysis. The decision tree, as shown earlier, assumes that the chance of particular events such as cure/partial cure/failure is stable over time. However, we know only too well that UI treatments may "look good" immediately after they are given (new drugs or surgery) but often begin to fail over the longer term. The receptor for the drug may become "resistant," or the surgical sutures may dissolve/become remodeled.

Markov models are set up to allow one to incorporate such changes over time. Patients can go through various cycles of moving from one treatment state to another, over time. The likelihood of moving from one state to another is given a mathematical probability (using techniques derived from matrix algebra). The final option is to become dead, a state from which the patient cannot move.

The author of the Markov model needs to define health states and the probability of moving from one to another, as in the decision tree. But also, the author determines the cycle length or time period over which one moves between states, e.g., weeks to months for pharmacotherapy and months to years for surgical studies. The outcome measure used to determine treatment effect is generally the QALY.

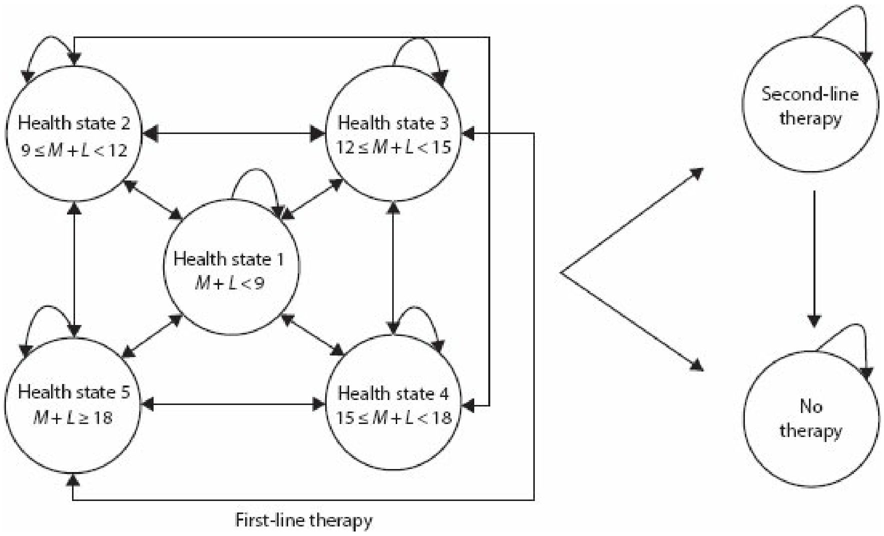

Figure 20.4 A Markov model comprising six health states, used to analyze solifenacin 5 mg/day versus oxybutynin 5 mg TDS, over 1 year. (Reproduced with permission from Hart, W.M. et al., *J. Med. Econ.*, 16, 1246, 2013.)

A recently published Markov model [39] compares the cost-effectiveness of solifenacin 5 mg/day versus oxybutynin 5 mg three times daily [39], based on the data obtained from the VECTOR RCT [40]. The cycle length was 1-month duration, repeated 12 times in the analysis. As shown in Figure

20.4, patients could move between five health states, dictated by their summated numbers of micturitions and leakages per day. Health State 1 (less than 9 micturitions or leaks per day) was considered “mild,” whereas Health State 5 (more than 18 micturitions or leaks per day) was considered “severe.” After 2 months of treatment, patients were assumed either to move to second-line therapy (tolterodine, 65% of cases) or to drop out from anticholinergic therapy (35% of cases), based upon published literature.

The costs were tallied from pad-usage data taken from the STAR study [41] and from GP visit costs in the United Kingdom. Utility values were taken from published data for patients using these medicines [42]. The annual costs of oxybutynin (£364) were lower than that of solifenacin (£504), but pad costs were higher for oxybutynin (40% of total) than for solifenacin (22% of total). The difference in QALYs between drugs was small (0.011, in favor of solifenacin).

PART TWO: HOW TO CONDUCT AN ECONOMIC ANALYSIS AND WHAT HAVE WE LEARNED FROM ANALYSES IN THE LAST TWO DECADES

How to Conduct a Cost-Utility Analysis

Clearly, the CUA is now the gold standard in economic analyses. The following paragraphs explain ten key points that must be included in a CUA—a “how to do it” guide to achieving the appropriate minimum standard for performing and reporting CUAs. Each point should be explicitly covered in every study [1].

1. The *research question, i.e., the hypothesis that treatment A will be more effective per unit of QALY than treatment B*, must be clearly stated. All CUAs must compare at least two different therapies. One of these should comprise the current standard practice. For example, when comparing surgeries for stress incontinence, one of the comparators should be a long-standing method; avoid comparing two new methods side by side.
2. The *Time Frame over which costs and benefits are measured should be long enough to capture the economic impact of an intervention* and all relevant future health outcomes such as treatment failure or complications. Pharmacology studies of 12-week duration give very little real economic information, and surgical complications/failures seldom emerge in less than 1–2 years.
3. *The perspective used by the author must be clearly stated.* Total society perspective (all payers) is the optimum (“gold standard”). Other perspectives, such as the payer or the patient’s out-of-pocket expenses, may be useful but must be stated clearly.

   When reading an economic analysis of continence treatments, usually comparing an older standard therapy with something new, one must be very careful. The writer may inadvertently have used a narrow perspective, for example, just looking at the treatment costs from the hospital provider perspective as regards savings in bed days or theater consumables.
4. *Probabilities* are needed for each “chance” event, if you are constructing a Markov model or a decision tree (i.e., chance of cure or chance of an adverse event). These should come from meta-analyses of RCTs (or from individual clinical trials if no meta-analysis).
5. *Costs* should be described in detail, including exactly how the “charges,” “bills,” or co-payments were derived. The year of the cost data should be given because studies are often not published until months or years after the data were actually collected.
6. *Outcome measure*: Measures of effectiveness depend on the type and objectives of analysis. QALYs are the gold standard, as described previously in this chapter.
7. *Analytic model*: If a real clinical study is not being used, but a Markov model or decision tree is being constructed, each intervention must be described and possible courses of events identified, including the expected course of disease, treatments, complications, and outcomes.
8. *Discounting*: Since the value of both costs and benefits may decrease over time, discounting is used to calculate the present value of money and health states that will occur in the future. Future costs and utilities should be discounted to present value; 3% per year is a recommended starting point.
9. *Incremental analysis*: The purpose of a CUA is to describe the relative value of one health-care strategy compared to another. An *ICER* is the incremental cost divided by the incremental effectiveness of intervention a compared to intervention b and is calculated as follows:

Averages should be used (*not* medians) because we want to see the effect of statistical outliers. The "leverage" or impact, of the outliers, should then be tested in a sensitivity analysis.

ICER= Average Costintervention a− Average Costintervention bAverage Utilityintervention a
−Average Utilityintervention b

10. *Sensitivity analysis*: A sensitivity analysis should allow the reader to understand whether the conclusion of the analysis would hold true if either the costs or the probabilities (of cure or complications) were to vary substantially. For example, if one treatment costs EUR€5000 and has a cure rate of 90% and the second treatment costs €2000 with a cure rate of 80%, then the ICER will assess whether the resultant benefit in QALY/QOL makes the first treatment worthwhile. The author should then vary the costs and the cure rates in the model to see how much variation in real life would be allowed for the conclusion to remain valid.

What Have We Learned from Economic Analyses in the Recent Past?

This overview of our current state of knowledge about incontinence costs is organized according to the type of incontinence (stress, urge, or mixed). Conservative treatments will be considered followed by surgical treatments.

Stress Incontinence: Conservative Therapy

There have been surprisingly little economic data generated about conservative treatment for stress incontinence. Neuman et al. [43] calculated the physiotherapy treatment costs for 274 women with stress incontinence in Australia. A median of 5 (Interquartile Range [IQR] 4–6) treatments were given, for a median cost of $250 (IQR 206–295) in 2005. Of the patients who completed the therapy, 84% were dry on stress test. Improvement was seen on the King's Health Questionnaire, but utilities were not collected (nor calculated as they could have been). Monz et al. [44] studied the total costs of physiotherapy treatment in France, Germany, Spain, Sweden, and the United Kingdom. These ranged from €64 to €467 (for a range of 4–10 prescribed visits).

As regards conservative therapy for mixed incontinence, Williams et al. [45], of the Leicestershire UK MRC Incontinence Study Team, undertook a large RCT of conservative therapy in 2005. Personal and treatment costs were measured (year 2001). A sample of 3746 men and women were randomized in a 4:1 ratio either to treatment by a specialist NCA (who provided conservative therapy and urodynamic testing) or to routine continence care by their GP and local continence nurse. Cure at 6 months occurred in 28% versus 19% (95% CI: 5–13, $p < 0.001$). The intervention costs at 6 months (£252, IQR 234–268) were greater than the routine costs (£73, IQR 53–93). Cost utilities were not collected.

Subak et al. [46] performed a *bottom-up* analysis of the personal "routine care" costs (pads and laundry questionnaire) of incontinence in 293 women age over 40 who had stress or urge leak more than 3 times per week, wanted help, but had not been treated in the previous 3 months. QOL was tested by the HUI-3 and WTP. Women were willing to pay $70 per month for 100% reduction in the frequency of incontinence. WTP increased 2.3-fold in the highest income bracket compared to the lowest. WTP for improvement exceeded the routine care costs by three- to sevenfold. On univariate analysis, women with daily incontinence had a 10% lower mean score on the HUI-3 compared to those with only weekly incontinence episodes (0.81 versus 0.90, $p = 0.02$). The scores of women with urge leak were 6% worse than those with stress leak.

Pinto et al. [47] studied the effect of weight loss on QOL in obese women with UI. QALY tests, which had not previously been used to measure response to incontinence treatments, were employed (the HUI-3, the SF-6D, and the estimated Quality of Well Being [e QWB]). In this RCT, 338 women who had at least 10 leakage episodes per week and a BMI of 25–50 were randomized to either a behavioral weight loss program (weekly small group sessions over 6 months, then fortnightly over 12 months) comprising a 1200–1800 cal/day diet, with regular physical activity, versus control (seven 1-hour group education sessions over 15 months). Weight loss at 6 months was 8% versus 1.6%, respectively ($p < 0.001$). At 8 months, difference was 5.5% versus 1.6% ($p < 0.001$). Reduction in incontinence episodes was significant at 6 months (−47% vs. −28%) but not at 18 months (−62% vs. −55%). Only basic incontinence management information was given.

The changes in HUI-3, SF-6D, or e QWB did not differ between active therapy and control, but for all participants, weight loss was directly correlated with benefit on the e QWB but not for the HUI-3 or SF-6D. Surprisingly, reduced UI did not correlate with improvement in these three QALYs.

Recently, Sjöström et al. [48], from Sweden, compared the treatment costs and QALY changes of 250 stress incontinent women enrolled in a RCT of 3 months of pelvic floor muscle training via an Internet-based program (that included continuous e-mail support from a physiotherapist) versus a training program sent in the post, versus no treatment. Costs were evaluated from a 1-year societal perspective, including all the staffing costs of the Internet program and all the patients' personal costs. The ICER for Internet treatment versus postal treatment was EU€21,797 per QALY, which is considered highly cost-effective.

In 2012, Albers-Heitner et al. [49], from the Netherlands, performed an economic evaluation of a RCT of the treatment for stress or mixed incontinence in 186 patients, who had therapy by a NCA, versus 198 subjects who had usual care by a GP in the Netherlands, using the EQ-5D to measure QALYs. Personal and indirect costs (but not intangible costs) were assessed at 1 year. Compared to usual care, the NCA treatment cost EU€16,740 per QALY gained, which was significantly more cost-effective than the usual care. The threshold for cost-effective therapy in the Netherlands (EU€40,000 per QALY gained) was justified by the use of NCA intervention. This publication is an excellent example of the incorporation of economic analysis into a RCT.

Ho et al. [50] performed a *bottom-up* study of the short- and long-term direct costs of conservative and surgical management of childbirth-related stress/mixed UI in 150 women. During the initial treatment, patients with stress UI treated conservatively incurred a median direct cost of AUD$658 per capita (IQR 476–$1191) compared to $6870 per capita for surgical treatment (IQR 6320–$7508). Similar cost difference was seen for the two treatments for mixed incontinence. Of regular clinic attendees, 39% of conservatively treated and 78% of surgically treated patients were cured. QALYs were not measured. At 6–13 years follow-up, 52% responded to a postal questionnaire, of whom 46% remained cured. The median treatment cost for the total group of postnatal incontinence (irrespective of continence status) was AUD$885 per capita per annum (IQR 338–$2589).

Before moving on to the cost-effectiveness of surgical treatments, a few words about *vaginal devices* are needed. Although a range of such continence devices have been manufactured (such as the Contigard vaginal sponge, Introl bladder neck support device, Femassist urethral occlusive device, Contiform vaginal ring, and continence dish), economic analyses of these are uncommon. However, a good lesson about the importance of such economic testing can be learned from the story of the Femassist device.

When it was first launched, the Femassist device was estimated to cost AUD$12.50 (in 1997, then about EUD€8) and was to be changed weekly by the patient. The staff from our unit developed an incontinence cost index [2] and then measured incontinence costs before and after using the Femassist [51]. The median person costs fell from AUD$6.52 per week (IQR 1.5–$10.6) down to a median of 1.57 per week (IQR 0.84–$4.89). Thus, the savings provided by the device in this group of 100 women with moderate leakage on pad test (typical of those who might want to use it) was not equivalent to the cost of the device. Unfortunately, the production of the device ceased about 10 years later.

Surgery for Stress Incontinence

Cody et al. [52] performed a systematic review of the cost-effectiveness of TVT versus open colposuspension. Such older studies remain as they are good examples of appropriate methodology. Using a Markov model, the TVT dominated the open colposuspension (lower costs with similar QALYS) within 5 years. The authors pointed out that there were no RCT data beyond 2 years however. Wu et al. [53] also developed a Markov model to compare TVT versus open colposuspension at 10 years, with similar findings but with a similar proviso that no long-term data exist. Much of the economic data used in the Markov models arose from the now-famous RCT of Manca et al. [54], which compared TVT to open colposuspension at 6 months. Procedural and convalescence resource costs were collected directly from the 344 trial participants, and then health-care consumption was estimated from the British NHS data, along with QALYS (on the EQ-5D). The TVT saved GBP£243 per patient and gave slightly higher QALY benefits (0.01 units per QALY). Dumville et al. [55] compared laparoscopic versus open colposuspension as part of a RCT. The analysis of costs and QALYS (on EQ-5D) at 6 months revealed a mean increase of £372 for the laparoscopic procedure, but a QALY benefit of 0.005, yielding an ICER of £74,4000 at 6 months for the benefit of the laparoscopic colposuspension. This

ICER falls below the recommended National Institute for Health and Care Excellence (NICE) guidelines for cost-effective therapy (£30,000 per QALY gained) (www.nice.org.uk).

In 2011, Lier and colleagues [56] performed a within trial CUA in a randomized trial of transobturator tape (TOT) compared with TVT among 194 women in Canada. The cure was assessed by objective pad tests. They assessed costs in 2007 Canadian dollars from the public payer's perspective, i.e., CAD$807 for surgical kits, plus day-only surgical costs, and 12 months of care costs. The 15D utility instrument was used to measure QALYs. At 1-year postsurgery, 81% of patients with TOT were dry on 24 hour pad test versus 77% of patients with TVT; 15% of the patients with TOT had groin pain (versus 6% of those with TVT), but whether this contributed to medical costs over 12 months was not clear. The TOT group had a nonsignificant average saving of $1133 (95% CI: −2793; 442), or 17%, with no difference in average QALYs between groups (95% CI: −0.02; 0.01). TOT was cost saving in over 80% of sensitivity analyses, suggesting that TOT would be cost-effective compared with TVT in the treatment of SUI. These results agreed with a Markov model (derived from Medicare data in the United States and published QALY data), which compared retropubic midurethral slings versus transobturator slings, over a 1-year period [57].

However, longer-term assessment of clinical and economic outcomes is needed to confirm this finding.

Recently, Subak et al. [58] have studied the out-of-pocket costs after Burch colposuspension or a fascial sling at 2 years, based upon the study of Subak et al. [37]. These patients were quite wet, with baseline 23 leaks per week. After surgery, both groups combined leaks per week fell by 86%. Pretreatment personal costs (US$16.6, ± $27) fell by 72% to US$ median $0.10, IQR 0–$3.39. Continence surgery was associated with improved disease-specific QOL scores, but QALYs were not measured.

Also, Richardson et al. [59] have evaluated the cos–effectiveness of a midurethal sling (MUS) at the time of abdominosacrocolpopexy for the prevention of occult stress incontinence. Only direct costs, obtained from Medicare payments, were included (no indirect or intangible costs were considered). Other options include the following: (1) only performing the MUS if stress incontinence was found postoperatively or (2) only performing the MUS if preoperative urodynamics revealed occult stress incontinence.

Based on the published literature, the QALY score for stress incontinence was 0.71, for those with no stress incontinence QALY = 0.93. The decision trees analysis at 12 months showed that the ICER for combined abdominosacrocolpopexy with midurethral sling (US$2,867 per QALY) was the most cost-effective approach. In the United States, an ICER of US$50,000 per QALY gained is considered cost-effective.

Urge Incontinence

As regards *conservative therapy of urge incontinence*, there have been no cost–effectiveness studies of first-line therapy and bladder retraining. However, many "economic studies" of pharmacotherapy have been undertaken, although most are funded by the relevant pharmaceutical company.

The Food and Drug Administration of the United States does not evaluate economic data when looking at a new drug, but insurance companies or government purchasers often require such data. In the United Kingdom, the NICE does require economic review; they have withheld approval for new drugs that have an ICER greater than £30,000 per QALY.

One of the few independently funded studies [60] performed economic evaluation of five antimuscarinic drugs (both immediate-release [IR] "usual" form and ER forms) for the treatment of OAB. They compared oxybutynin, oxybutynin ER, transdermal oxybutynin, tolterodine, tolterodine ER, trospium, solifenacin, and darifenacin. Solifenacin had the lowest costs and greatest effectiveness for OAB. However, their analysis did not comply with the 10 steps recommended for CEA (see page x). The perspective was that of the payer (rather than a societal perspective), the time frame was too short (3 months) and complete continence was the main effectiveness measure (rather than QALYs).

The *UTIN group* [61] is currently conducting a clinical trial comparing behavioral treatments to medications for urge incontinence. This important study will measure costs and utilities. Through a NIH-funded substudy, separate researchers will conduct parallel economic evaluation of this trial. Recruitment was completed in the late 2013, data not yet published.

Solifenacin studies: Milsom et al. [62] performed a CEA of solifenacin (5–10 mg) versus tolterodine

4 mg sustained release, based upon the STAR RCT [41] and 2 other RCTs of solifenacin versus tolterodine and placebo. QALYs were not included in the original trials, but the EQ-5D was estimated from original HRQOL data collected in 1997. The cost differences between solifenacin and tolterodine ranged from €6 to €127. The authors concluded that flexible-dose solifenacin was more cost-effective than tolterodine 4 mg. This study was supported by Astellas.

Herschorn et al. [42] undertook a Markov model based upon the VECTOR study, which compared solifenacin 5 mg/day versus oxybutynin 15 mg/day in Canada. The withdrawal rate due to side effects of oxybutynin (19%) was much greater than that for solifenacin (3%). No QALY data were included in the original VECTOR study. Their 8-week efficacy data were projected over 1 year, which is an arguable model. Solifenacin yielded a cost saving of CAD$1,830 per annum, giving an ICER of CAD$14,000. This study was funded by Astellas.

Cardozo et al. [63] performed a decision tree analysis of solifenacin versus fesoterodine, oxybutynin ER, propiverine, and tolterodine ER and IR in the United Kingdom. In this 1-year model, success was individually defined for frequency, urgency, and urge incontinence. The model assumed if the patient had no success on a drug that was only available in one dose, then the patient was given no further treatment. The original study did not include QALY data, which were calculated from WTP data published by Kobelt et al. [64]. Because oxybutynin was so much cheaper than the other drugs (20% of total costs versus 60%–70% of total costs for the other therapies), oxybutynin was dominant for 2 of the 3 outcomes.

Darifenacin: Short-term efficacy (12 weeks) and longer-term effects (24 and 52 weeks) of darifenacin have been evaluated [65,66]. Abrams et al. [65] found that darifenacin was associated with significant improvements in QOL as measured by the King's Health Questionnaire at 12 weeks relative to placebo. Chancellor et al. [66] found that darifenacin and darifenacin combined with a behavioral modification plan both resulted in improvements in symptoms and QOL, as measured by the Overactive Bladder Questionnaire (OAB-q), but there were no differences between the two groups. Unfortunately, neither study measured utilities.

Tolterodine: Burgio et al. (the UTIN group) studied 10 weeks of open-label, tolterodine ER alone ($n = 153$) or combined with behavioral training ($n = 154$). The aim was to allow discontinuation of therapy, with follow-up at 8 months [67]. The rate of successful discontinuation of therapy at 8 months was the same in the combination therapy versus drug therapy alone groups (41% in both groups). However, more patients who received combination therapy (versus drug therapy alone) achieved a 70% greater reduction in leakage at 10 weeks (69% vs. 80%; 11% difference [CI: −0.3% to 22.1%]). Women in the combination therapy group had greater benefit on the UDI and the OAB-q (both $p < 0.001$). The addition of behavioral training to drug therapy did reduce incontinence frequency during active treatment. However, it did not improve the ability to discontinue drug therapy (yet maintain improvement in continence status). This finding is counterintuitive to clinical practice.

Two studies evaluating the cost–effectiveness of tolterodine versus PTNS have been published. In 2009, Robinson et al. [68] performed a cost-minimization study of PTNS versus tolterodine ER 4mg, involving 1–2 year follow-up, from the perspective of the NHS. The model assumed that the two treatments had equivalent efficacy (based on unpublished data). Adverse effects were considered to be cost neutral. The patients having tolterodine were followed for 2 years; the duration of follow-up for PTNS was not clearly stated. Tolterodine appeared to be the cheaper treatment but alteration of the variables in the model had a large effect. The report of Chen et al. [35] has already been discussed under decision tree analysis.

Studies of multiple antimuscarinic agents: Nilsson et al. [69] performed a decision tree analysis of anticholinergic medicines available in Sweden. The costs of medicines and incontinence pads were carefully costed from national data. The costs of doctor visits were not included. QALY data were transformed from the King's Health Questionnaire results, obtained from the pooled data of two RCTs regarding fesoterodine (as per standard method discussed). The overall framework was to compare an older drug (oxybutynin IR) with the newer drugs as a group (tolterodine, solifenacin, fesoterodine, darifenacin, and oxybutynin patch), including continuation rates over 1 year from the national drug register. The option of "no treatment" was also included.

The Markov model was carefully constructed and closely resembles the standard clinical practice. The results show that treatment with the newer drugs cost EUR€301 more per annum versus no treatment, but the average gain in QALY (0.046) was substantial. The cost per QALY gained by treatment with newer drugs versus oxybutynin was €37,119, which remains cost-effective. A full range of sensitivity analyses were conducted. No pharmaceutical company was a sponsor of this study.

Also in 2012, Armstrong et al. [70] performed a decision tree analysis of 11 different anticholinergic medicines, using 11 published reports of patients with “OAB-wet.” The primary outcome was cost per treatment success (defined as no incontinence episode for 3–7 consecutive days).

Costs for pads were not included but costs of comorbidities such as UTI, skin infections, bone fractures, and depression were obtained from the U.S. literature. Medication costs were carefully tabulated, ranging from oxybutynin 5 mg BD (US$37 per 3 months) to oxybutynin transdermal patch 3× per week (US$545 per 3 months). Solifenacin 5 mg daily costs US$459 per 3 months. These figures may be quite different in other countries. Cost utility was derived from WTP studies that were not referenced. Using “cost per additional continent patient,” the ICER of solifenacin dominated oxybutynin 5 mg BD by $1,338 per annum. Sensitivity analyses were conducted. The senior author was an employee of Astellas.

Surgery for Urge Incontinence

Studies regarding botulinum toxin type A (Botox A) injections: Three studies comparing Botox A with other current treatments have been performed. Wu et al. performed a Markov model analysis of Botox A versus anticholinergic medication [71], over 2 years, assuming that only 33% of patients would comply with anticholinergic therapy over this time. The Botox treatment cycles were more expensive (US$4,400) than the anticholinergic medication (US$2,560), but the Botox was more effective (QALY gain 1.63 versus 1.50), yielding an ICER of $14,377.

Wefer et al. from Germany evaluated Botox A injections in 214 patients with neuropathic DO [72]. A total of 300 IU of Botox were injected on an inpatient basis (which is common practice in neuropathic DO but varies from some clinical practice in idiopathic DO). Pad costs were reduced from EUR€2.11 per day to €1.05, and medications for UTI fell by half (from €162 per annum to €80 per annum). No QALY measurements were performed.

Robinson et al. [73] undertook a Markov model study comparing Botox with PTNS over 2 years in refractory idiopathic DO. Repeat Botox injections were assumed to occur every 8 months; 20% of patients were assumed to perform clean intermittent self-catheterization (CISC) for 4 months. QALY data were taken from the literature. PTNS was cheaper than Botox (GBP£1,700 versus £4,067) and had a lower ICER (£50,133 versus £111,953) but neither would satisfy UK NICE guidelines for cost–effectiveness (i.e., not less than £30,000 per QALY).

Sacral nerve stimulation (SNS): SNS is a second-line treatment for refractory OAB. Five recent papers present different aspects of cost analysis and cost–effectiveness of SNS.

Aboseif et al. [74] retrospectively reviewed the costs related to SNS 1 year from pre- to postimplantation in the United States. In a heterogeneous group of patients (including retention and chronic pelvic pain), SNS treatment reduced 92% of outpatient visits and diagnostic/therapeutic procedure costs, along with a 30% reduction in drug costs. The costs of the neuromodulation implant itself, nor the surgical implantation costs, were not included. QALYs were not ascertained.

A large multicenter cohort study in France [75] evaluated the costs of 190 OAB-wet patients and neuropathic DO, as well as another 85 patients with OAB-wet plus fecal incontinence (double incontinence). Treatment costs included insertion of preliminary tined leads under GA as an outpatient, then permanent implant as an inpatient. Inpatient Botox injections were the comparator, but patients having routine care were also compared. Travel costs were also included, which extended for 2 years after the SNS implant procedure.

The median overall cost per OAB-wet patient (for 2 years of SNS) was EUR€16,403. This was on average €8,525 more per patient, compared to those on alternative treatments. These comprised conservative measures (medication and diapers/pads), botulinum toxin injection, enterocystoplasty, or urinary diversion. Devices and hospital stays accounted for 40% and 52% of the total cost, respectively. Although a limited CEA was performed over 2 years, the interpretation of the results is difficult because of the heterogeneity of the study population and surgical procedures and the lack of clear descriptions of the cost–effectiveness parameters. Their data suggest that SNS for OAB-wet is not cost–effective over a 2-year period. This is in agreement with the data from Siddiqui et al. [76], and not surprising since the initial device costs are very high. Interestingly, their data suggest that SNS may be cost-effective even in the short term for patients with double incontinence [75].

Siddiqui et al. [76] performed a CEA of SNS vs. intravesical Botox A in patients with idiopathic "OAB-wet" in the United States over 2 years. Interventions comprised a staged implant procedure for SNS using a tined lead and office injections of 200 units of botulinum toxin A. For the SNS strategy, no information about the procedures was provided (local vs. general anesthesia; outpatient vs. inpatient clinic). Based upon their Markov model, the base case SNS treatment was more expensive ($15,743 vs. $4,392) but also more effective (1.73 vs. 1.63 QALYs) than botulinum toxin A. During the 2-year period, SNS was not cost-effective with an ICER of $116,427 [76]. This study reiterates the notion that CEA over just 2 years for a costly implant device is open to question.

Two cost–effectiveness studies have considered the longer term, comparing SNS and botulinum toxin A in the Netherlands [77] and Spain [78]. In the Netherlands, Leong et al. [77] showed that SNS becomes cost-effective from the fourth year postimplant on, given an ICER threshold of €40,000/QALY [77]. These data are based upon two procedures under general anesthesia: (1) a staged SNS procedure involving a tined lead test phase in the operating theater on an outpatient basis, followed by an inpatient stay for device implant and (2) inpatient stay for botulinum toxin A injection in the operating theater.

The Dutch study is in keeping with the Spanish study by Arlandis et al. [78] that showed SNS to be cost-effective from 5 years postimplant onward (using an ICER threshold of €30,000/QALY). These results are based on (1) a staged SNS procedure involving a tined lead test phase and (2) 100 units of botulinum toxin A. No further data were provided on the procedure (inpatient vs. outpatient; local vs. general anesthesia). In both studies [77,78], several assumptions had to be made due to the lack of long-term data beyond 1 year for botulinum toxin A injections and 5 years for SNS therapy, such as therapy transition rates after failure and dropout rates. To what extent these assumptions are valid is unknown.

Because there is no standard protocol of botulinum toxin A injection, a different protocol using 200 units every 14 months was evaluated in the Arlandis study [78], which proved cost-effective on the ICER < €30,000/QALY threshold.

Furthermore, both studies quote a 1-year success rate for SNS of 90%, based upon Van Voskuilen et al. [79] that describes the effect of SNS in 39 patients with OAB over 15.5 months follow-up. However, in that study 10 patients were lost to follow and were excluded from the analysis. Therefore, the 90% success rate may be an overestimation. In the worst case scenario (considering ten lost-to-follow-up patients as failures), both studies would give a 61% success rate. This would obviously influence the cost–effectiveness evaluation. A similar consideration applies to the 5 years success rate of 70%, based upon Van Kerrebroeck et al. [80], which considers patients lost to follow up as last observation carried forward.

Sensitivity analyses for several parameters estimated by expert opinion have been performed. In the Netherlands, SNS remained cost-effective over a 5-year period (ICER < €40,000/QALY) when the estimated dropout rate of 4.3% for both treatments was changed to 2% or 6% and when utility value for incontinence was changed from 0.73 to 0.80. SNS was no longer cost-effective over 5 years in the following cases: (1) if botulinum toxin injections is done under local anesthesia (common practice in several countries), (2) if the peripheral nerve evaluation (PNE) test for SNS screening is used (because of the lower success rate of 55% for PNE compared to 75% for tined lead screening), (3) if bilateral testing is done, and (4) if the new and smaller stimulator (Interstim II) is used.

For a full and detailed review of all direct costs (personal and treatment, including all of the earlier therapies) along with indirect and intangible costs of urge incontinence, readers are recommended to the recent publication by Coyne et al. [81].

SUMMARY AND CONCLUSIONS

Looking at the past three decades of economic studies for UI, we have certainly come a long way. Twenty-five years ago, we were still trying to establish the basic COI in a range of countries and health-care models. In the last 15 years, more continence clinicians have collaborated with health economists. We are now seeing formal economic analyses of the important questions in this field.

Twenty-five years ago, doctors essentially controlled the health-care budget. As long as we could show efficacy and safety, the treatment was usually implemented.

As government bodies such as NICE (and the American insurance companies/health maintenance organizations) gain ever more control of the outflow of monies to patients and health services, we need to generate economic data to show that a new treatment is not just more *effective*, but is more *cost-*

effective, than the old standard. If we clinicians don't generate the raw data, then the health economists will create *top-down* economic simulations such as decision trees or Markov models, to be used instead of real economic data from RCTs. If the conclusions drawn from such theoretical models don't mirror real-life data, we have only ourselves to blame for the lack of true economic data, and for the health policies that may be derived from these mathematical models.

NOTE REGARDING: PROLAPSE

Unfortunately, to date there does not appear to be a QOL test that is sensitive to change after treatment for prolapse. Therefore, economic analyses does not appear to be feasible for prolapse treatments. However, the recent chapters on prolapse, and economic analyses, in the 5th International Consultation on Incontinence [1,82], contain a summary of COI and cost-minimization studies for prolapse (pp. 1853–1854 and pp. 1429–1430, respectively).

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Section III

Structure and Function of the Lower Urinary and Anorectal Tracts in Women

21 Anatomy

John O.L. DeLancey

FUNCTIONAL ANATOMY OF THE LOWER URINARY TRACT

The inseparable relationship between structure and function in living organisms is one of the common themes found in biology. The anatomy and clinical behavior of the lower urinary tract exemplify this immutable link. The following descriptions are intended to offer a brief overview of some clinically relevant aspects of lower urinary tract structure that help us understand the normal and abnormal behavior of this system. Because of the importance of the pelvic floor to lower urinary tract function, comments on the structure of the lower urinary tract organs are followed by a section describing the structure of the pelvic floor as it relates to micturition, continence, and pelvic organ support.

The lower urinary tract can be divided into the bladder and urethra. At the junction of these two continuous, yet discrete, structures lies the vesical neck. This hybrid structure represents that part of the lower urinary tract where the urethral lumen traverses the bladder wall before becoming surrounded by the urethral wall. It contains portions of the bladder muscle and also elements that continue into the urethra.

The vesical neck is considered separately because of its functional differentiation from the bladder and the urethra. The spatial relationships of this region are illustrated in Figure 21.1 and described in Table 21.1.

Bladder

The bladder consists of the detrusor muscle, covered by an adventitia and serosa over its dome and lined by a submucosa and transitional cell epithelium. The muscular layers of the detrusor are not discrete; nevertheless, in general, the outer and inner layers of the detrusor musculature tend to be longitudinal, with an intervening circular–oblique layer.

Two prominent bands on the dorsal aspect of the bladder form one of the prominent landmarks of detrusor musculature [1]. They are derived from the outer longitudinal layer and pass beside the urethra to form a loop on its anterior aspect, called the detrusor loop. On the anterior aspect of this loop, some detrusor fibers leave the region of the vesical neck and attach to the pubic bones and pelvic walls; these are called the pubovesical muscles and are discussed in the succeeding texts.

Trigone

Within the bladder, there is a visible triangular area known as the vesical trigone. The two ureteral orifices and the internal urinary meatus form its apices. The base of the triangle, the interureteric ridge, forms a useful landmark in cystoscopic identification of the ureteral orifices. This triangular elevation is caused by the presence of a specialized group of smooth muscle fibers that lie within the detrusor and arise from a separate embryological primordium. They are continuous above with the ureteral smooth muscle [2]; below, they continue down the urethra. In addition to their visible triangular elevation, these muscle fibers form a ring inside the detrusor loop at the level of the internal urinary meatus [3] (Figure 21.2).

Some fibers continue down the dorsal surface of the urethra and lie between the ends of the U-shaped striated sphincter muscles of the urethra. These smooth muscle fibers of the trigone are clearly separable from those of the detrusor by the smaller size of their fascicles and greater density of surrounding connective tissue. The mucosa over the trigone frequently undergoes squamous metaplasia and therefore differs from that in the rest of the bladder. The circumferential distribution of the trigonal ring fibers at the vesical neck might contribute to closure of the lumen of the vesical neck in this area, but its role has yet to be fully elucidated.

Urethra

The urethra holds urine in the bladder and is therefore an important structure that helps determine urinary continence. Although for many years the urethra was thought to be relatively unimportant in the cause of stress urinary incontinence, recent research has indicated that it is actually the primary factor responsible for stress incontinence. Proper matching of cases with stress incontinence and true asymptomatic controls has revealed that more than 50% of stress incontinence is directly attributable to maximum urethra closure pressure [4].

The urethra is a complex tubular viscus extending below the bladder. In its upper third, it is clearly separable from the adjacent vagina, but its lower portion is fused with the wall of the latter structure. Embedded within its substance are a number of elements that are important to lower urinary tract function; their locations are summarized in Table 21.1 [5]. MRI is being used more frequently to visualize the components of the urethra and suggests functional interpretations of findings in an effort to correlate clinical anatomy with pathophysiology of incontinence [6–8].

Striated Urogenital Sphincter

The outer layer of the urethra is formed by the muscle of the striated urogenital sphincter (Figures 21.3 and 21.4), which is found from approximately 20%–80% of the total urethral length (measured as a percentage of the distance from the internal urinary meatus to the external urinary meatus). In its upper two-thirds, the sphincter fibers lie in a primarily circular orientation; distally, they leave the confines of the urethra and either encircle the vaginal wall as the urethrovaginal sphincter or extend along the inferior pubic ramus above the perineal membrane (urogenital diaphragm) as the compressor urethrae. This muscle is composed largely of slow-twitch muscle fibers [9], which are well suited to maintaining the constant tone exhibited by this muscle. In addition, voluntary muscle activation increases urethral constriction during times when increased closure pressure is needed. In the distal urethra, this striated muscle compresses the urethra from above; proximally, it constricts the lumen. Studies of skeletal muscle blockade suggest that this muscle is responsible for approximately one-third of resting urethral closure pressure [10].

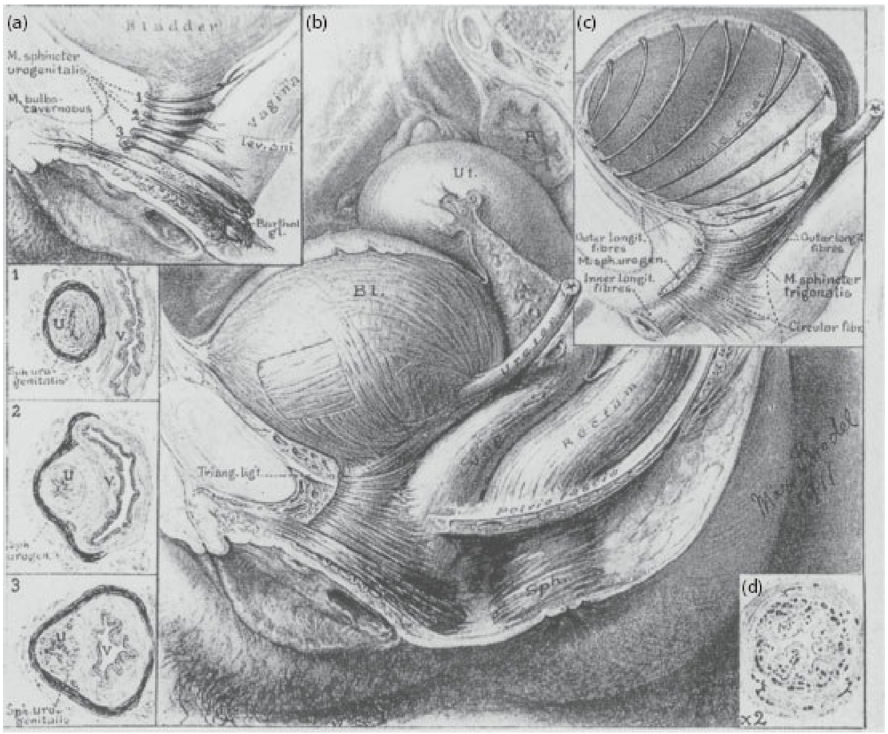

Figure 21.1 The lower urinary tract, including the striated urogenital sphincter muscle. Panel a shows the components of the striated urogenital sphincter muscle with the numbered elements 1, 2, and 3 shown in the following cross section. Panel b represents the relationship of the urethral muscles to the surrounding pelvic organs. Panel c displays the fiber direction of muscles within the detrusor. Panel d indicates the urethra's

vascularity in cross section.

Table 21.1 Topography of Urethral and Paraurethral Structures[a]

Approximate location[b]	Region of the urethra	Paraurethral structures
0–20	Intramural urethra	Urethral lumen traverses the bladder wall
20–60	Midurethra	Sphincter urethrae muscle Pubovesical muscle Vaginolevator attachment
60–80	Perineal membrane	Compressor urethrae muscle Urethrovaginal sphincter muscle
80–100	Distal urethra	Bulbocavernosus muscle

Source: Reproduced from DeLancey JOL, *Obstet Gynecol*, 68, 91, 1986. With permission.

[a] Smooth muscle of the urethra was not considered.

[b] Expressed as a percentage of total urethral length.

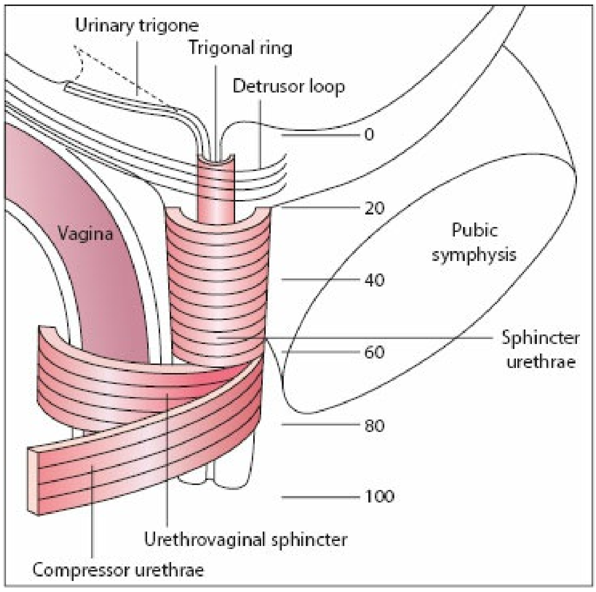

Figure 21.2 Striated urogenital sphincter muscle and trigonal musculature within the bladder base and urethra (cut in sagittal section). The ruler indicates the locations of structures along the urethral length.

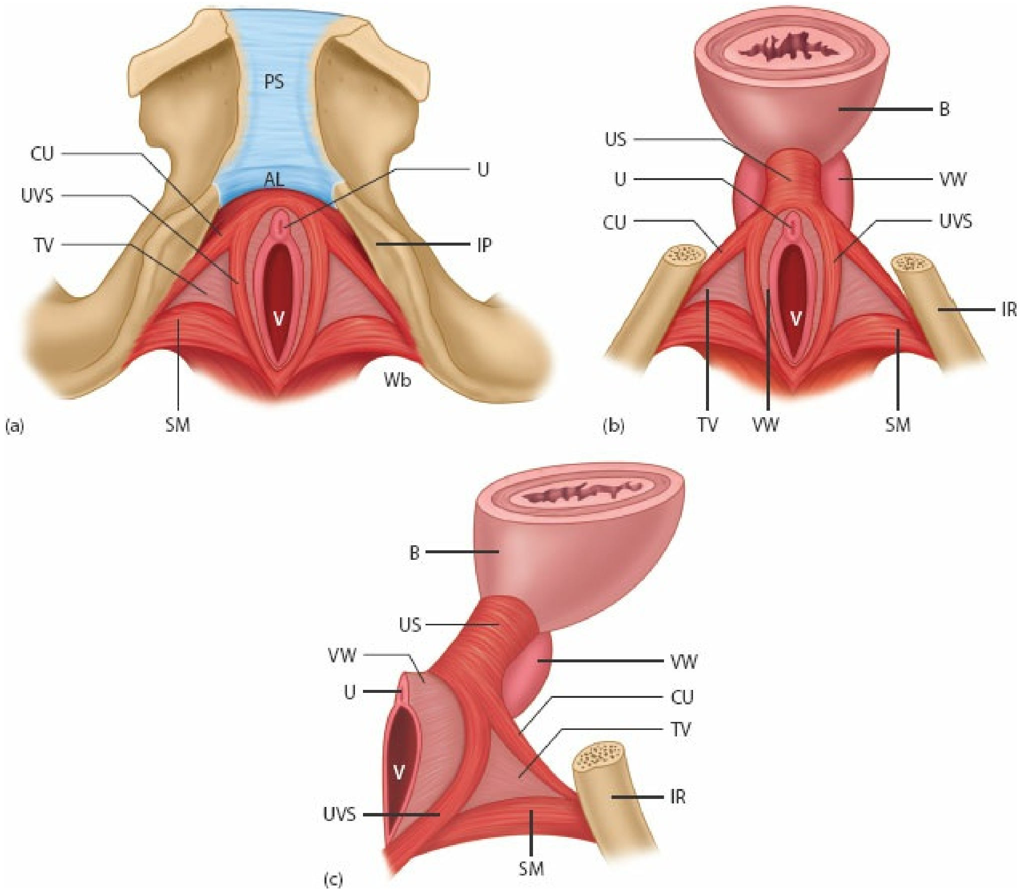

Figure 21.3 Striated urogenital sphincter muscle seen from below after removal of the perineal membrane (a) and pubic bones (b, c). *Abbreviations*: AL, arcuate pubic ligament; B, bladder; CU, compressor urethrae; IP, ischiopubic ramus; IR, ischiopubic ramus; PS, pubic symphysis; SM, smooth muscle; TV, transverse vaginal muscle; U, urethra; US, urethral sphincter; UVS, urethrovaginal sphincter; V, vagina; VW, vaginal wall. (Reproduced from Oelrich TM, *Anat Rec*, 205, 223, 1983. With permission.)

Recent research has shown that the amount of striated muscle declines considerably with age [11]. This is associated with a decline in innervating nerves [12]. First, vaginal delivery also results in changes in electromyographic patterns of striated sphincter musculature that is consistent with impaired muscular function persisting for at least 6 months beyond delivery [13].

Urethral Smooth Muscle

The smooth muscle of the urethra is contiguous with that of the trigone and detrusor but can be separated from these other muscles on embryological, topographical, and morphological grounds [3,14]. It has an inner longitudinal layer and a thin outer circular layer, with the former being by far the more prominent of the two (Figure 21.5). The layers lie inside the striated urogenital sphincter muscle and are present throughout the upper four-fifths of the urethra. With advancing age, the smooth muscle becomes less dense, a change that may contribute to the decline in urethral closure pressure as women get older [15,16]. The configuration of the circular muscle suggests a role in constricting the lumen, and the longitudinal muscle may help to shorten and funnel the urethra during voiding.

Submucosal Vasculature

Lying within the urethra is a surprisingly well-developed vascular plexus that is more prominent than one would expect for the ordinary demands of so small an organ [17]. These vessels have been studied in serial reconstruction by Huisman [3], who has demonstrated the presence of several specialized types of arteriovenous anastomosis. They are formed in such a way that the flow of blood into large venules can be controlled to inflate or deflate them. This would assist in forming a watertight closure of the mucosal surfaces and offer the possibility of rapid increases in their filling from the pressure on the abdominal vessels that supply them. Occlusion of the arterial inflow to these venous reservoirs has been shown to influence urethral closure pressure [10]. In addition, these appear to be hormonally sensitive [3], which may help to explain some individuals' response to estrogen supplementation.

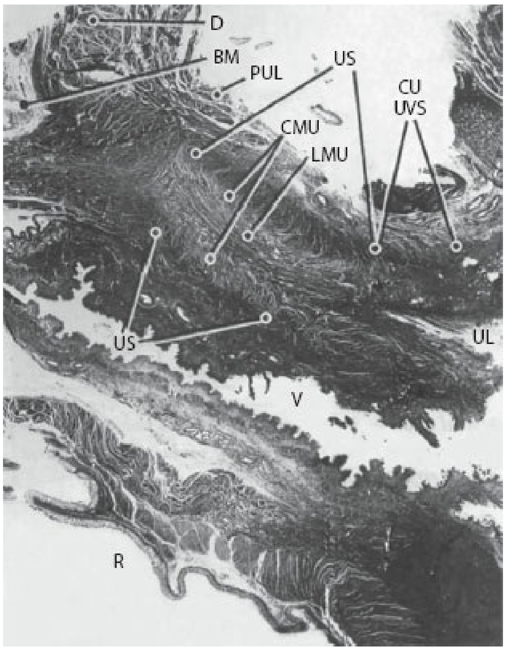

Figure 21.4 Sagittal section from a 29-year-old cadaver, cut just lateral to the midline and not quite parallel to it. The section contains tissue nearer the midline in the distal urethra where the lumen can be seen at the vesical neck. *Abbreviations*: BM, bladder mucosa; CMU, circular smooth muscle of the urethra; CU, compressor urethrae; D, detrusor muscle; LMU, longitudinal smooth muscles of the urethra; PUL, pubourethral ligament; R, rectum; UL, urethral lumen; US, urethral sphincter; UVS, urethrovaginal sphincter; V, vagina. (Reproduced from DeLancey JOL, *Obstet Gynecol*, 68, 91, 1986. With permission.)

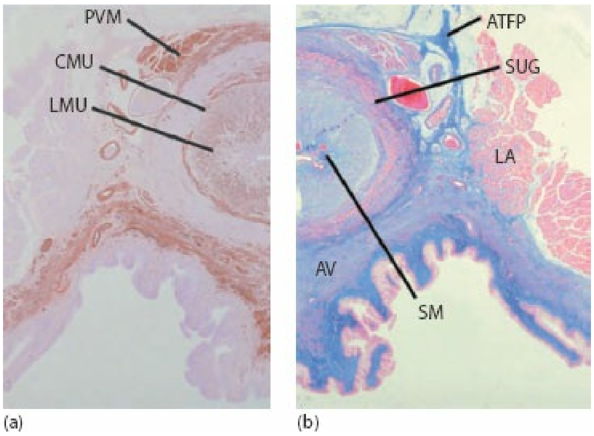

Figure 21.5 Axial midurethral actin immunoperoxidase histological section for smooth muscle (a) and mirrored Mallory trichrome histological section (b) from the same specimen. A few small spots are identified in the submucosa (SM). The longitudinal (LMU) and circular (CMU) smooth muscle of the urethra, the pubovesical muscle (PVM), and the smooth muscle layer of the anterior vaginal wall (AV) are easily identified on the actin-stained immunoperoxidase preparation, whereas the striated urogenital sphincter muscle (SUG) does not stain with actin. *Abbreviations*: ATFP, arcus tendineus fasciae pelvis; LA, levator ani muscles.

Mucosa

The mucosal lining of the urethra is continuous above with the transitional epithelium of the bladder and below with the nonkeratinizing squamous epithelium of the vestibule. This mucosa shares a common derivation from the urogenital sinus with the lower vagina and vestibule. Like these other areas, its mucosa is hormonally sensitive and undergoes significant change, depending on its state of stimulation.

Connective Tissue

In addition to the contractile and vascular tissue of the urethra, there is a considerable quantity of connective tissue interspersed within the muscle and the submucosa. This tissue contains both collagenous and elastin fibers. Studies that have sought to abolish the active aspects of urethral closure have suggested that the noncontractile elements contribute to urethral closure [3]. However, it is difficult to study the function of these tissues because there is no specific way to block their action pharmacologically or surgically.

Glands

A series of glands are found in the submucosa, primarily along the dorsal (vaginal) surface of the urethra [18]. They are most concentrated in the lower and middle thirds and vary in number. The location of urethral diverticula (which are derived from cystic dilation of these glands) follows this distribution, being the most common distally and usually originating along the dorsal surface of the urethra. In addition, their origin within the submucosa indicates that the fascia of the urethra must be stretched and attenuated over their surface and indicates the need for its approximation after diverticular excision.

Vesical Neck

The term “vesical neck” is both a regional and a functional one, as previously discussed. It does not refer to a single anatomic entity; it denotes that area, at the base of the bladder, where the urethral lumen passes through the thickened musculature of the bladder base. Therefore, it is sometimes considered as part of the bladder musculature, but it also contains the urethral lumen studied during urethral pressure profilometry. It is a region where the detrusor musculature, including the detrusor loop, surrounds the trigonal ring and the internal urinary meatus.

The vesical neck has come to be considered separately from the bladder and urethra because it has unique functional characteristics. Specifically, sympathetic denervation or damage of this area results in its remaining open at rest [19]; when this happens in association with stress incontinence, simple urethral suspension is often ineffective in curing this problem [20].

Functional Terms

A number of terms have been used to describe functional units within the vesicourethral unit, based upon radiographic observations of the activities of these viscera. The term “extrinsic continence mechanism” or “external sphincteric mechanism” usually refers to that group of structures that respond when an individual is instructed to stop the urine stream. The two phenomena observed during this effort are a constriction of the urethral lumen by the striated urogenital sphincter and an elevation of the vesical neck, caused by contraction of the levator ani muscles, as described in the following texts. The intrinsic continence mechanism then consists of the structures that lie within the vesical neck and are not specifically activated by contraction of the voluntary muscles. It is this system that fails in patients whose vesical neck can be seen to be open at rest.

PELVIC FLOOR

The position and mobility of the bladder and urethra are recognized as important to urinary continence [21]. Although urethral support plays a secondary role in causing stress incontinence, it is still an independent and important factor [4]. Because these two organs are limp and formless when removed from the body, they must depend upon attachments to the pelvic floor for their shape and position. Fluoroscopic examination has shown that the upper portions of the urethra and vesical neck are normally mobile structures, whereas the distal urethra remains fixed in position [22,23]. The pelvic floor muscles and fasciae determine these aspects of support and fixation. The term “pelvic floor” is used in different ways by different authors. Sometimes, especially in the colorectal field, the term is used to refer to the levator ani muscles. In this chapter, it will be given its broader interpretation because the anatomic term “pelvic diaphragm” serves to identify levator ani muscles and their covering fascia, leaving the term “pelvic floor” to identify the complex structural unit that lies at the bottom of the abdominal cavity.

The pelvic floor consists of several components lying between the pelvic peritoneum and the vulvar skin. These are (from above downward) the peritoneum, viscera and endopelvic fascia, levator ani muscles, perineal membrane, and external genital muscles. The eventual support for all of these structures comes from their connection to the bony pelvis and its attached muscles. The viscera are often thought of as being supported by the pelvic floor; however, they are actually a part of it. Through such structures as the cardinal (CL) and uterosacral ligaments (USLs) and the pubocervical fascia, the viscera have an important role in forming the pelvic floor.

Endopelvic Fascia

Viscerofascial Layer

The top layer of the pelvic floor is provided by the endopelvic fascia that attaches the pelvic organs to the pelvic walls, thereby suspending the pelvic organs [24–26]. Because this layer is a combination of the pelvic viscera and the endopelvic fascia, it is referred to here as the viscerofascial layer. It is common to speak of the fasciae and ligaments alone, separate from the pelvic organs as if they had a discrete identity; however, unless these fibrous structures have something to attach to (the pelvic organs), they can have no mechanical effect.

On each side of the pelvis, the endopelvic fascia attaches the uterus and vagina to the pelvic wall (Figures 21.6 through 21.8). This fascia forms a continuous sheetlike mesentery, extending from the uterine artery at its cephalic margin to the point at which the vagina fuses with the levator ani muscles below. The part that attaches to the uterus is called the parametrium and that which attaches to the vagina, the paracolpium.

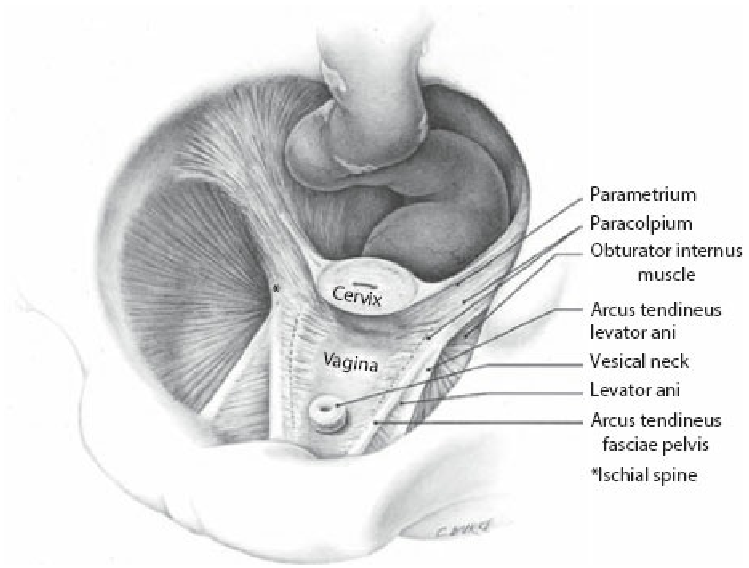
Parametrium
Paracolpium
Obturator internus muscle
Arcus tendineus levator ani
Vesical neck
Levator ani
Arcus tendineus fasciae pelvis
*Ischial spine
Cervix
Vagina
*

Figure 21.6 Supportive tissues of the cervix and upper vagina. Bladder has been removed above the vesical neck.

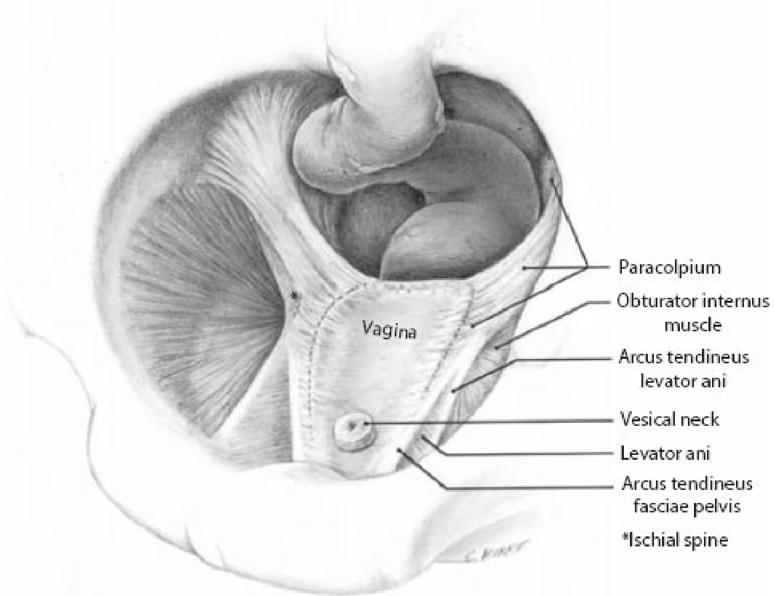
Paracolpium
Obturator internus muscle
Arcus tendineus levator ani
Vesical neck
Levator ani
Arcus tendineus fasciae pelvis
*Ischial spine
Vagina

Figure 21.7 Vagina and supportive structures drawn from dissection of a 56-year-old cadaver after hysterectomy. The paracolpium extends along the lateral wall of the vagina. (Reproduced from DeLancey JOL, *Am J Obstet Gynecol*, 166, 1717, 1992. With permission.)

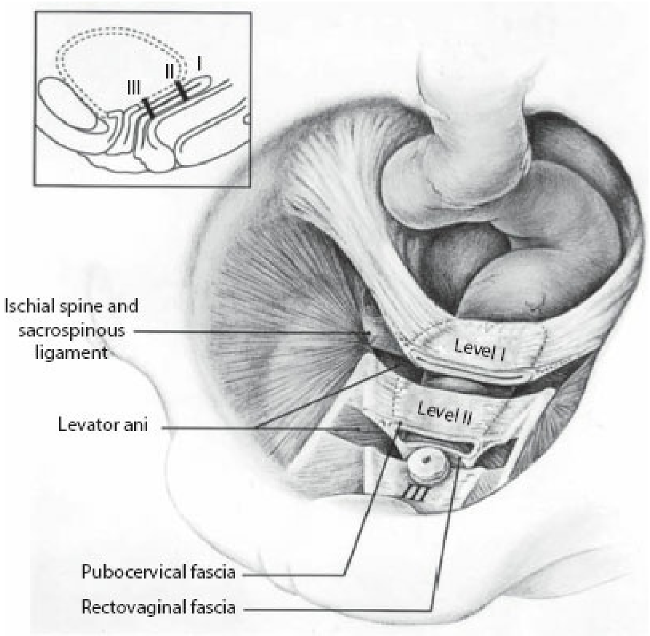

Figure 21.8 Level I (suspension) and level II (attachment). In level I, the paracolpium suspends the vagina from the lateral pelvic walls. Fibers of level I extend both vertically and posteriorly toward the sacrum. In level II, the vagina is attached to the arcus tendineus fasciae pelvis and superior fascia of levator ani. (Reproduced from DeLancey JOL, *Am J Obstet Gynecol*, 166, 1717, 1992. With permission.)

The parametria are made up of what are clinically referred to as the CL and USL [27,28].

Although the cardinal and uterosacrals are termed “ligaments” and “fasciae,” they are not the same type of tissue as that seen in the “fascia” of the rectus abdominis muscle or in the ligaments of the knee, both of which are composed of parallel collagen fibers forming dense, regular, connective tissue. The CL consists of blood vessels, nerves, and fibrous connective tissue and can be thought of as mesenteries that supply the genital tract bilaterally. The USL contains a specific body of smooth muscle not contained in the CL that attaches to the dorsal surface of the cervix. The ridge formed by these tissues when the uterus is elevated is visible when the cul de sac is viewed from above and is the most familiar view of this structure but looks entirely different when the uterus is drawn downward, the action that demonstrates its supportive function.

The structural effect of the CL and USL is most evident when the uterine cervix is pulled downward with a tenaculum, as occurs during dilation and curettage. After a certain amount of descent within the elastic range of the fascia, the parametria become tight and arrest the further cervical descent. Similarly, downward descent of the vaginal apex after hysterectomy is resisted by the paracolpium. The fact that these ligaments do not determine the position of the uterus in normal healthy women is attested to by the observation that the cervix may be pulled down to the level of the hymen with little difficulty [29], and significant differences exist between the location of the cervix during Valsalva in the clinic and with traction in the operating room. In women with normal support, there is a difference of 5 cm or more in most instances [30].

Although it is traditional to focus attention on the ligaments that suspend the uterus, the attachments of the vagina to the pelvic walls are equally important and are responsible for normal support of the vagina, bladder, and rectum, even after hysterectomy. The location of damage to these supports determines whether a woman has a cystocele, rectocele, or vaginal vault prolapse; understanding the different characteristics of this support helps in the understanding of the different types of prolapse that can occur.

After hysterectomy, the upper two-thirds of the vagina is suspended and attached to the pelvic walls by the paracolpium [26]. This paracolpium has two portions (see Figure 21.8): the upper portion (level I) consists of a relatively long sheet of tissue that suspends the vagina by attaching it to the pelvic wall; in the midportion of the vagina, the paracolpium attaches the vagina laterally and more directly to the pelvic walls (level II). This attachment stretches the vagina transversely between the bladder and rectum and has functional significance. The structural layer that supports the bladder (“pubocervical fascia”) is composed of the anterior vaginal wall and its attachment through the endopelvic fascia to the pelvic wall. It is not a layer separate from the vagina, as sometimes suggested, but is a combination of the anterior vaginal wall and its attachments to the pelvic wall. Similarly, the posterior vaginal wall and endopelvic fascia (rectovaginal fascia) form the restraining layer that prevents the rectum from protruding forward, blocking the formation of a rectocele. In the distal vagina (level III), the vaginal wall is directly attached to surrounding structures without any intervening paracolpium: anteriorly it fuses with the urethra, posteriorly with the perineal body, and laterally with the levator ani muscles.

Loss of level II support occurs because of detachment of the arcus tendineus from the ischial spine rather than from the pubic bone [31]. This allows the trapezoidal-shaped anterior vaginal wall to swing downward, resulting in the characteristic cystocele seen clinically. There is also some failure of the midline vaginal wall in these patients, and the relationship between these two defects remains to be clarified.

With the advent of high-resolution MRI, it has been possible to examine the distinct anatomy of the CL and the deep uterosacral ligament (USLd) that comprise the parametrium. Although the superficial USLs that are seen during abdominal hysterectomy are not visible on MRI, the USLds are; their anatomy can, therefore, be studied [32]. The orientation of the CL and USLd and also the changes that occur during increases in abdominal pressure can be studied using models based on women with and without pelvic organ prolapse (Figure 21.9) [33]. In normal women, the CLs are 18.1° ± 6.8° (SD) from the vertical body axis (head to foot) going from their origin at the top of the greater sciatic foramen to their insertion on the cervix and upper vagina. The USLds are dorsally directed at 92.5° ± 13.5 from the body axis coursing from their origin near the sacral foramina S2–S4. The CLs are longer and more curved than USL. When simulated loads are applied in biomechanical models, the theoretical calculated tension on CL is 52% larger than that on USL [34]. These ligament tensions are affected by their orientations.

The differences between these ligaments in women with (cases) and without (controls) prolapse have also been studied. The curved length of the CL at rest was 71 ± 16 mm (cases) vs. 59 ± 9 mm (controls; $p = 0.05$). For the deep uterosacral values, these values were 38 ± 16 mm vs. 36 ± 11 mm ($p = 0.8$), respectively. Similarly, the increase in CL length from rest to strain was 30 ± 16 mm vs. 15 ± 9 mm ($p = 0.03$), and USLd was 15 ± 12 mm vs. 7 ± 4 mm ($p = 0.09$). The change in deep uterosacral angle from rest to Valsalva was significantly different from the CL ($p < 0.001$). These data reveal that CL elongation was greater in women with prolapse than in women with normal support, whereas USL length change was not. The USLd exhibited greater changes in ligament inclination angle [35] (see

Figure 21.10).

The mechanical properties of these ligaments have been studied in vivo by applying known amounts of traction force on the cervix while measuring cervical displacement. In these studies, the length of the CL (indicated by the location of the cervix) seems to be the primary factor associated with cervix position during clinical examination with ligament stiffness playing a relatively minor role [36]. Changes in apical support have clinical importance to both uterine prolapse and cystocele because slightly more than half of cystocele size is associated with the degree to which the cervix prolapses [37].

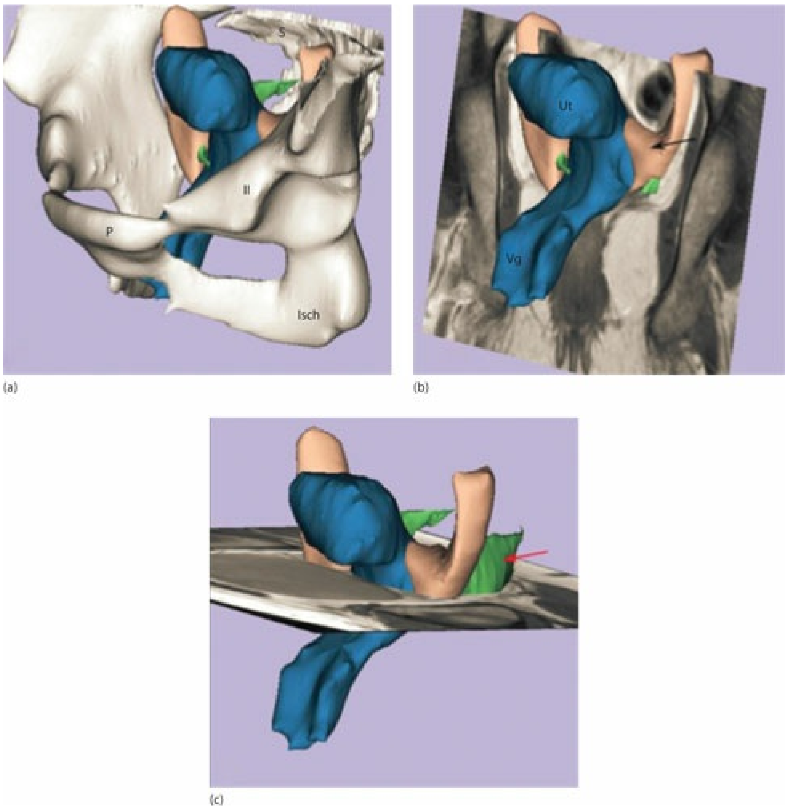

Figure 21.9 A 3D model of the cardinal ligament and uterosacral ligament is oriented relative to the coronal and axial planes. (a) The bony pelvis, including the pubis (P), ilium (Il), ischium (Isch), and sacrum (S), is displayed. (b) Positioning of the uterus (Ut), cardinal ligament (black arrow), and vagina (Vg) can be seen in this coronal image. (c) Note the location of the uterosacral ligament (red arrow) in this axial MR scan. (Courtesy of DeLancey.)

Pelvic Diaphragm and Levator Ani Muscles

Subjecting connective tissue to constant force will stretch any such tissue within the body. Skin expanders used in plastic surgery stretch the dense and resistant dermis to extraordinary degrees, and flexibility exercises practiced by dancers and athletes elongate leg ligaments with as little as 10 minutes of stretching a day. Both of these observations underscore the malleable nature of connective tissue when subjected to force overtime. If the ligaments and fasciae within the pelvis were subjected to the continuous stress imposed on the pelvic floor by the great weight of abdominal pressure, they would stretch; this stretching does not occur because the pelvic floor muscles close the pelvic floor and carry the weight of the abdominal and pelvic organs, preventing constant strain on the ligaments. Recent research has demonstrated the importance of levator ani muscle defects in the occurrence of pelvic organ prolapse [38]. Fifty-five percent of women with prolapse have major injuries to their levator ani muscles. Only 16% of the normal population have this level of injury. Therefore, women with prolapse are much more likely to have major levator muscle injury. This injury is associated with loss of levator contraction force and a larger urogenital hiatus. There is also evidence that poorly functioning levator ani muscles are associated with surgical failure [39].

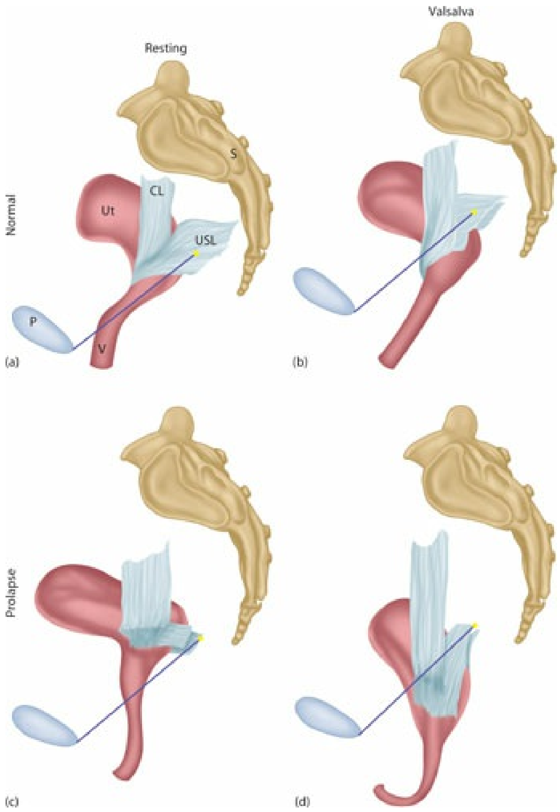

Figure 21.10 Normal and prolapse ligament comparison under resting and maximal Valsalva. Left side view of 3D models of one healthy individual at rest (a) and at maximal Valsalva (b), with their relationship to the normalized arcus tendineus fasciae pelvis (ATFP) (turquoise lines extending from the pubic symphysis [PS] to the ischial spines [yellow squares] or the pubic symphysis to the ischial spine line for spatial reference). Left side view of models of one individual with prolapse at rest (c) and at maximal Valsalva (d). PS and sacrum are shown in the midsagittal plane. *Abbreviations*: Ut, uterus; V, vagina; CL, cardinal ligament; USLd, deep uterosacral ligament. (Courtesy of DeLancey.)

Below the viscerofascial layer is the levator ani group of muscles [40] (Figure 21.11). They have a connective tissue covering on both superior and inferior surfaces, known as the superior and inferior fasciae of the levator ani, respectively. When these muscles and their fasciae are considered together, the combined structure is termed the “pelvic diaphragm.” Although there have been disagreements about the terminology for this muscle, recent review of the literature shows good unanimity regarding anatomy, and a consistent nomenclature based on standardized anatomic terminology is possible [41].

There are three portions of the levator ani muscle: the pubovisceral (pubococcygeal), puborectal, and iliococcygeal [42,43]. The pubovisceral and puborectal muscles arise from the pubic bones on either side of the midline. The pubovisceral muscle lies medial to the puborectal muscle and has several identifiable portions, each with a specific insertion point: The puboperineal portion attaches to the perineal body, the pubovaginal portion attaches to the lateral vaginal wall just inside the hymen, and the puboanal portion has fibers insert into the space between the internal and external anal sphincter. The puborectal muscle originates near the pubic bone and from the superior surface of the perineal membrane and forms a sling dorsal to the anorectal angle, just cranial to the external anal sphincter. Laterally, the iliococcygeal muscle arises from a fibrous band on the pelvic wall (arcus tendineus levator ani [ATLA]) and forms a relatively horizontal sheet that spans the opening within the pelvis and provides a shelf on which the organs may rest. The muscle inserts into the iliococcygeal raphe that is connected to the inner surface of the coccyx and sacrum.

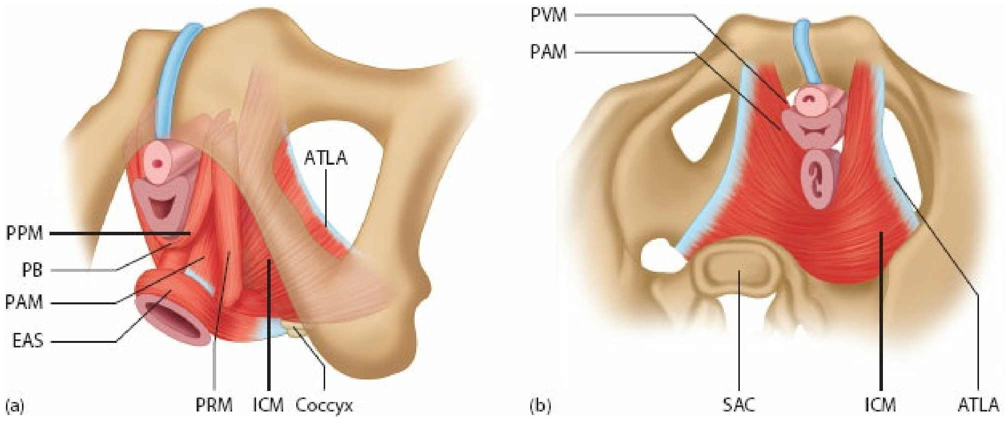

Figure 21.11 (a) The levator ani muscles from below after the vulvar structures and perineal membrane have been removed showing the arcus tendineus levator ani (ATLA), external anal sphincter (EAS), puboanal muscle (PAM), perineal body (PB) uniting the two ends of the puboperineal muscle (PPM), iliococcygeal muscle (ICM), and puborectal muscle (PRM). The urethra and vagina have been transected just above the hymenal ring. (b) The levator ani muscle seen from above looking over the sacral promontory (SAC) showing the pubovaginal muscle (PVM; other abbreviations as in Figure 21.11a). The urethra, vagina, and rectum have been transected just above the pelvic floor. *Note*: The internal obturator muscles have been removed to clarify levator muscle origins. (Reproduced from Kearney R et al., *Obstet Gynecol*, 104, 168, 2004. With permission.)

The opening within the levator ani muscle through which the urethra and vagina pass (and through which prolapse occurs) is called the urogenital hiatus of the levator ani. The rectum also passes through this opening; however, because the levator ani muscles attach directly to the anus, it is not included in the name of the hiatus. The hiatus, therefore, is bounded ventrally (anteriorly) by the pubic bones, laterally by the levator ani muscles, and dorsally (posteriorly) by the perineal body and external anal sphincter. The normal baseline activity of the levator ani muscle keeps the urogenital hiatus closed: it squeezes the vagina, urethra, and rectum closed by compressing them against the pubic bone and it lifts the floor and organs in a cephalic direction.

The levator ani muscles have constant activity [44], like that of other postural muscles. This continuous contraction is similar to the continuous activity of the external anal sphincter muscle and closes the lumen of the vagina in a way similar to that by which the anal sphincter closes the anus. This constant action eliminates any opening within the pelvic floor through which prolapse could occur and forms a relatively horizontal shelf on which the pelvic organs are supported [45,46]. The mechanical action of a muscle is determined by the direction of its fibers. Within the levator ani muscles, there is a 60° differences in muscle fiber direction between the puborectal and pubovisceral muscles [47] (Figure 21.12).

The mechanical consequences of this difference can be appreciated by resolving the muscle fiber directions into a horizontal component that would lead to closure of the levator hiatus and a vertical component that would result in elevation (Figure 21.13). Both the pubovisceral and puborectal components have a significant horizontal component that would compress the hiatus closed. By contrast, only the pubovisceral muscle has an upward vertical vector that could play a role in elevation. The vertical vector of the puborectal muscle is actually in a slight downward direction. The fact that birth-associated injury to the levator ani muscle only affects the pubococcygeal muscle [48] means that distinguishing between these muscles is important in understanding the consequences of levator injury.

Interaction between the Muscle and Connective Tissue

It is important to recognize that the degree of ligament impairment and the degree of prolapse are influenced by and interact with the status of the levator ani muscles as well [49–51]. Figure 21.14 explains this interaction [52]. With normal levator function, (a) the vaginal walls are in apposition, and anterior and posterior pressures are balanced. Levator damage (b) results in hiatal opening. In this situation, the vagina becomes exposed to a pressure differential between abdominal and atmospheric pressures. This pressure differential (c) creates a traction force on the CL and USL.

The importance of understanding the relationship of musculature support and connective tissue support [50,51].

As long as the levator ani muscles function properly, the pelvic floor is closed and the ligaments and fascia are under no tension; the fasciae simply act to stabilize the organs in their position above the levator ani muscles. When the pelvic floor muscles relax or are damaged, the pelvic floor opens and the vagina lies between the high abdominal pressure and low atmospheric pressure; in this situation, it must be held in place by the ligaments. Although the ligaments can sustain these loads for short periods of time, if the pelvic floor muscles do not close the pelvic floor, then the connective tissue must carry this load for long periods and will eventually fail to hold the vagina in place. Song and colleagues have recently shown that there is a decrease in collagen type III in premenopausal women with stress incontinence, suggesting that less flexibility of connective tissue may be associated with greater likelihood of eventual loss of vaginal support [53].

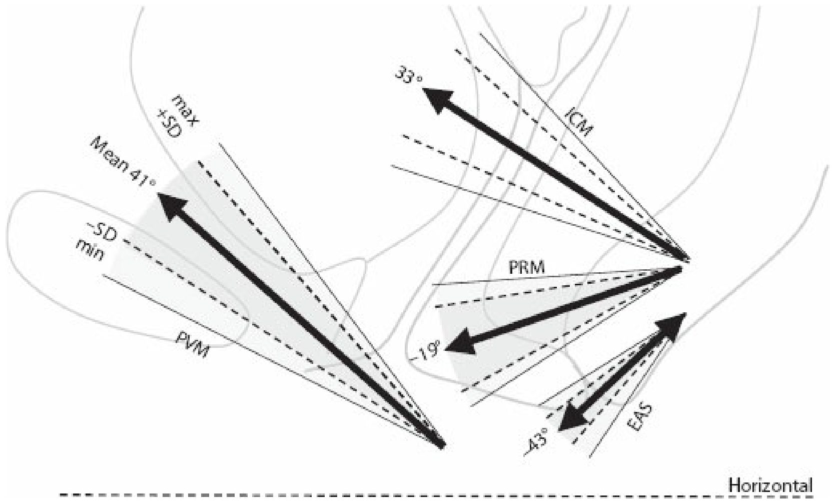

Figure 21.12 The thick arrow displays the mean direction to the horizontal line in a 2D graphic while the shaded areas reflect the standard deviations and range. The dashed line is the horizontal line from which the angles are measured. Angles above the horizontal line have a "±" sign and those below the horizontal line a "−" sign. (Courtesy of DeLancey.)

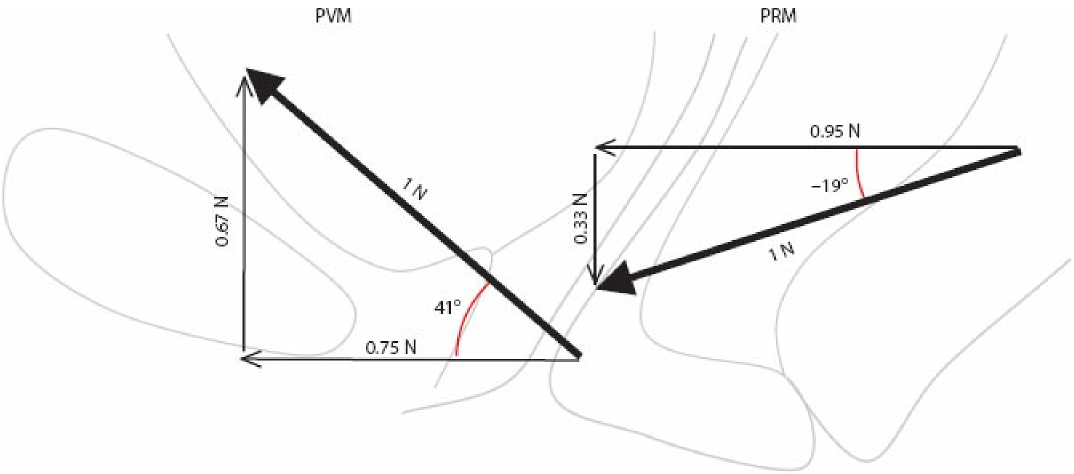

Figure 21.13 Horizontal and vertical components of the pubovaginal muscle (PVM) and puborectal muscle (PRM) in the standing position. The thick arrows show the average direction of the lines of action of the PVM and PRM relative to the horizontal with a theoretical 1 N force. Thin lines indicate the portion of each force related to a closing and lifting function. (*Note*: Vectors are shown larger than the background anatomy to avoid an overlap in the display.) (Courtesy of DeLancey.)

This support of the uterus has been likened to a ship in its berth, floating on the water attached by ropes on either side to a dock [54]. The ship is analogous to the uterus, the ropes to the ligaments, and the water to the supportive layer formed by the pelvic floor muscles. The ropes (ligaments) function to hold the ship (uterus) in the center of its berth as it rests on the water (pelvic floor muscles). If, however, the water level were to fall so far that the ropes would be required to hold the ship without the support of the water, the ropes would break. The analogous situation in the pelvic floor involves the pelvic floor muscles supporting the uterus and vagina that are stabilized in position by the ligaments and fasciae: once the pelvic floor musculature becomes damaged and no longer holds the organs in place, the connective tissue fails because of significant overload.

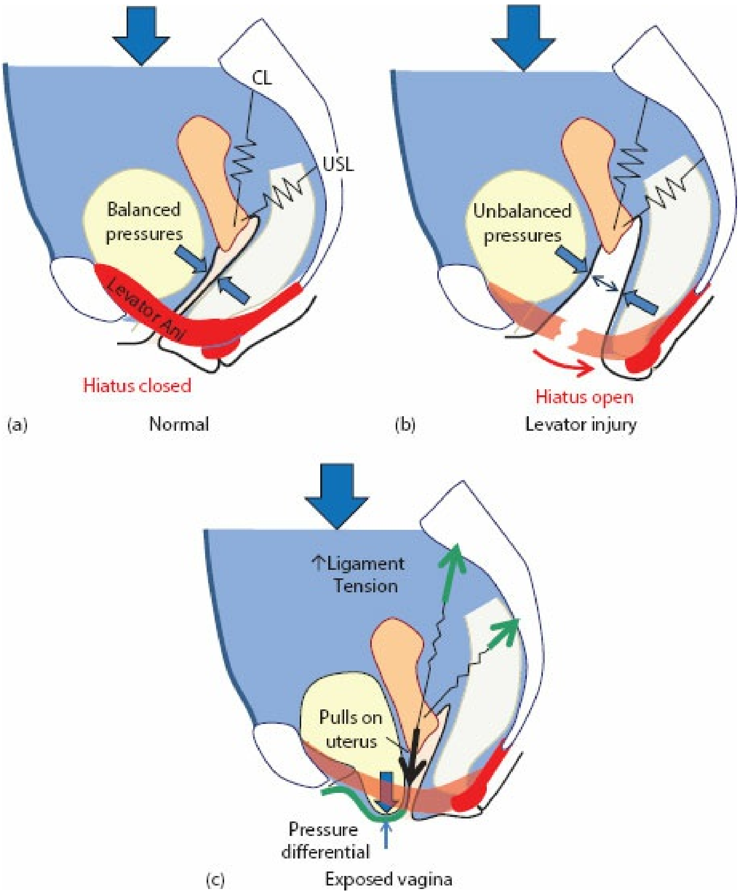

Figure 21.14 Diagrammatic representation of interactions between levator ani muscle, anterior vaginal wall prolapse, and cardinal/uterosacral ligament suspension. (a) Normal levator, pressures balanced; (b) damaged levator, hiatus opens; and (c) pressure differential, upward ligament tension. (Courtesy of DeLancey.)

Perineal Membrane and External Genital Muscles

In the anterior portion of the pelvis, below the pelvic diaphragm, is a dense triangular membrane containing a central opening called the perineal membrane (urogenital diaphragm). This lies at the level of the hymenal ring and attaches the urethra, vagina, and perineal body to the ischiopubic rami. Just above the perineal membrane are the compressor urethrae and urethrovaginal sphincter muscles, previously discussed as part of the striated urogenital sphincter muscle.

Recent dissections show the intimate relationship between the perineal membrane and the levator ani muscle (Figure 21.15); these are in close proximity and so the action of the muscle certainly could influence the position of the perineal membrane [55].

The term "perineal membrane" replaces the old term "urogenital diaphragm," reflecting more accurate recent anatomic information [56]. Previous concepts of the urogenital diaphragm show two fascial layers, with a transversely orientated muscle between them (the deep transverse perineal muscle). Observations based on serial histology and gross dissection, however, reveal a single connective tissue membrane, with these muscles and the levator ani muscles lying immediately above.

The correct anatomy explains the observation that pressures during a cough are greatest in the distal urethra [57,58], where the compressor urethrae and urethrovaginal sphincter can squeeze the lumen in anticipation of a cough [59]. The perineal membrane has been visualized in normal women by MRI examination [8].

Position and Mobility of the Urethra

When the importance of urethral position to determining urinary continence was recognized, anatomic observations revealed an attachment of the tissues around the urethra to the pubic bones. These connections were referred to as the pubourethral ligaments [60] and were found to be continuous with the connective tissue of the perineal membrane [61]. Further studies [59,62,63] have expanded these observations and revealed several separate structural elements contained within these—tissues that have functional importance to urinary—continences [64].

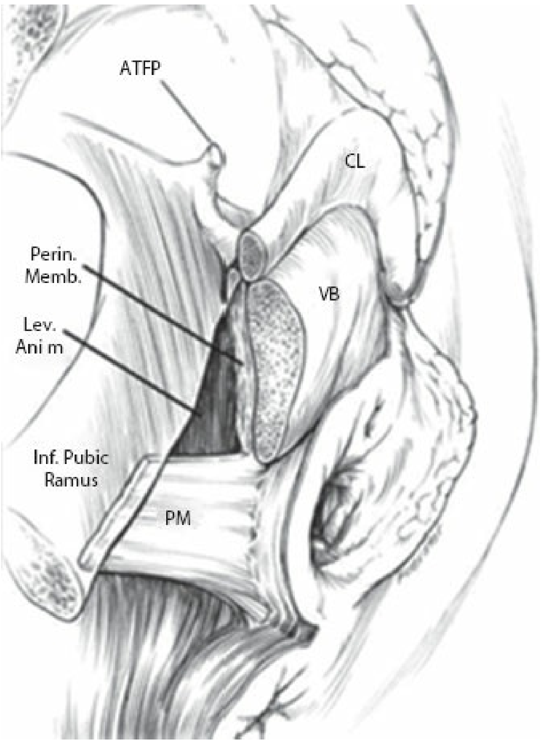

Figure 21.15 Drawing of dissection revealing the perineal membrane showing its lateral attachment to the inferior pubic ramus. A window in the perineal membrane has been cut to reveal the attachment of the levator ani muscle and its fusion with the vestibular bulb. Extension to the arcus tendineus fasciae pelvis is also shown, which is seen inside the pubic bone attaching to its inner surface, clitoris. (From Stein TA and DeLancey JO, *Obstet Gynecol*, 111, 686, 2008. Copyright DeLancey.)

As mentioned earlier in this chapter, urethral support is dynamic rather than static. Fluoroscopic and topographic observations [22,23] suggest that urethral position is determined both by attachments to the bone and by those to the levator ani muscles. The role of the connection between the ureteral supports and those to the levator ani is probably more important than previously thought for the following reasons:

- The resting position of the proximal urethra is high within the pelvis, some 3 cm above the inferior aspect of the pubic bones [65] (Figure 21.16) and above the insertion of the “posterior pubourethral ligaments,” which attach near the lower margin of the pubic bones [60].
- Maintenance of this position would be best explained by the constant muscular activity of the levator ani. In addition, the upper two-thirds of the urethra is mobile [22,23,66] and under voluntary control.
- At the onset of micturition, relaxation of the levator ani muscles allows the urethra to descend

and obliterates the posterior urethrovesical angle (Figure 21.16).

- Resumption of the normal tonic contraction of the muscle at the end of micturition returns the vesical neck to its normal position.

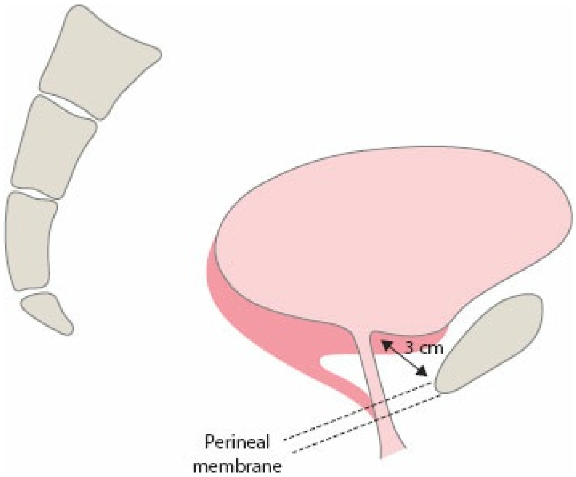

Figure 21.16 Topography and mobility of the normal proximal urethra and vesical neck based upon resting (▪) and voiding (▪) in nulliparae.

Both urethral function and urethral support play a role in urinary continence. Although previously it was thought that support was the predominant factor, it is now clear that urethral function (maximal urethral closure pressure) is the primary determinant of whether or not a woman has stress incontinence [4]. Urethral support is probably more influential in younger women with stress urinary incontinence because they have relatively good urethral function. As urethral function declines with age, the role that maximum urethral closure pressure plays begins to predominate. In women with de novo stress incontinence after first birth, injury to the levator ani muscle is seen twice as often as individuals who deliver and are continent [67]. Later on in life, this seems, however, to disappear [4].

The anterior vaginal wall and urethra arise from the urogenital sinus and are intimately connected. The support of the urethra does not depend on attachments of the urethra itself to adjacent structures, but on the connection of the vagina and periurethral tissues to the muscles and fasciae of the pelvic wall. Surgeons are most familiar with seeing this anatomy through the space of Retzius, and this view is also helpful in understanding urethral support (Figure 21.17). On either side of the pelvis, the arcus tendineus fasciae pelvis (ATFP) is found as a band of connective tissue attached at one end to the lower one-sixth of the pubic bone, 1 cm from the midline, and at the other end to the ischial spine. The anterior portion of this band lies on the inner surface of the levator ani muscle that arises some 3 cm above the ATFP. Posteriorly, the levator ani arises from a second arcus, the ATLA, which fuses with the ATFP near the ischial spine.

The layer of tissue that provides urethral support has two lateral attachments: a fascial attachment and a muscular attachment (Figure 21.18). The fascial attachments of the urethral supports connect the periurethral tissues and anterior vaginal wall to the ATFP and have been termed the “paravaginal fascial attachments” [62]. The muscular attachment connects these same periurethral tissues to the medial border of the levator ani muscle. These attachments allow the normal resting tone of the levator ani to maintain the position of the vesical neck, supported by the fascial attachments (Figure 21.19). When the muscle relaxes at the onset of micturition, it allows the vesical neck to rotate downward to the limit of the elasticity of the fascial attachments; at the end of micturition, contraction allows it to resume its normal position.

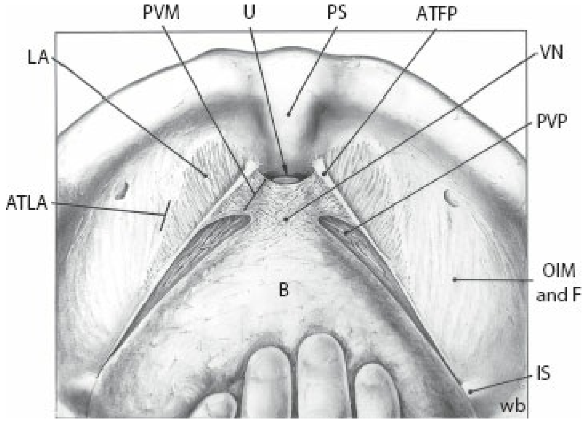

Figure 21.17 Space of Retzius (drawn from cadaver dissection). Pubovesical muscle can be seen going from vesical neck to arcus tendineus fasciae pelvis and running over the paraurethral vascular plexus. *Abbreviations*: ATLA, arcus tendineus levator ani; B, bladder; IS, ischial spine; LA, levator ani muscles; OIM and F obturator internus muscle and fascia; PS, pubic symphysis; U, urethra. (Reproduced from DeLancey JOL, *Neurourol Urodyn*, 8, 53, 1989. With permission.)

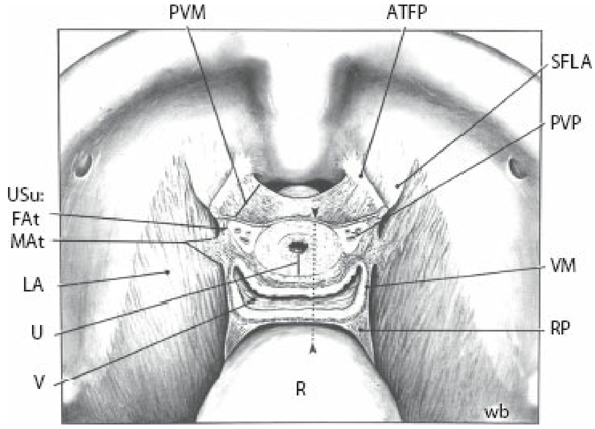

Figure 21.18 Relationship of the supportive tissues of the urethra (USu) to the pubovesical muscles (PVM). Cross section of the urethra (U), vagina (V), arcus tendineus fasciae pelvis (ATFP), and superior fascia of levator ani (SFLA) just below the vesical neck (drawn from cadaver dissection). The PVM lie anterior to the urethra, and anterior and superior to the paraurethral vascular plexus. The USu ("the pubourethral ligaments") attach the vagina and vaginal surface of the urethra to the levator ani (LA) muscles (muscular attachment) and to the SFLA (fascial attachment). *Abbreviations*: R, rectum; RP, rectal pillar; VM, vaginal wall muscularis. (Reproduced from DeLancey JOL, *Neurourol Urodyn*, 8, 53, 1989. With permission.)

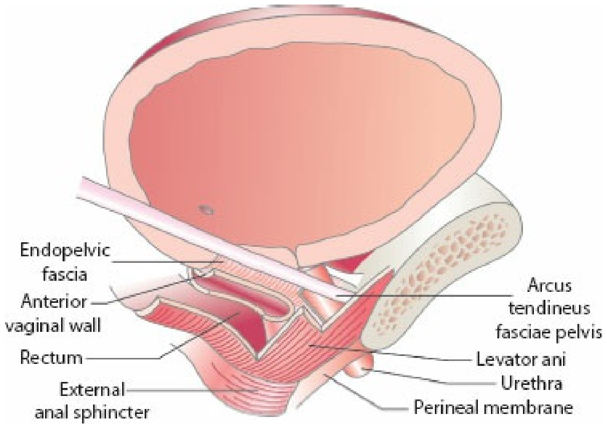

Figure 21.19 Lateral view of the pelvic floor structures related to urethral support, seen from the side in the

standing position cut just lateral to the midline. Note that windows have been cut in the levator ani muscles, vagina, and endopelvic fascia so that the urethra and anterior vaginal walls can be seen.

Also within this region are the pubovesical muscles, which are extensions of the detrusor muscle [1,68,69]. They lie within the connective tissue; when both muscular and fibrous elements are considered together, they are termed the "pubovesical ligaments," in much the same way that the smooth muscle of the ligamentum teres is referred to as the round ligament (see Figures 21.4, 21.5, 21.17, and 21.18). Although the terms "pubovesical ligament" and "pubourethral ligament" have sometimes been considered to be synonymous, the pubovesical ligaments are different structures from the urethral supportive tissues. Fibers of the detrusor muscle are able to undergo great elongation, and these weak tissues are, therefore, not suited to maintain urethral position under stress. In addition, they run in front of the vesical neck rather than underneath it, where one would expect supportive tissues to be found. It is not surprising, therefore, that these detrusor fibers do not differ, in stress-incontinent patients, from those in patients without this condition [70]. The tissues that support the urethra are separated from the pubovesical ligaments by a prominent vascular plexus and are easily parted from them. Rather than supporting the urethra, the pubovesical muscles may be responsible for assisting in vesical neck opening at the onset of micturition by contracting to pull the anterior vesical neck forward, as some have suggested [71].

This mechanism influences incontinence by determining how the urethra is supported, not by how high or low the urethra is in the pelvis. In examining anatomic specimens, simulated increases in abdominal pressure reveal that the urethra lies in a position where it can be compressed against the supporting hammock by rises in abdominal pressure (Figure 21.19). In this model, it is the stability of this supporting layer under the urethra rather than the height of the urethra that determines stress continence. In an individual with a firm supportive layer, the urethra would be compressed between abdominal pressure and pelvic fascia (Figure 21.20) in much the same way that the flow of water through a garden hose can be stopped by stepping on and compressing it against underlying paving. If, however, the layer under the urethra becomes unstable and does not provide a firm backstop against which the urethra can be compressed by abdominal pressure, the opposing force that causes closure is lost and the occlusive action is diminished. This latter situation is similar to an attempt to stop the flow of water through a garden hose by stepping on it while it lies on soft soil.

The structural and functional aspects of the body must always be in agreement. As new functional observations are made of the lower urinary tract, it will be necessary to reexamine our anatomic concepts; doubtless, some of the structural arrangements described in this chapter will be corrected, expanded upon, and improved. This will continue to enhance our ability to understand the variety of patients with lower urinary tract dysfunction and will improve our ability to restore normal urinary control.

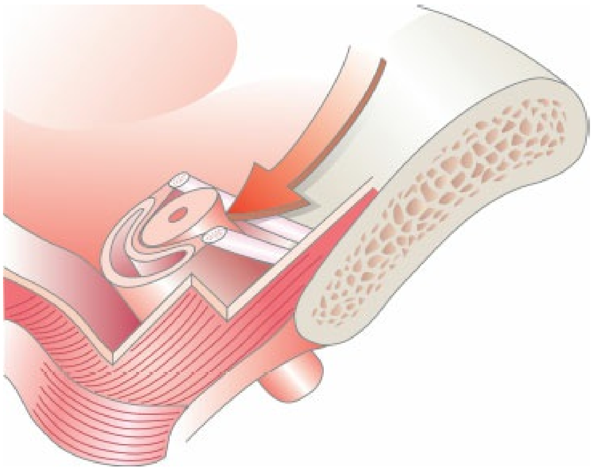

Figure 21.20 Lateral view of pelvic floor with the urethra, vagina, and fascial tissues transected at the level of the vesical neck, drawn from 3D reconstruction indicating compression of the urethra by downward force (arrow) against the supportive tissues indicating the influence of abdominal pressure on the urethra (arrow).

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22

Embryology of the Female Urogenital System and Clinical Applications

Dana Weiss and Stephen A. Zderic

INTRODUCTION

The first goal of this chapter is to provide an overview of the embryological events that lead to the formation of the upper and lower urinary tract in women. Normal female lower urinary tract development cannot be discussed in isolation from that of the rectum, anus, and vagina. Therefore, a good deal of attention will be focused on the embryology of the cloaca and the process whereby it is transformed into the perineum. The traditional embryology literature was highly descriptive based on clinical observations and two-dimensional line drawings. The modern world of developmental biology has changed as embryology may now be visualized in three dimensions, and congenital defects can be examined during the course of development using mice with targeted genetic anomalies. The second goal of this chapter is to briefly discuss the genetic and molecular signals that enable these complex structures to develop. The final goal of this chapter is to provide clinical examples of malformations that arise when deviations from this path of normal development occur.

A growing database of murine genitourinary development exists within the GenitoUrinary Development Molecular Anatomy Project (gudmap.org), which includes serial sections of murine embryos at various stages of development. Over the past 10 years, this multicenter collaboration has compiled a large database containing the results of in situ hybridizations and immunohistochemistry performed for specific gene and protein expression, as well as microarray data. These results are available as a common resource for all investigators via the online portal and serve as a rich starting point from which new work can be planned or current findings can be compared with.

EARLY EMBRYOGENESIS

After initial fertilization of two gametes, the resultant zygote undergoes a series of cell divisions. If this process occurs properly, the embryo ultimately implants within the endometrial wall of the uterine cavity. Pluripotent stem cells then begin to differentiate into three basic germ cell layers. By 22 days of gestation, the embryo is a disc-shaped structure containing the 3 germ cell layers: the ectoderm-lined amniotic cavity, the mesoderm, and the endoderm arising within the yolk sac. At the cranial and caudal ends, the ectoderm and endoderm are in direct contact, and these bilaminar areas are described as the oropharyngeal and cloacal membranes (Figure 22.1a) [1]. With further growth, this disc folds progressively both craniocaudally and laterally, resulting in yolk sac invagination. Over the ensuing 6 weeks, the yolk sac tubularizes and differentiates into the stomach, small intestine, and large intestine completing this process by week 10 of embryonic development [1]. During the course of this yolk sac tubularization, the intestines are extruded from the abdominal cavity by means of the incompletely developed anterior abdominal wall. Simultaneously with the abdominal wall closure, the developing intestine returns to the abdominal cavity and undergoes a 245° counterclockwise rotation around the superior mesenteric artery. This process is complete by 10 weeks of age and explains why the cecum is found in the right lower quadrant.

The development of the ureters, bladder, and urethra starts at the caudal end of the embryo at the cloacal membrane and within the adjacent mesenchyme. Via differential growth rates of the adjacent mesenchyme, the distal primitive hindgut begins to form a dilated chamber known as the cloaca. To appreciate the development of the lower urinary tract and female perineum, one must understand the transition from the 4 mm (4 weeks) to the 36 mm (10 weeks) embryo as the cloaca is partitioned into anterior (urogenital) and posterior (rectal) components.

DIVISION OF THE CLOACA

Following the invagination of the yolk sac at day 28, the primitive hindgut begins to form a dilated chamber, referred to as the cloaca. From this develops a ventral outgrowth orientated toward the umbilicus referred to as the allantois (Figure 22.2a). At this stage, the cloacal membrane that separates the internal cloaca (lined with endoderm derived from the yolk sac) from the external cloaca (composed of ectoderm) remains intact [2]. Part of the allantois will contribute to bladder development; those portions closest to the umbilicus will atrophy forming the urachus. However, in order for these structures to form, the internal cloaca must be partitioned into the ventral (urogenital) and dorsal (rectal) cloaca. This division of the cloaca begins during the fifth week within the upper portions of the chamber and is completed during the seventh week of gestation with resulting rupture of the cloacal membrane (Figure 22.2b) [2]. In classic descriptions from the 1800s, Rathke [3] claimed that this partition takes place by median fusion of two lateral ridges of the cloacal wall in a caudal direction, whereas Tourneaux [4] described a descending septum fusing with the cloacal membrane. By the beginning of the eighth week of gestation, the cloaca has been divided into anterior (ventral) and posterior (dorsal) components, and there is free communication between the internal and external cloacae due to the rupture of the cloacal membrane.

Several complex cellular signaling pathways are required for normal cloacal differentiation, which are being defined through the use of transgenic mice capable of labeling specific cell populations at specific time points. Using a murine model of fetal exposure to all-trans-retinoic acid on the ninth day of conception, Sasaki et al. [5] demonstrated that all fetal survivors had a short tail and imperforate anus. In females, this was manifest as a common cloaca in which the urethra, vagina, and rectum merged. The process of normal cloacal differentiation is under the control of the sonic hedgehog (Shh) signaling pathway (Figure 22.3a) [6]. Shh immunoreactivity was prominent in the rectal, urethral, and bladder epithelium in normal mice, but was absent in those with anorectal malformations (ARM). Bone morphogenetic protein type 4 (BMP4) immunoreactivity was noted in the mesenchyme below the epithelium staining for Shh expression in normal mice, but was absent in the population with ARM. In a second model using a knockout mouse model for Shh, Sukegawa et al. demonstrated that Shh signaling is critical to the concentric development of the hindgut [7]. Recent murine models demonstrate that Wnt5a and Axin2, both downstream of the Shh signaling, are absent in mice with ARM providing evidence of their importance in normal cloacal development [8]. Mice lacking two zinc finger transcription factors, Gli2 and Gli3, which participate in Shh signaling, display imperforate anus, rectourethral fistula, and anal stenosis [9]. Using a knockout mouse, Xu et al. provided evidence for an important role for BMP7 in the partitioning of the cloaca [10]. These BMP7 knockout mice demonstrated a persisting cloacal membrane that was associated with a hypoplastic rectum and a common urogenital sinus. Their data also show that deletion of BMP7 results in marked apoptosis of the cloacal endoderm (CE) (Figure 22.4). In addition, loss of BMP7 expression was associated with a failure of maturation of urethral keratin 8 into the keratin 14 isoform. The literature using these experimental models to delineate the molecular basis of the cloacal partitioning will expand as additional strains of genetically modified mice are available for study.

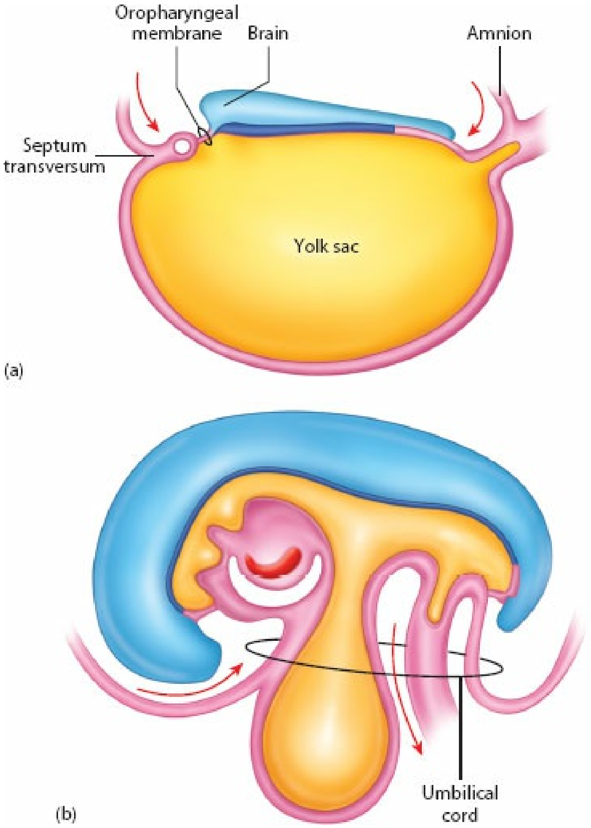

Figure 22.1 (a) Sagittal section of the discoid 22-day-old embryo, showing the relationship of the yolk sac to the neural and mesenchymal layers prior to the folding. The arrows show the direction of the subsequent folding that takes place by day 28. The oropharyngeal and cloacal membranes are already developing at the cranial and caudal ends of the neural tube. (b) Sagittal section of the embryo at day 28, showing the residual yolk sac contained within the developing umbilical cord. The second smaller extension of the yolk sac into the cord (which forms the basis of the allantois) can be seen. The cloacal membrane is just to the right of the umbilical cord. (Reprinted with permission from Stephens FD et al., *Congenital Anomalies of the Kidney, Urinary and Genital Tract*, 2nd ed., Martin Dunitz Limited, London, U.K., 2002, pp. 3–12, Fig. 1.1.)

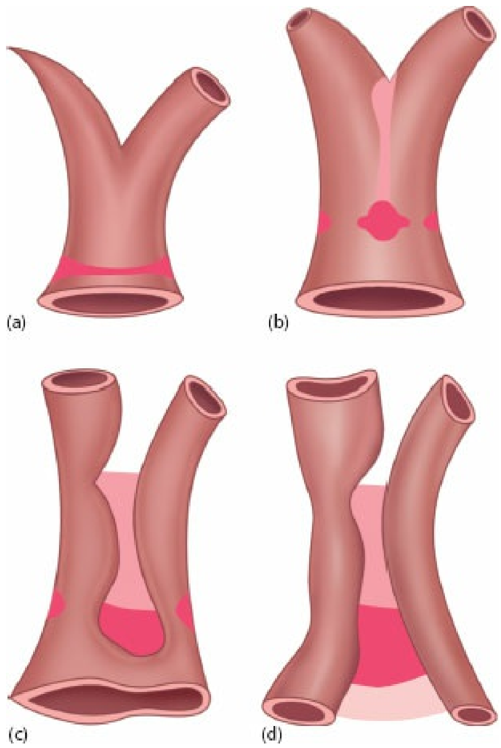

Figure 22.2 (a) Undivided internal cloaca at the 4 mm stage of development. The developing urorectal septum separates the allantois from the hindgut. The allantoic extension to the left leads to the umbilical cord and the future navel; this extension forms the basis of the urachal remnant. (b) Division of the internal cloaca is completed in this sequence, and the cloacal membrane has now ruptured, allowing for communication between the internal and external cloacal chambers. (c) With further growth, the external cloaca is partitioned by an extension of the urorectal septum and an ingrowth of the genital folds. (d) Fusion of the genital folds in the midline completes the separation of the urethra anteriorly from the rectum posteriorly. (Reprinted with permission from Stephens FD et al., *Congenital Anomalies of the Kidney, Urinary and Genital Tract*, 2nd ed., Martin Dunitz Limited, London, U.K., 2002, pp. 3–12, Fig. 1.2.)

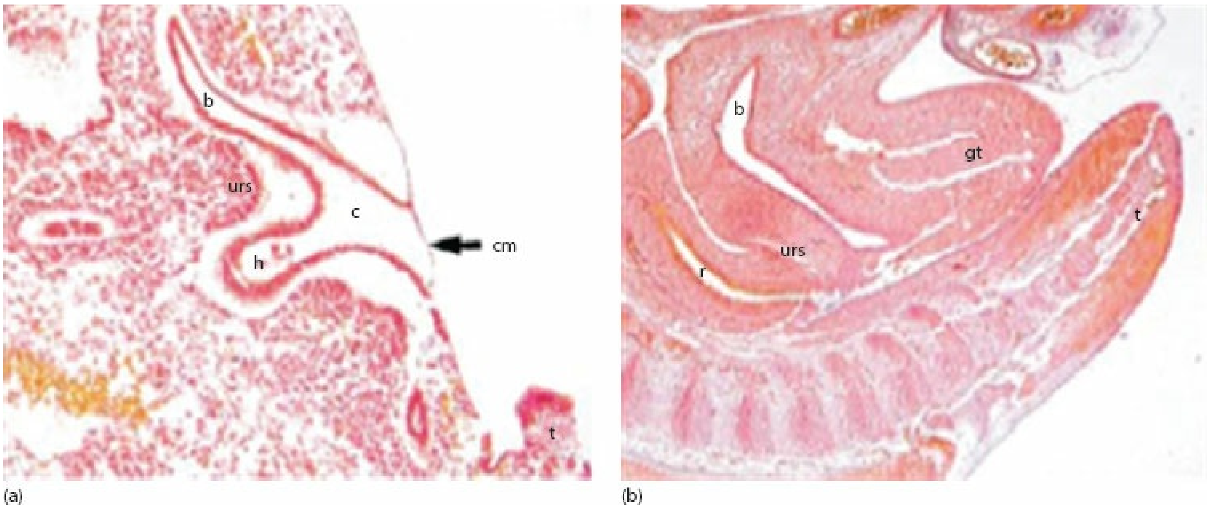

Figure 22.3 (a) Midsagittal section taken through a mouse embryo with a deletion of Shh expression shows a persistent cloaca covered by a thin cloacal membrane (cm). The bladder (b) and hindgut (h) are partially separated by the urorectal septum (urs). The proximal portion of the tail (t) can be seen. (b) In comparison a midsagittal section taken through a wild-type embryo showing almost complete separation of the bladder and urogenital sinus from the rectum (r). (With permission from Perriton CL et al., *Dev Biol*, 247, 26, 2002.)

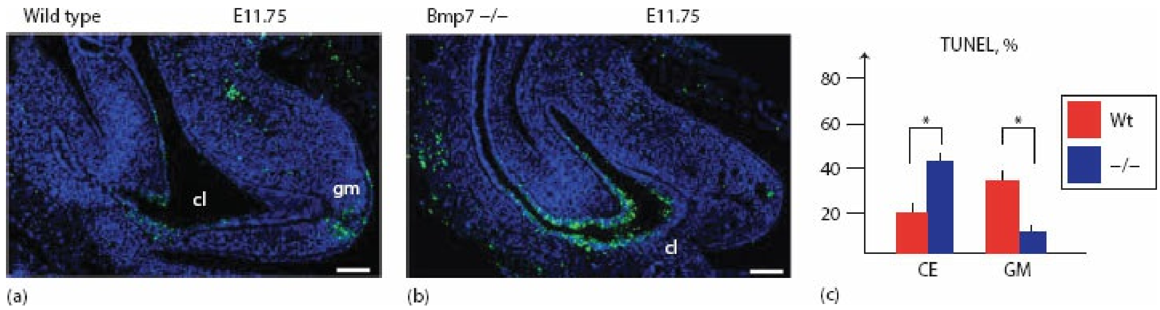

Figure 22.4 Bmp7 promotes cell survival in the cloacal endoderm (CE) as shown in sagittal sections of wild-type (a) and Bmp7-null (b) mice at E12.5. Zones of apoptosis were detected using a TUNEL assay (green fluorescence), and all nuclei were stained with DAPI (blue). (c) Graph shows the percentage of TUNEL-positive cells in CE and genital mesenchyme (gm). * indicates that $p < 0.05$ when comparing CE to GM. (With permission from Xu K et al., *PLOS ONE*, 7(1), e29372, 2012.)

Simultaneously with the septation of the internal cloaca, the external cloaca also undergoes partitioning in order for the normal perineum to develop and the process of external sexual differentiation begins. Partitioning of the external cloaca begins in part as a distal extension of the urorectal septum (Figure 22.2c) coupled to an inward migration of the genital folds to create the short female perineal body and median raphe (Figure 22.2d). In contrast, in males, the perineal body is elongated, and there is an anterior deflection of the proximal urethra, a process that is regulated by androgens. This phase also marks the onset of Müllerian differentiation in the female embryo.

Genital patterning is initiated 2 weeks prior to steroid synthesis in part through Shh-dependent signaling pathways. These concepts are nicely demonstrated in a mouse with a deletion of Shh expression; external genitalia are absent and a primitive persistent cloaca develops instead (Figure 22.3a) [6]. It appears that with Shh deletion, there is also a simultaneous downregulation of BMP2, BMP4, Fgf8, Fgf10, and Wnt5a, and increased apoptosis occurs within the genitalia [6]. Wang et al. studied the effects from the deletion of the *Six1* and *Six2* family of genes on perineal development [11]. These genes were strongly expressed in the pericloacal mesenchyme, and their deletion resulted in a urogenital sinus. They suggested that these genes program for an asymmetric growth pattern that leads to a narrowing of the cloaca that results in the perineal body. Some of the pathways must be androgen dependent of which ephrin B signaling in the developing urethral seam is one such example [12].

MÜLLERIAN DIFFERENTIATION

Primitive Müllerian ducts are present in both sexes during embryogenesis, but in males these involute due to the expression of Müllerian-inhibiting substance (MIS), which is secreted by the Sertoli cells of the testes. Mouse studies suggest the transcription factors Pax2, Pax8, Lim1, Emx2, Hoxa13, and Dach1 play a major role in Müllerian development. In Lim1-null mice, ovarian development still occurs but the female neonates lack uteri and fallopian tubes [13]. Other signaling molecules are postulated to be required for normal Müllerian development such as Wnt9b and Wnt4, which act via a paracrine mechanism [14] and retinoic acid [15]. Despite these findings in murine models, a study of 25 women affected by the Mayer–Rokitansky–Kuster–Hauser syndrome, characterized by varying degrees of uterine duplication or agenesis and renal findings, failed to support the role of Wnt4 and the retinoic acid receptor pathways [16]. These discrepancies between experimental and clinical observations are not surprising, because the genetic deletion in the mouse often targets the first step in a long complex cascade, whereas clinical syndromes may have defects much farther along in the same pathways.

By week 6, the Müllerian ducts form from the intermediate mesoderm located laterally to the Wolffian ducts and develop along the anterior–posterior axis of the embryo. Lineage tracing experiments in chicks and mice reveal that these ducts are all derived from different populations of coelomic epithelium without any direct cellular contribution from the adjacent Wolffian ducts [17]. Although cells derived from the Wolffian duct do not contribute to the Müllerian duct, cell–cell signaling between these ducts mediated by Wnt9b and Wnt4 induces Müllerian development. Indeed, close contact with the Wolffian duct is necessary for Müllerian duct elongation [18]. The Müllerian ducts begin as solid cords that likely tubularize on the basis of apoptosis during their differentiation.

Proximal parts of these ducts form the fallopian tubes; distally, they fuse in the midline producing the uterus, cervix, and proximal two-thirds of the vagina [19]. By week 7, the caudal ends of the Müllerian ducts migrate through the urorectal septum to penetrate the posterior aspect of the urethra [20] at the Müllerian tubercle between the two openings of the Wolffian ducts (Figure 22.5a) [19]. The urethra and Müllerian structures terminate in the common urogenital sinus (Figure 22.5b) prior to the separation of the urethra and vagina that proceeds as a result of differential growth (Figure 22.5c) and an anterior turn of the distal urethra (Figure 22.5d). Failures in distal migration of the Müllerian ducts to form the urogenital sinus may result in distal vaginal atresia.

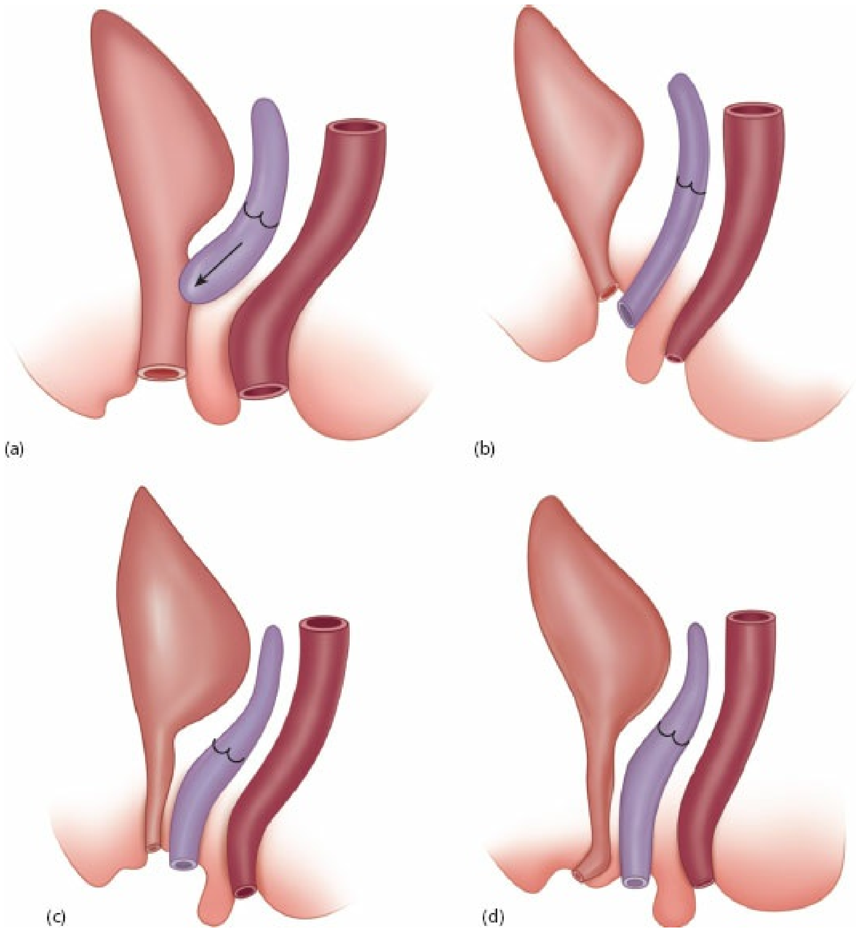

Figure 22.5 (a) The Müllerian ducts migrate to and penetrate the posterior urethra at week 7. The Müllerian ducts are guided to this point in the posterior urethra by the Wolffian ducts. (b) The ducts migrate caudally, and the urogenital sinus becomes a shallow channel. At this point, there is a good separation between the urethra and vagina. (c) With continued growth, the urogenital sinus disappears, as both the urethra and vaginal introitus are now at the perineal surface. The distal vagina is formed from sinus epithelium, which streams into the vaginal vault. (d) With continued growth, the urethra turns anteriorly to reach its final location. (Reprinted with permission from Stephens FD et al., *Congenital Anomalies of the Kidney, Urinary and Genital Tract*, 2nd ed., Martin Dunitz Limited, London, U.K., 2002, pp. 50–62, Fig. 4.1.)

It is important to appreciate the interaction between the Wolffian and Müllerian systems leading to formation of the urogenital sinus [21]. The Wolffian ducts serve to guide the Müllerian ducts to the urogenital sinus and are then carried toward the perineum in the lateral walls of the vagina and undergo involution in the course of normal differentiation. If the Wolffian ducts fail to involute properly, they can remain as small cysts within the lateral vaginal wall or the cervix that can enlarge, become infected, and present clinically as Gartner’s duct cysts. This embryology is also clinically relevant because the ureteral buds arise from the Wolffian system; as a result, the lateral walls of the vagina are a potential site for the rare insertion of an ectopic ureter.

DEVELOPMENT OF THE UROTHELIUM

The urothelium precedes development of the smooth muscle of the bladder wall and ureters. Within the ureter and the trigone, the urothelium has been postulated to arise from mesodermal origins. In contrast, the remainder of the bladder and proximal urethra are thought to arise from endodermal cell lines, whereas the distal urethra arises from ectoderm. Liang et al. have shown that urothelium derived from these distinct anatomic locations has unique patterns of expression of the uroplakins and keratins and that these are maintained in cell culture [22]. In addition, they showed that the urothelium undergoes squamous metaplasia in response to vitamin A deficiency, characterized by keratin expression restricted to the trigone and bottom half of the bladder. The key concept in this work is that the urothelium may look the same in these areas of the upper and lower urinary tract, but it is actually very heterogeneous.

SMOOTH MUSCLE DIFFERENTIATION

The connective tissue and smooth muscle of the urethra and bladder are subsequently derived from adjacent mesenchyme. The developing urethra and bladder contain no muscle in the early stages of development, and the endoderm of the urogenital sinus remains a single layer of epithelium up to the seventh week and then gradually assumes the appearance of transitional epithelium in the third month. The earliest muscle layers arise within the bladder, and the urethral smooth muscle layers are induced 1 week later implying that these smooth muscle bodies are distinct entities despite their close approximation at the bladder neck [23]. This should not be particularly surprising given the pharmacological differences and functional demands between these two intravesical regions of smooth muscle.

The mechanism by which epithelial mesenchymal interactions induce smooth muscle development has been described. Using fetal rat primitive mesenchyme grafted below the renal capsule in nude mice, Baskin et al. demonstrated that a transformation of this mesenchyme into smooth muscle was possible only if urothelium was also implanted simultaneously [24,25]. The growth factors, such as Shh, secreted by such epithelial regions are powerful driving forces for differentiation [26,27]. Further growth of smooth muscle is accompanied by complex serial changes in muscle-specific protein expression and cell turnover, as shown in a detailed study of mouse detrusor development [28].

DEVELOPMENT OF THE SPHINCTERS

Little data exist regarding the development of the internal, or smooth muscle, sphincter (i.e., the bladder neck). In contrast, more efforts have been expended in trying to better characterize the development of the striated external sphincter. Evidence supports the notion of transdifferentiation from smooth to striated muscle, which could then account for the development of the external sphincter [29]. As an alternative explanation, anatomic observations in female fetal specimens confirm that by 9 weeks of gestation, there is the condensation of undifferentiated mesenchyme immediately adjacent to the urethra. By 10 weeks of gestation, this mesenchyme has differentiated into striated muscle, which forms the omega-shaped external sphincter [30,31]. In this study, there was no evidence that concentric development of this striated muscle group is then followed by a selective loss of muscle to produce the omega-shaped characteristic of this sphincter. Similar observations were reported by Yucel and Baskin [32], who also noted that this striated sphincter is always distinct from the levator muscle group and commented on the innervation of this sphincter by both myelinated fibers and neurons that stained positively for nNOS [33]. A recent study examining 28 human female fetuses confirmed the presence of a discrete external urethral sphincter primordium at week 9 of gestation. Additionally, at week 15 the smooth sphincter and rhabdosphincter could be clearly identified. Both muscular complexes were located in the middle third of the urethra but only the muscle fibers of the smooth sphincter intermingled with the detrusor muscle [34].

DEVELOPMENT OF THE TRIGONE AND UPPER URINARY TRACT

The pronephros develops at the fourth week and differentiates into the mesonephric ducts and the mesonephros. The mesonephros consists of glomeruli and tubules, which open into the mesonephric (Wolffian) ducts derived from the pronephric ducts. The mesonephric ducts extend caudally and drain into the cloaca [1], and an outgrowth of the ducts near their insertion at the cloaca gives rise to the ureteral buds (Figures 22.6 and 22.7) [35,36]. The ureteral buds grow cranially until they contact the metanephric mesenchyme at which point a series of complex reciprocal interactions between the bud and the mesoderm result in differentiation to the metanephros and ultimately a functioning kidney; fetal urine production is evident by the ninth week of gestation. The initiation location of the ureteral bud is critical for the formation of the trigone, the development of a normal vesicoureteral junction, and ultimately the formation of a normal kidney. In 1975, Mackie and Stephens [37] proposed the ureteral bud hypothesis that stated that a bud arising from an abnormal location along the Wolffian duct would lead to abnormal nephrogenesis (Figure 22.8) [38]. They proposed that if the bud appeared too close to the cloaca, it would ultimately be incorporated into the trigone in a very lateral position leaving it more prone to reflux, and in extreme cases, abnormal nephrogenesis would occur. Clinically, this might become apparent in the neonate who presents with antenatally diagnosed hydronephrosis, who in the first days of life undergoes a VCUG demonstrating high-grade reflux and who on sonography has abnormal renal parenchyma and an elevated creatinine. They also noted that if the bud arose too far away from the cloaca, it would be carried out into an ectopic position either within the bladder neck, the urethra, or even the lateral walls of the vagina in females. Many of these ectopic ureters are associated with a small volume of dysplastic renal parenchyma.

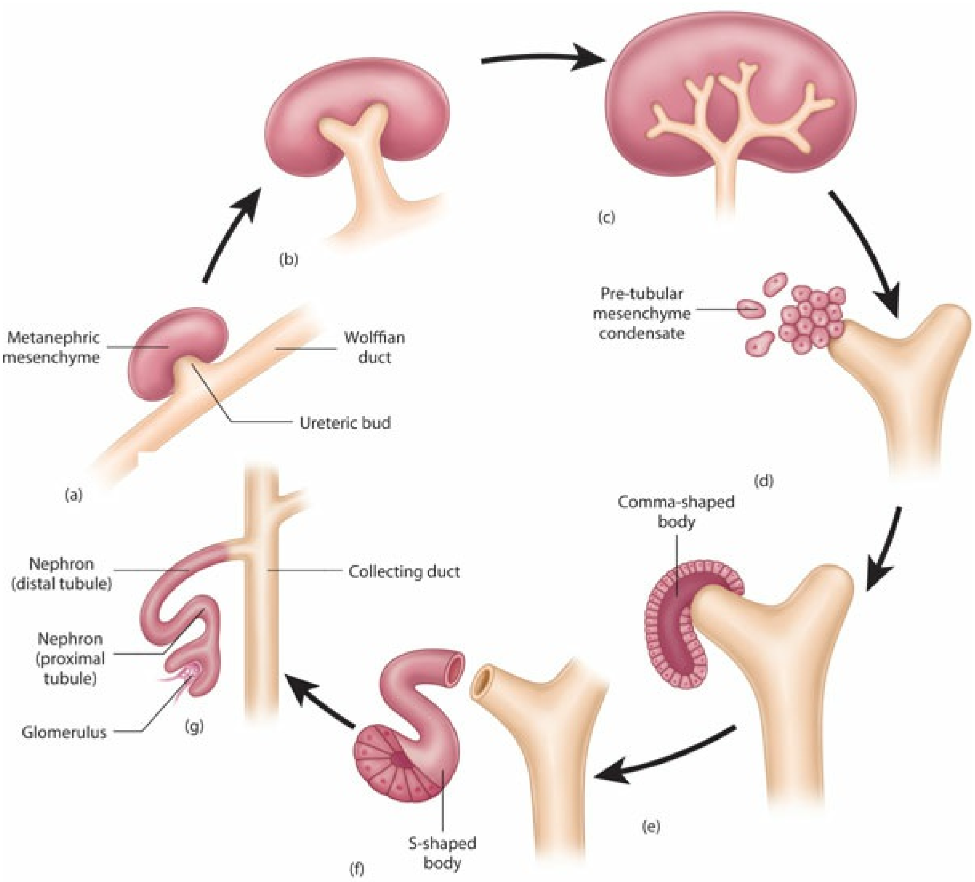

Figure 22.6 Stages of the renal branching morphogenesis: (a) Ureteral bud outgrowth from the Wolffian duct is induced by signals from the metanephric mesenchyme. (b, c) Invasion of the metanephric mesenchyme by the ureteral bud results in branching. (d) At the tips of the branches, the epithelium induces the mesenchyme to form pretubular aggregates, which are stimulated to undergo mesenchymal to epithelial transformation through the formation of comma-shaped (e) and S-shaped (f) bodies to form components of the nephron. (g) The renal tubules merge with the epithelial and vascular components of the glomerulus. (With permission from Shah MM et al., *Development*, 131, 1449, 2004.)

Normal trigonal development is essential to the prevention of vesicoureteral reflux, a common clinical entity in young girls. Its embryological origins remain a source of debate as the trigone was traditionally thought to be of mesodermal origin deriving from the common nephric duct and the ureter [39]. In order for the ureteral bud to become incorporated into the developing urogenital sinus, the common nephric duct must become absorbed into this sinus. Thus, it would stand to reason that at least part of the trigone is of mesodermal origin. Others have postulated that the detrusor muscle contributed to the trigone [40]. Indeed, recent studies using transgenic mice suggest that in fact the trigone is of endodermal origin [41]. Examination of murine models has demonstrated that the majority of the trigone is derived from detrusor muscle but interdigitating ureteral fibers do contribute to the final trigonal structure. These data were obtained via immunohistochemical analysis of both murine and human fetal tissue [42]. Apoptosis plays an integral role in trigone formation; the common nephric duct undergoes apoptosis resulting in separation of the ureter from the Wolffian duct and apoptosis is required to create a patent ureteral orifice [43–45]. It is also likely that the final position of the ureteral orifice also depends on the growth of the bladder itself [46].

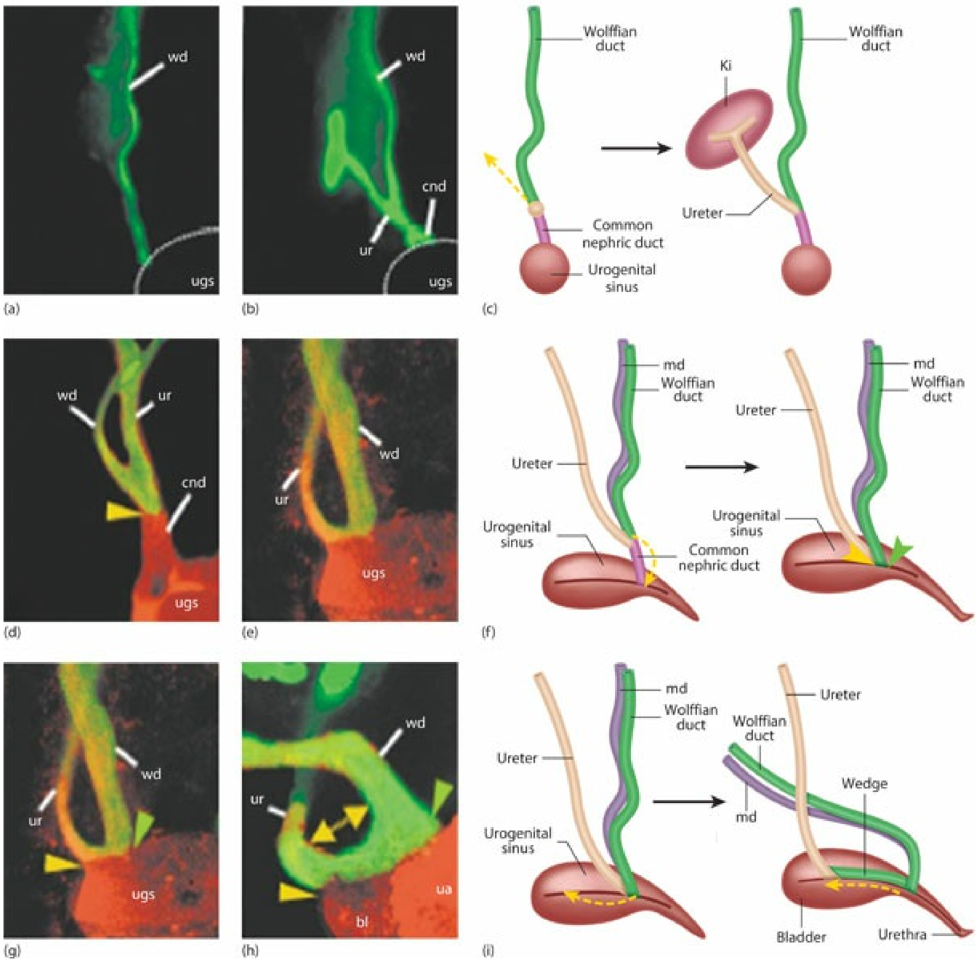

Figure 22.7 Visualization of the three stages of ureter maturation in vivo in Hoxb7-GFP mice that express green fluorescent protein in epithelia of the fetal excretory system. (a–c) Ureteral bud formation and outgrowth: The distal ureter (ur) remains attached to the Wolffian duct (wd). The distal ureter starts to separate from the primitive bladder (ugs) by a terminal Wolffian duct segment, the common nephric duct (cnd). (d–f) Vertical displacement: The distal ureter descends and contacts the urogenital sinus. The yellow arrow indicates the common nephric duct. Broken yellow arrow shows the downward movement of the ureter toward the urogenital sinus. Yellow and green arrows indicate the final position of the distal ureter and Wolffian duct. (g–i) Lateral displacement: The distal ureter separates from the Wolffian duct and moves to the final position at bladder base. Yellow and green arrows mark the position of the distal ureter and Wolffian duct before and after separation. Double-headed yellow arrow indicates epithelial wedge, an epithelial outgrowth, which facilitates the separation. Color code for (c, f, i): Wolffian duct and trigonal wedge, green; urogenital sinus, grey; Müllerian duct, pink; common nephric duct, red; kidney and ureter, blue. (With permission from Batourina E et al., *Nat Genet*, 32, 109, 2002.)

The kidney develops as a result of complex reciprocal signaling between the ureteral bud and the primitive metanephric mesenchyme [47,48]. Once this signaling is initiated, the bud elongates to penetrate the blastema, and the process of branching begins. In order for the final form of a single human kidney to have 500,000 to 1 million nephrons, the ureteral bud must undergo branching morphogenesis (Figure 22.6) [28]. Iterative branching of the ureteral bud must occur about 15 times during human development in order to lead to this number of nephrons. As this division of the terminal ureteral bud takes place to produce a treelike structure, lateral branches differentiate into terminal bifid branches. In these terminal bifid branches, the ureteral bud tip will attach itself to a nephron and remove itself from further bifurcations. This attachment of the bud to a primitive nephron then initiates the formation of a full nephron. Critical to this view is the notion that the final population of nephrons is ultimately determined by the branching and proper functioning of the ureteral bud, a view espoused by Mackie and Stephens over 30 years ago [37]. Equally critical to establishing normal renal function are the acquisition of the renal artery(ies) and subsequent vascular development (for a more detailed review of renal development, the reader is referred to Shah [47]).

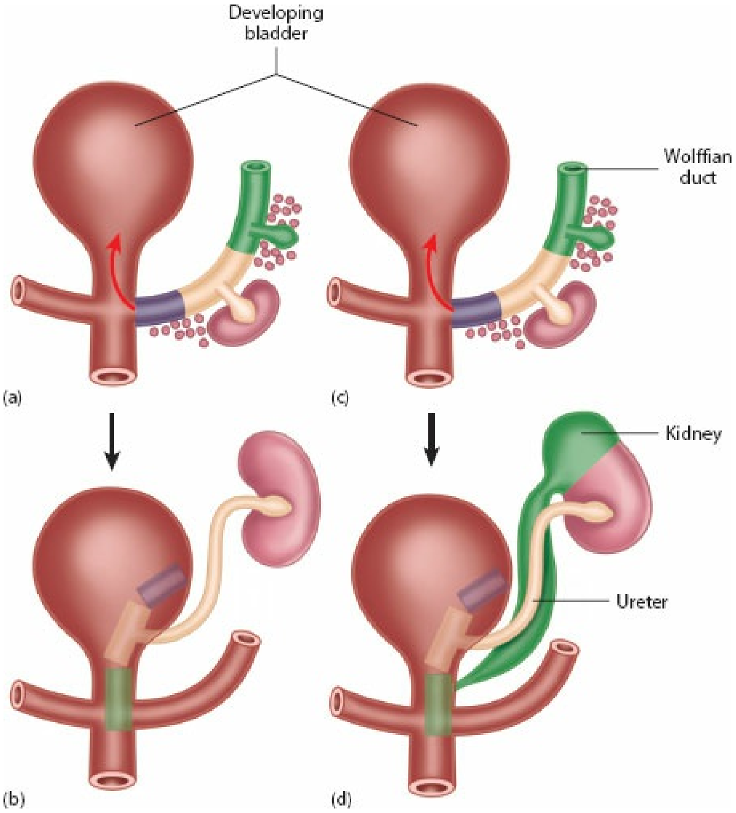

Figure 22.8 The ureteral bud hypothesis described by Mackie and Stephens [38]. (a, b) Normal kidney development: Single ureteral bud is induced and grows into the nephric mesenchyme (small dots). The caudal end of the Wolffian duct is incorporated into the developing bladder (red arrow). The yellow-marked region contributes to the trigone, the green one to the urethra, and blue for the lateral bladder. (c, d) Ectopic ureter development: A second, ectopic ureteral bud is induced more anteriorly than normal (green region at Wolffian duct) and interacts with the adjacent nephrogenic mesenchyme giving rise to a duplex system. This ectopic ureter opens into the urethra with the abnormal outflow and development of hydroureter. (With permission from Kume T et al., *Development*, 127, 1387, 2000.)

With current methods of molecular biology, the complex chemistry underlying these reciprocal interactions is being clarified, and several examples are offered here. Transcription factor PAX2 is expressed during normal kidney development and activates Wnt4 gene expression. PAX2 knockout mice are anephric, while a heterozygous PAX2 mutation results in a 60% decrease in Wnt4 mRNA [49]. In vitro studies have shown that glial cell–derived neurotrophic factor (GDNF) secreted by the metanephric mesenchyme serves to induce ureteral budding [38]. This is supported by the observation that the ureters and kidney do not develop in GDNF knockout mice. It has also been shown that gene products that antagonize GDNF expression such as FOXc1 (Figure 22.9) [38] or BMP4 [50] can result in multiple bud formation and duplex collecting systems. There is also a role for retinoic acid–mediated signaling in the development of the ureteral buds and trigone as shown in a model using targeted deletion of the retinoic acid receptors [36]. Abnormal vesicoureteral development has also been demonstrated in the presence of targeted RET overexpression [51] or the deletion of the type 2 angiotensin receptor [52].

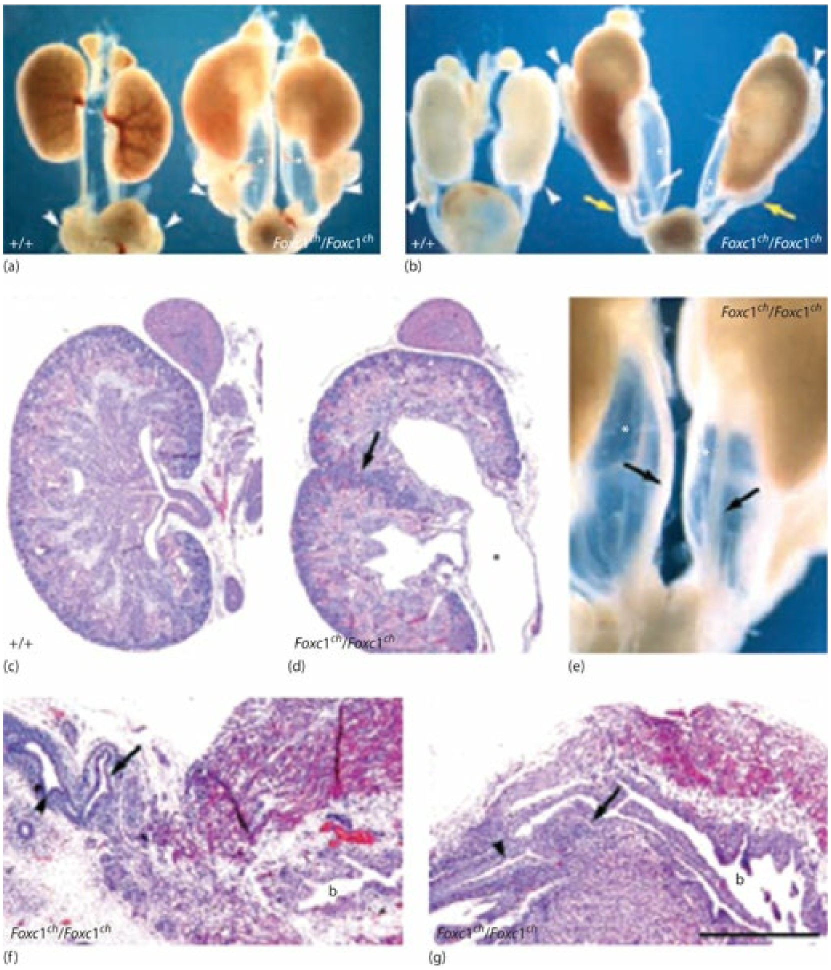
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Figure 22.9 Kidney and ureter abnormalities in mice homozygous for Foxc1ch. (a, b) Wild-type and mutant (a) in male: hydroureter (asterisks) and testis (arrows) located more anteriorly in mutant type compared to wild type. (b) In female with hydroureter (asterisks) and normal ureter (white arrow) behind and mutant ovaries located more anteriorly (arrowhead). (c, d) Section of wild-type (c) and mutant (d) kidneys with a duplex kidney in the mutant and clear boundary of the peripheral metanephrogenic mesenchyme (arrow). The upper part of the kidney connects to the hydroureter (asterisk). (e) Dorsal view of mutant kidney with normal ureters (arrows) and ectopic hydroureter (asterisks). (f, g) Sections showing an abnormal position of hydroureters in mutants (f) in male: hydroureter (arrow) does not connect to the bladder (b). (g) In female: hydroureter (arrow) ends blindly, while normal ureter (arrowhead) connects to bladder (b). (With permission from Kume T et al., *Development*, 127, 1387, 2000.)

GROWTH OF THE BLADDER

With the development of the trigone and the sphincter complex, the bladder can begin its cycle of filling and emptying. This is crucial for normal development since fetal urine serves as amniotic fluid, which is essential for normal lung development. However, bladder cycling is also crucial for development of bladder capacity. Experimental, as well as clinical, evidence supports this concept. In experimental work in a canine model of urinary diversion, Chun et al. [53] showed that with diversion, the bladder mass declined, as did muscarinic receptor density and the bladder's response to pharmacological agonists. These proved to be reversible upon reimplantation of the ureters into the bladder. Matsumoto et al. demonstrated that ureteral diversion in the fetal sheep resulted in a smaller bladder with poor compliance and diminished responses to pharmacological agonists [54]. Urinary diversion in the fetal sheep model was also associated with altered patterns of collagen expression [55] and decreased cell proliferation and apoptosis [56] in the bladder wall. Thus, there is ample support for the concept that mechanical distention is an essential contributor to normal bladder development. This is supported by the clinical observations in patients with bilateral ectopic ureters and bladder exstrophy, which are two conditions in which the bladder wall fails to cycle. Both conditions are characterized by small-capacity bladders and poor wall compliance.

INNERVATION

The common origins of the bladder and rectum from the cloaca are also reflected in their patterns of innervation. Contraction of the bladder is mediated by the pelvic nerve that arises from the sacral segments $S_{2,3,4}$. Sensory fibers from the bladder are also directed to these same sacral segments. Given their common embryological origins, it is not surprising that sensory fibers from the rectum are also directed to the same segments. Experimental work done in rat models using viral vectors expressing red or green fluorescent proteins has shown that there is a cross talk between these two organ systems. As an example using modified pseudorabies virus tagged to express green fluorescent protein injected into the bladder and the modified pseudorabies virus tagged to express beta galactosidase in the rectum, Rouzade-Dominguez et al. [57] showed that Barrington's nucleus receives innervation from both systems (Figure 22.10). Many of the nuclei in Barrington's nucleus were stained either green (reflecting sensory input from the bladder) or red (reflecting sensory input from the rectum because the beta galactosidase was visualized with an antibody tagged with red fluorescent protein). However, when imaged under dual fluorescent conditions, a substantial fraction of these nerves stained yellow *indicating that these individual nerves were receiving sensory input from both the bladder and the rectum*.

This image is of clinical relevance because constipation is a major contributing factor to bladder dysfunction because it can affect both the sensory and motor pathways. Evidence for this comes from ample clinical observations that children with incontinence improve following treatment of their underlying constipation [59]. Further evidence comes from a clinical study of women undergoing urodynamic evaluations in which a balloon catheter was placed in the rectum; the results of the urodynamic parameters varied substantially once the balloon was inflated to mimic the rectal distention seen with constipation [60]. Using an experimental approach in the rat, Miyazato et al. were able to show that rectal dilation with a balloon increased the intercontraction interval and diminished the detrusor pressure and that these changes were mediated by glycinergic and GABAergic mechanisms [61].

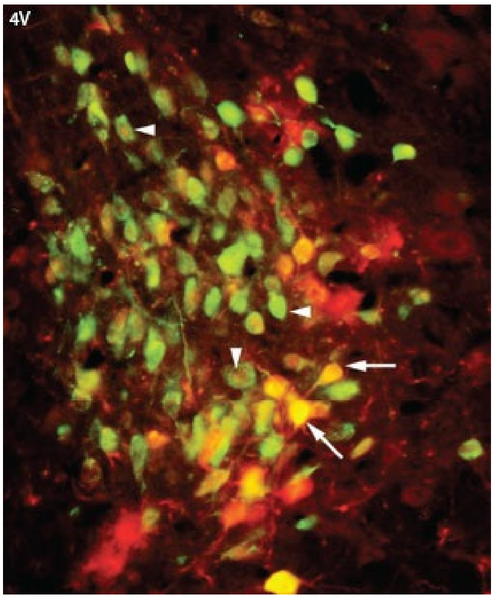
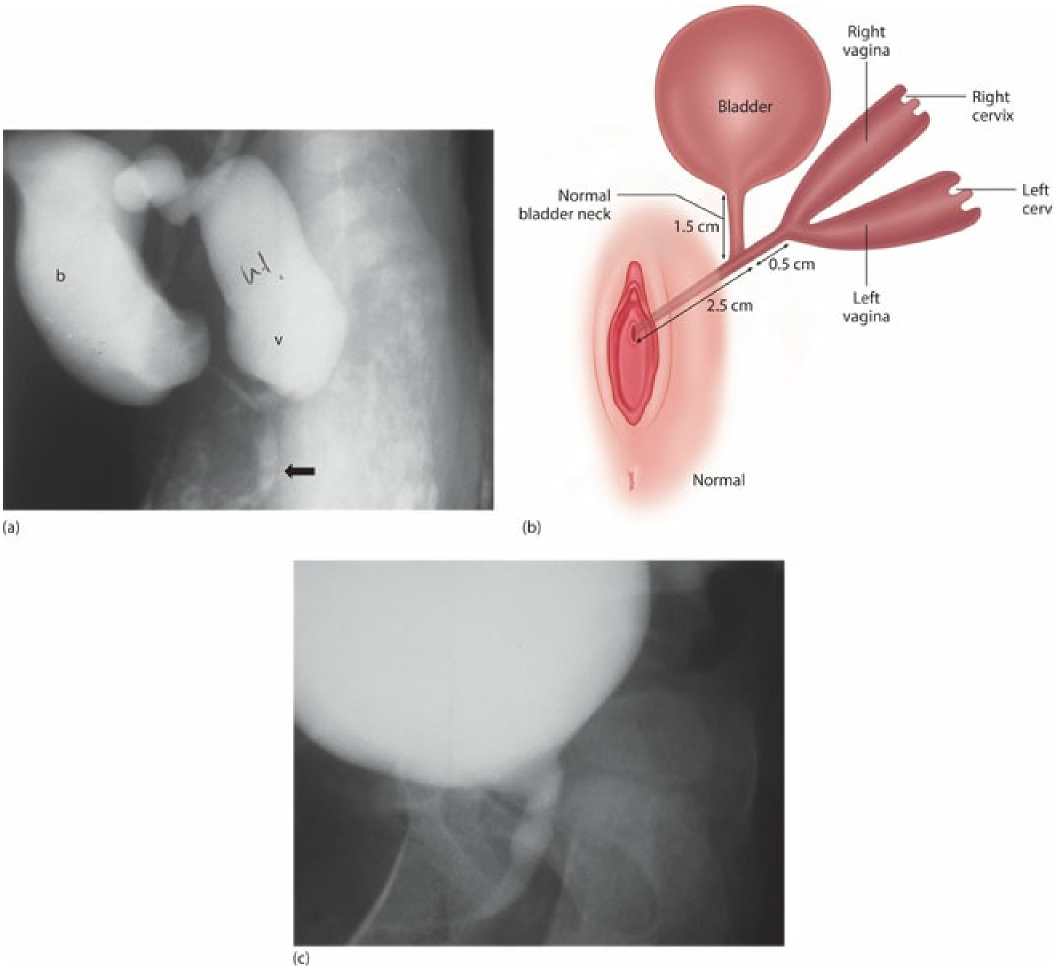


Figure 22.10 Dual fluorescent microscopy of Barrington's nucleus in a rat. These neurons were labeled with pseudorabies virus expressing green fluorescent protein that was injected into the bladder (green) and pseudorabies virus expressing β-galactosidase (red) that was injected into the distal colon. A substantial population of these neurons are labeled with both viruses appearing as either yellow or orange (arrows) or cells that have a red nucleus and green cytoplasm (arrowheads). (With permission from Rouzade-Dominguez ML et al., *Eur J Neurosci,* 18, 3311, 2003.)

CLINICAL APPLICATIONS

Urogenital Sinus

Persistence of the urogenital sinus can occur as an isolated malformation or in association with other conditions such as congenital adrenal hyperplasia. In these patients, the urethra and the vagina converge in a short common channel, and the convergence is close to the perineum. In some cases, the voided urine is trapped within the vagina, resulting in hydrocolpos. These patients may present with a palpable pelvic mass requiring decompression, infection of obstructed urine, or overflow incontinence. The rectum is often displaced anteriorly, but it functions normally. A review of Figure 22.5 should allow the reader to understand the embryological basis for this anomaly. The distal Müllerian ducts fuse with the urethra and then migrate caudally during normal perineal development. Arrest of this distal migration at any point will result in a urogenital sinus as the fused urethra and vagina drain into a common channel. On physical examination, the vaginal introitus is absent with a single opening in the urethral position, although the labia majora and minora might be normal in appearance. Urogenital sinuses are usually separated into those with a low confluence, or short common channel, and those with a high confluence, or long common channel. Separation into these two categories dictates the type of surgical repair that can be performed. The distance from the bladder neck to the confluence is also paramount in determining the surgical technique and outcome [62].



(a) (b)

(c)

Figure 22.11 (a) Genitogram demonstrating a common urogenital sinus (arrow) dividing into the bladder (b) and dilated vagina (v). (b) Summary of the anatomy as revealed by endoscopic examination. (c) Postoperative result after reconstruction and conversion of the urogenital sinus into urethra.

The diagnosis of a urogenital sinus is confirmed radiographically with a retrograde contrast injection, i.e., a genitogram (Figure 22.11a). If the genitogram is inconclusive and does not reveal the level of confluence, a cystoscopy and retrograde contrast study should be performed. Depending on the length of the common channel and the complexity of related malformations, different surgical procedures are available. The objectives of the surgical repair are (1) the separation of urogenital tract to allow for normal voiding and (2) the creation of an adequate vaginal introitus. A urogenital sinus with a low confluence can be managed with a "cutback" operation combined with an inverted U-flap to widen the introitus to prevent stenosis [63]. When the common channel exceeds 3 cm, the modified total urogenital sinus mobilization is the preferred approach [64,65]. This technique avoids separation of the urethra from the vagina and circumferentially dissects the urogenital sinus as a single unit. The urogenital sinus mobilization technique has been modified since the original description. Rink and colleagues advocate utilizing the mobilized sinus tissue to create a mucosal vestibule or a posterior vaginal flap [66]. Additionally, the same group has described a partial urogenital mobilization that limits dissection to remain distal to the pubourethral ligament in hopes of avoiding dissection around the innervation of the urinary sphincter and clitoris [67]. Once the urogenital sinus has been mobilized distally, a perineal flap can be introduced into the posterior wall of the vagina providing a normal caliber vaginal opening. Depending on the length of the common channel and related anatomic malformations, a more complex surgical repair may be necessary [68,69].

Case: A 1-day-old female was noted to have a palpable mass in her lower abdomen, and sonography revealed distended fluid-filled collections in her pelvis. On physical exam, her lower abdomen was filled with a tense mass, the rectum was normally placed, but no vaginal opening could be appreciated. Via the one opening near her introitus, a genitogram was performed (Figure 22.11a), demonstrating a common UG sinus with a bifurcation leading to the bladder and a dilated vagina. A subsequent endoscopic examination revealed the anatomy shown in Figure 22.11 and allowed for a plan of reconstruction to be developed. Using a posterior sagittal approach, the urethrovaginal trifurcation was divided, and the urogenital sinus was converted into the urethra. The duplex vaginas were then mobilized and moved down into the perineum with a perineal skin flap to complete the vaginoplasty.

Common Cloaca

Rarely patients may present with a common cloaca in which the urethra, vagina, and rectum converge into one common sinus that exits at the perineum. Many of these patients often present with the associated findings of spinal cord tethering and a neurogenic bladder. The association of these anomalies was initially described in 1961 by Duhamel and termed caudal regression syndrome [70]. As the somites develop from cranial to caudal during early gestation, it is possible that an isolated cloacal anomaly represents a late defect in somite development and a milder form of caudal regression syndrome. Rodent models have demonstrated that the known teratogen retinoic acid can result in spina bifida, imperforate anus, genitourinary anomalies, omphalocele, and limb abnormalities when administered on gestational day eight (equivalent to gestational week four in humans) [71,72]. In contrast, the administration of the same teratogen on gestational day nine results in anal atresia, urethral atresia, and tail deformities providing evidence that these anomalies are part of a spectrum [73]. An example of this association may be found in patients with the VACTERL (vertebral anomalies, anal atresia, cardiac defects, tracheoesophageal fistula, esophageal atresia, renal anomalies, radial/limb anomalies) syndrome.

Congenital Vaginal Anomalies

Though rare, a variety of congenital vaginal anomalies have been described in the urological and gynecological literature. Such anomalies include transverse vaginal septum, vaginal duplication, distal vaginal atresia, and vaginal agenesis. Increasingly these diagnoses may be made in the neonatal period because of the widespread use of prenatal sonography. Ultrasound can reveal hydrocolpos, duplications, or associated anomalies, such as unilateral renal agenesis, which raise suspicion for a vaginal anomaly. But many vaginal anomalies will only become apparent with the onset of puberty. A thorough medical history and physical examination in conjunction with pelvic ultrasonography and magnetic resonance imaging can usually determine the exact diagnosis [74]. The constellation of vaginal agenesis, or the absence of the proximal vagina, and unilateral renal agenesis is the classic description of Mayer–Rokitansky–Kuster–Hauser syndrome [19]. This association between anomalies of renal and vaginal development can be related to the complex relationship between the Wolffian ducts and Müllerian ducts (Figure 22.5). Disturbances in the paracrine signaling required for the normal development of the genitourinary tract in women can likely result in abnormal renal and vaginal development. Thus, a condition in which ipsilateral and/or bilateral vaginal agenesis or stenosis is associated with unilateral renal agenesis is not surprising.

Case: A previously healthy and normally developed 12-year-old female presented with multiple 1-week episodes of abdominal pain occurring on a monthly basis; she was amenorrheic. Breast development was present as was pubic hair, and the urethra was normally placed above a blind-ending vaginal introitus. Further imaging with ultrasound and MRI revealed a huge hematocolpos with dilated fallopian tubes on both sides (Figure 22.12) without any other malformations of the upper or lower urinary tract. Evaluation under anesthesia revealed a complete distal atresia of the vagina; the vaginal to perineal surface distance was measured at 10 cm. She was managed with a combined laparoscopic mobilization of the proximal vagina, with a simultaneous perineal exploration and vaginal pull-through in combination with a perineal skin flap.

The normal urethral development seen in this case illustrates the concept that there was most likely a failure of fusion between the distal Müllerian ducts and the urethra (Figure 22.5) [20]. Subsequently urethral migration proceeded distally leaving the distal Müllerian remnants in a position far from the perineal body. Normal urethral migration to the perineum is also seen in patients with androgen resistance syndromes despite the absence of the upper two-thirds of the vagina, uterus, and fallopian tubes.

Ectopic Ureter

A ureter that opens anywhere outside of the trigone is considered ectopic and is the result of a displaced ureteral bud. Ureteral buds that develop very low along the mesonephric duct will be sited in a laterocranial ectopic position, often associated with a significant vesicoureteral reflux. In contrast, if a bud develops high along the mesonephric duct, it bypasses the trigone and inserts within the urethra, vestibule, or vagina. An ectopic ureter can drain a single system [75], but about 70% are associated with complete ureteral duplication with the ectopic ureter draining the upper moiety of a complete pyeloureteral duplication. Complete ureteral duplication occurs when two separate ureteral buds arise independently from the mesonephric duct. A duplex kidney is induced when these two buds meet the metanephric blastema. During the development of the trigone, the most cranial ureter that drains the upper moiety of the duplex kidney rotates inwardly on its long axis and crosses the lower pole ureter. A normal duplex kidney develops, if the two ureters originate close to each other and both ureteral orifices terminate on the trigone. However, if the ureteral buds arise from widely separate positions on the mesonephric duct, the upper pole ureter is incorporated into the urogenital sinus at a later stage of development, and the resulting orifice is situated in an ectopic position, inferior to the trigone. This accounts for the Meyer–Weigert law that states that the upper pole ureter shall always be found distal to that ureter, which drains the lower renal unit. Mackie and Stephens [37] have postulated that induction of the metanephric blastema either too caudally or too cranially along the metanephric blastema will result in renal dysplasia. This is the reason for impaired renal function of the renal unit draining into an ectopic ureter, whereas refluxing ureters most often drain normally functioning renal units.

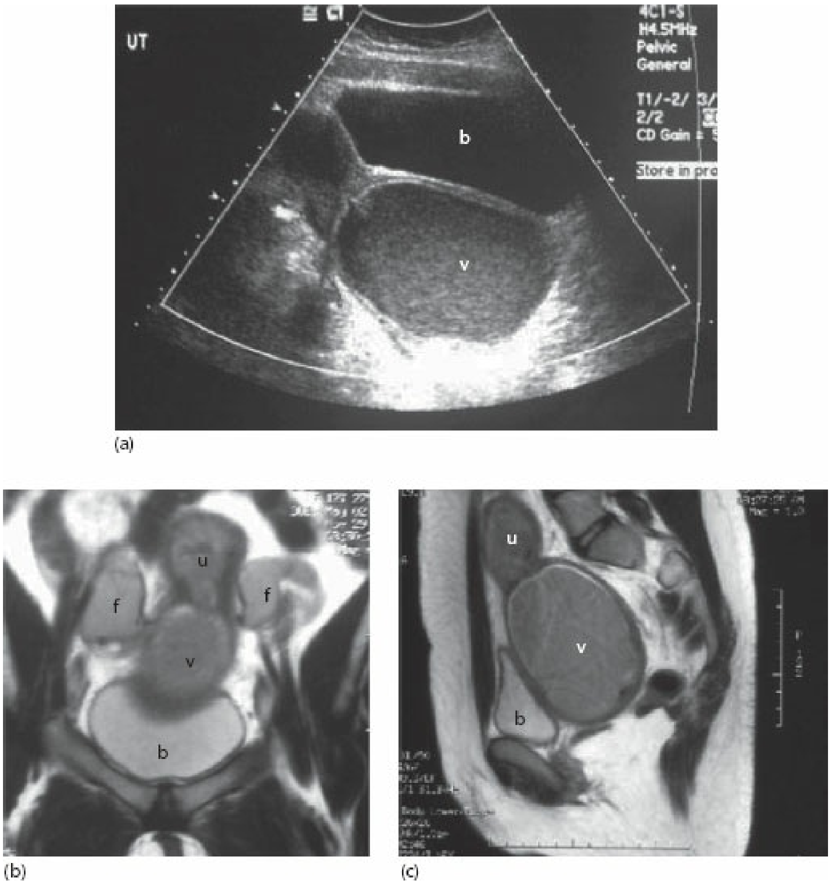

(a)
(b)
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Figure 22.12 (a) Pelvic ultrasound (sagittal) demonstrating the blood-filled vagina (v) behind the bladder (b). (b) MRI furthermore revealed dilated fallopian tubes (f) on both sides. (v) Vagina, (u) uterus. (c) MRI in coronal view.

If the ureter opens below the internal sphincter, the patient with such an ectopic ureter can present with incontinence. If the ureteral bud arises very high along the mesonephric duct, it fails to become incorporated into the lower urinary tract and remains confluent with the mesonephric duct. These vestiges of the mesonephric system track along the lateral vagina wall and may become clinically manifest as Gartner’s duct cysts. This also provides an embryological basis for the rare vaginal ectopic ureter. Approximately one-half of female patients with ectopic ureters present with continuous dribbling of urine, despite normal bladder emptying due to the normally situated ipsilateral or contralateral ureteral orifices [75,76]. If the ectopic ureter is draining a dysplastic or hypoplastic kidney or upper pole, infection or vaginal discharge may be the only complaint. Today, most of these cases are diagnosed by prenatal ultrasound, since most ectopic ureters are associated with significant hydronephrosis. On occasion, this diagnosis is not established before toilet training and some patients are mistakenly diagnosed with voiding dysfunction.

The traditional imaging workup included a cyclic VCUG, which demonstrates reflux into the ectopic ureter in 70%–80% of cases, and an IV urogram or CT scan. More recently, the application of MR urography has provided a global view of the malformation, including renal dysplasia and dilated ureter, even in the presence of diminished renal function, thus making it a gold standard [77]. Depending on renal function, the treatment varies from ureteroureterostomy in duplicated systems, upper pole resection with or without ureterectomy, various ureteroneocystostomy procedures, or nephroureterectomy.

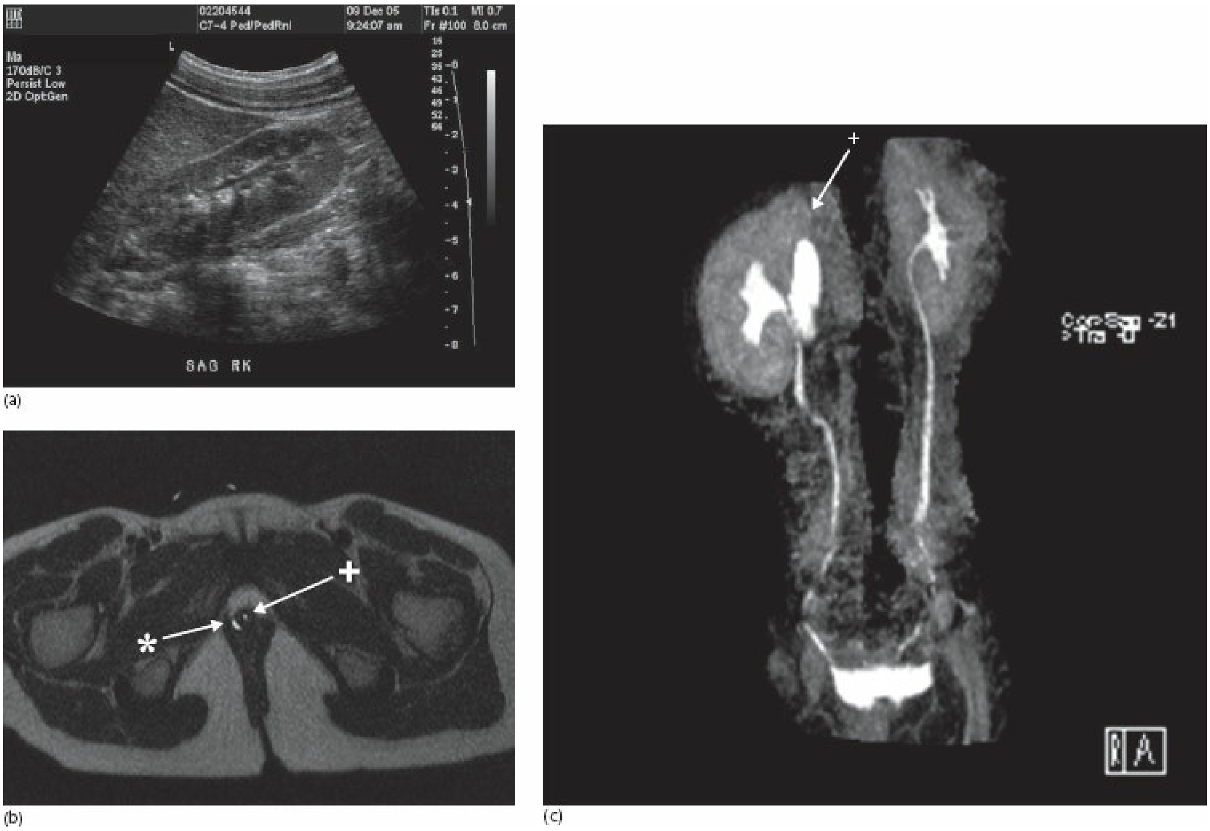

Figure 22.13 (a) Renal ultrasound demonstrating a normal right kidney with no signs of a ureteral duplication. (b) Transverse pelvic images showing the insertion of the ectopic ureter (*) into the urethra adjacent to the Foley catheter (+) placed at the time of the MRI urogram. (c) Coronal sections of the abdomen on MRI showing a ureteral duplication (+). At surgical exploration this ureter was found to connect with a tiny remnant of renal parenchyma.

Case: A 7-year-old female presented for the evaluation of continuous urinary incontinence. A renal bladder ultrasound ordered by her pediatrician was reviewed and found to be normal. She voided at regular intervals and was not constipated. A voiding log confirmed her good voiding habits, and a urinary flow rate revealed a normal bell-shaped curve with no residual urine as determined by office sonography (Figure 22.13). An MRI urogram was obtained, which confirmed the presence of a small upper pole duplication associated with an ectopic ureter to the urethra. Following upper pole partial nephrectomy, she reported immediate continence of urine.

In rare instances, bilateral ureteral budding may occur at a cranial location along the mesonephric duct and result in bilateral ectopic ureters. These patients present with total urinary incontinence, a deficient internal sphincter, and a noncompliant bladder with small capacity. These cases serve to illustrate the importance of early bladder cycling for the acquisition of normal capacity and compliance, a concept that has been confirmed in fetal experimental models [55]. For these patients, urinary continence will require complex surgery most often consisting of a bladder neck reconstruction, ureteral reimplantation, and augmentation.

Gartner's Duct Cyst

Remnants of the Wolffian ducts may be found in the lateral vaginal wall and may become clinically apparent if they swell or become infected. If these rupture, and if there is enough poorly functioning renal parenchyma associated with the system, the patient will be left with a continuous low-grade incontinence.

Case: A 4-month-old female presented with a prenatal history significant for an ultrasound, which demonstrated an absent right kidney. At the time of this presentation, she had 2 cm cystic structure within her labia that was covered by a thin membrane (Figure 22.14). An ultrasound showed a solitary left kidney and no evidence of a ureterocele, and a VCUG showed high-grade reflux into the left kidney. The MRI showed a solitary left kidney and an ectopic remnant of a right kidney (Figure 22.14c) that was associated with a cystic dilation, which ultimately was traced into the right wall of the vagina and led to the cystic mass seen on physical examination (shown from the posterior projection in Figure 22.14). The cyst was decompressed by endoscopic incision and marsupialization into the vagina in order to prevent infection. However, her reflux persisted and the family reported her perineum was consistently wet. At 2 years of age, she underwent a robotic left ureteral reimplant and a right nephrectomy of the atrophic dysplastic kidney. The family now reports a dry perineum.

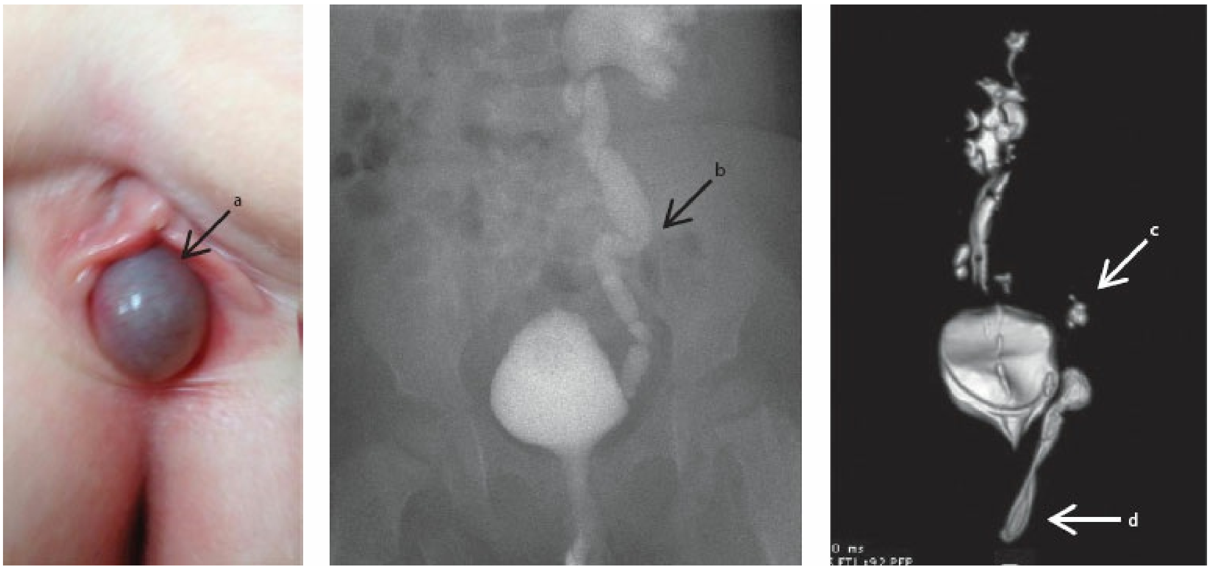

Figure 22.14 This 3-month-old infant female presented with a bulging mass within her labia (a) and a history of antenatal sonography showing a solitary kidney. A renal bladder ultrasound (not shown) confirmed that she had a solitary left kidney into which there was high-grade vesicoureteral reflux as shown on a VCUG (b). An MRI with a three-dimensional reconstruction was performed and rotated to demonstrate the posterior view. This revealed a solitary right kidney with a duplication and a small atrophic remnant of primitive renal tubules on the left (c). This dysplastic left kidney could be traced to the Gartner's duct cyst, which traveled in the lateral right vaginal wall (d).

Ureterocele

A ureterocele is a cystic dilation of the lower end of the ureter, which protrudes into the bladder. The origin of the defect begins in the eighth week of gestation. This anomaly has been attributed to a failure of Chwalle's epithelial membrane to regress during the incorporation of the ureteral bud into the developing trigone [78]. Ureteroceles are associated with duplex systems in 80% of cases, and girls are affected four times more frequently than boys [79,80]. Since most ureteroceles are associated with hydronephrosis, the vast majority of these patients are now being diagnosed with antenatal ultrasound [81]. Prenatal diagnosis and early postnatal management of duplex-system ureteroceles are beneficial to decrease morbidity and potential adverse outcomes related to infection [82]. Clinically, ureteroceles are the most common cause of urinary retention in female infants [83].

The initial workup of these patients should include a renal and bladder ultrasound, a voiding cystourethrogram to detect whether there is associated reflux, and a renal scan to determine the functional contribution of the system (especially in the case of the rare single-system ureterocele). Patients with ureteroceles have a high incidence of associated vesicoureteral reflux into the ipsilateral lower pole and less commonly the contralateral collecting system [84]. The presence or absence of reflux may affect the type of surgical intervention performed and therefore must be established. A large number of options exist for management of these patients: complete upper and lower urinary tract reconstruction, upper pole heminephrectomy (simplified approach) and ureterocele decompression, and endoscopic incision [85–88]. While endoscopic decompression may be definitive treatment for intravesical ureteroceles, partial nephrectomy appears to be more definitive for extravesical ureteroceles. Other groups advocate primary endoscopic puncture even for patients with ectopic and duplex ureteroceles, because a third of patients are definitively treated and early decompression is presumed to reduce the risk of pyelonephritis [87].

Incontinence may be seen after the initial treatment of ectopic ureteroceles and was thought to be related to iatrogenic bladder neck or external urinary sphincter injury at surgery. However, Husmann et al. observed that, in patients treated with partial nephrectomy alone, 10% subsequently developed urinary stress incontinence, despite the absence of any bladder neck surgery [89]. It seems that large ureteroceles are capable of significantly distorting the developing bladder neck and urethra, which will not become apparent until the system is decompressed. In a more recent study [90], the authors concluded that children with ectopic ureteroceles presenting with incontinence are at high risk for a high-capacity bladder with incomplete emptying and bladder dysfunction following bladder neck procedures. They concluded that this was not related to the operative intervention, but rather was an integral part of the underlying disorder.

Case: An 11-year-old continent girl presented with recurrent febrile urinary tract infections. Sonography revealed duplications of both kidneys and a large ectopic ureterocele draining the upper moiety of the right kidney. The VCUG demonstrated right-sided reflux into both moieties on the right side. An endoscopic examination revealed a ureterocele that extended into the bladder neck and upper one-third of the urethra. An endoscopic puncture and decompression of the ureterocele was performed. Postoperatively, the patient experienced moderate stress incontinence that she had not manifested preoperatively and a VCUG revealed persisting right high-grade reflux. A right-sided common sheath reimplant, ureterocele excision, and bladder neck reconstruction were performed. Five years later, she remains continent and free of infections off antibiotic prophylaxis.

This clinical evidence would suggest that once a large ectopic ureterocele is deflated, function of the bladder neck and urethra may be impaired due to distortion of these structures by the long-standing distention.

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23 Physiology of Micturition

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INTRODUCTION

Micturition describes a dynamic process that alternates between phases of storage and expulsion of urine stored in the urinary bladder. The storage phase typically extends for hours, whereas the expulsion phase lasts for a few seconds. Reciprocal contraction and relaxation of smooth muscle in the bladder and urethra is required for these two phases of different duration to happen, which is accomplished by the complex interactions among smooth muscle, connective tissue, urothelium, and supportive structures with innervation. The relay of afferent input from the bladder to the neural circuitry in the brainstem, in particular the periaqueductal gray (PAG) and the pontine micturition center (PMC), switches on the periodic transformation of the lower urinary tract from the mode of bladder filling to voiding [1–3] (Figure 23.1). The volitional control over this dynamic process is lacking in infants, but is gained through learning by the age of 5 in most individuals. The micturition in both sexes is influenced by neural, biomechanical, biochemical, and morphologic properties of the bladder and urethra, as well as the hormonal influences and unique pelvic and perineal anatomy [4].

Role of Bladder Anatomy in Micturition Reflex

The muscular and membranous structure of bladder is well suited for the storage phase of micturition that can last up to several hours in healthy individuals. The storage function of bladder is therefore dependent on the stretching of a compliant bladder wall, which allows it to store a socially adequate volume of urine without significant rise in bladder wall tension. Bladder emptying requires a synchronous activation of all the smooth muscles. Uneven spread of contraction across bladder wall may cause stretching of contracted regions and prevent the rise in pressure necessary for urine to be expelled through the urethra.

Histological examination of the bladder body reveals that bladder wall is an interlacing bundle of disorganized smooth muscle, where myofibrils are arranged into fascicles in random directions [5]. This architecture differs from the discrete circular and longitudinal smooth muscle layers in the ureter or gastrointestinal tract. The bladder outlet is composed of the bladder base, urethra, and external urethral sphincter (EUS). The bladder base has a laminar architecture with a superficial longitudinal layer lying beneath the trigone. A muscle layer deep to the superficial layer is continuous with the detrusor [6–8] and the smaller muscle bundles in the bladder base exhibit a predominantly circular orientation.

Detrusor smooth muscles have a broad length–tension relationship, which allows tension to be developed over a large range of resting muscle lengths [9]. Elastic characteristics of bladder wall play a role in the development of bladder wall tension [10]. Although spontaneous mechanical activity is noted in isolated detrusor strips of small mammals [11] and humans, the fused tetanic contractions typically seen in smooth muscles from the gastrointestinal tract and uterus are almost never seen in the normal bladder. The lack of tetanic contractions suggests that electrical coupling of detrusor smooth muscle cells [12] is absent.

Furthermore, tissue impedance measurement also supports the relatively poor electrical coupling of detrusor smooth muscles compared to other smooth muscles [13,14]. Poor electrical coupling may assist in the prevention of synchronous activation of the smooth muscle cells during bladder filling. Nevertheless, the existence of some degree of coupling within a muscle bundle cannot be ruled out as the length constant of a bundle can be easily measured [13,14]. Studies on postnatal development of the rat bladder have shown that electrical couplings between detrusor cells seem to be higher in neonates compared to adults because coordinated, large-amplitude, low-frequency contractile activity seen in the neonates declines and is replaced by low-amplitude, high-frequency, more irregular activity in older rats, which appears to depend on the disruption of the intercellular smooth muscle communication [15].

Instead of electrical coupling, there has been evidence reported of gap junction coupling between detrusor smooth muscle cells of the human and guinea pig bladder from whole-cell patch-clamp recordings [16] and Ca^2 imaging [17]. In addition, the significant expression of connexin 43 and 45 gap junction proteins has been reported in human detrusor muscles (Figure 23.2) [16,18]. Gap junction connexin proteins oligomerize into hexameric assemblies called connexons, which dock head to head with partner connexons positioned on neighboring cells to provide channels for paracrine messengers [19]. Recent studies on mouse bladder suggest that the circadian oscillation of Cx43 contributes to increased bladder capacity during day seen in rodents [20]. It is surmised that the uninhibited detrusor contractions occurring in the overactive and aging bladders may be due to reversal in the properties of the cell coupling [21–25] from gap junction [26] back to the electrical as seen in neonates.

Another important subcellular structure important for detrusor signaling is the caveolae, which are specialized regions of the cell membrane that modulate signal transduction, by clustering muscarinic and purinergic receptors within the sarcolemma. Postnatal development of bladder in rats is associated with increase in caveolin protein expression [27]. In contrast, decreased density of caveolin-2 and caveolin-3 protein expression was noted in rat detrusor smooth cells from 12-month-old rats relative to 12-week-old rats [28]. Age-dependent changes in caveolar morphology also revealed the reversal of infantile expression of caveolin protein at old age. Estrogens are known to promote the survival of smooth muscle cells and neurons by increase in caveolae [27], whereas depletion of estrogen is known to decrease the caveolae.

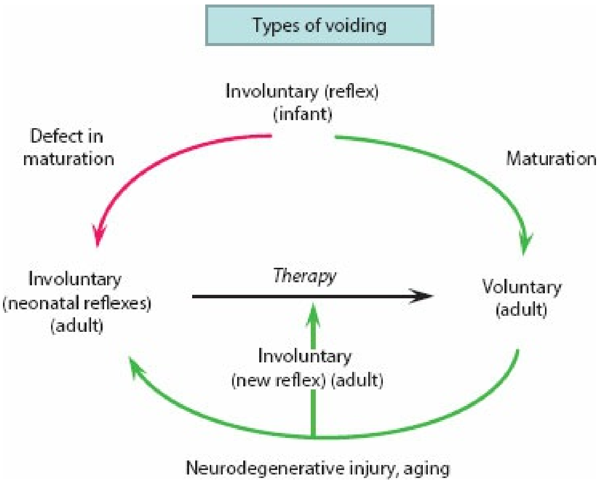

Types of voiding
Involuntary (reflex) (infant)
Defect in maturation
Maturation
Involuntary (neonatal reflexes) (adult)
Therapy
Voluntary (adult)
Involuntary (new reflex) (adult)
Neurodegenerative injury, aging

Figure 23.1 Bladder's "circle of life" by influence of maturation, pathologic processes, and aging. In infants, voiding is initiated and coordinated by reflex circuits. After maturation of central neural pathways, voiding is controlled voluntarily by neural circuitry in higher centers in the brain. A defect in neural maturation allows involuntary voiding to persist in adults. Aging, neural injury, or diseases such as benign prostatic hyperplasia can disrupt the central voluntary micturition neural pathways. Pathologic processes can lead to the formation of new reflex circuitry by reemergence of primitive reflex mechanisms that were present in the infant or that appear as the result of synaptic remodeling. The goal of therapy is to reverse the pathologic process and to reestablish normal voluntary control of voiding.

Role of Urothelium

The superficial cell layer of bladder known as urothelium was traditionally considered to play the role of blood–bladder barrier, which blocks the ingress of toxic constituents from stored urine and thereby prevents uremia. Urothelium has to expand in size during filling phase when detrusor smooth muscles are relaxing and expanding the size of the bladder. Expansion of urothelium while maintaining barrier function protects the smooth muscle and intrinsic nerves from urine exposure [29]. Recent investigations have revealed that urothelium conveys the stimulus of bladder distension, which initiates activity in low-threshold mechanoreceptive afferents during storage and also conveys the magnitude of detrusor contractions during voiding. Urothelium is considered to act as a lumenal sensor–transducer and communicate directly with the suburothelial afferent nerves by releasing various autocrine and paracrine factors [30].

Autonomous detrusor activity detected during storage is known to facilitate the generation of bladder sensation and afferent activity. Although the source of autonomous detrusor activity is unclear, spontaneous contractile activity of detrusor myocytes was suspected to trigger spontaneous contractions through gap junctions [31]. Alternatively, another population of cells located in various sites the bladder known as interstitial cells have been proposed for the pacemaking role in spontaneous activity of the bladder [32,33]. Interstitial cells have been identified in human and guinea pig ureter, urethra, and bladder body [33–35]. Urothelium is believed to secrete paracrine factors that seem to reduce the spontaneous activity of detrusor [30] because the frequency of whole-cell Ca^2 flashes of detrusor smooth muscle cells was higher in preparations with intact urothelium relative to those with denuded urothelium.

Suburothelial Interstitial Cells

Distension of bladder during filling of urine stretches the urothelium and causes the nonneuronal release of acetylcholine (ACh) or adenosine triphosphate (ATP) from pannexin-1 hemichannels [36]. ATP exerts a prominent role on afferent arm of micturition reflex as it initiates the voiding reflex *via* the activation of $P2X_3$ receptors on suburothelial sensory nerve fibers [35]. The stretch-evoked ATP release is increased in diseased condition such as chronic spinal cord injury [37,38]. The ATP release from stretched urothelium is reported to be further augmented in aging and in obstructed bladder [39–43], which may be related to increased voiding frequency and enhanced low-threshold afferent nerve activity noted in these conditions. Elevated expression of $P2X_3$ receptor in urothelium and interstitial cells has been reported in association with aging [40] and in rat model of bladder obstruction [44]. ATP is also a cotransmitter of ACh in the parasympathetic nerves and participates in both afferent and efferent transmissions of micturition reflex [45].

Suburothelial (or lamina propria) interstitial cells in the human bladder have also been termed myofibroblasts as they stain for vimentin and alpha-smooth muscle actin but not for desmin [46]. Immunohistochemical studies show the expression of P2Y receptors, most notably $P2Y_6$ receptors [22] and M_3 muscarinic receptors in the suburothelial interstitial cells from guinea pigs [21–25]. These cells are linked by gap junctions composed of connexin 43 proteins, which make close appositions with C-fiber nerve endings in the suburothelium to suggest that there is a network of functionally connected interstitial cells immediately below the urothelium that can be modulated by other nerve fibers [22] (Figure 23.2).

Isolated suburothelial interstitial cells respond to application of ATP by inducing inward currents associated with elevated intracellular Ca^2 [35]. Because ATP or ACh is known to be released from the urothelium during bladder stretch, suburothelial interstitial cells that respond to ATP via P2Y receptor activation [21–25] are in an ideal position between the urothelium and nerve endings to modify a sensory feedback mechanism [21–25]. In the human bladder, increased expression of muscarinic M_2 and M_3 receptors in suburothelial interstitial cells is found and correlated with urgency score in humans with idiopathic detrusor overactivity [47].

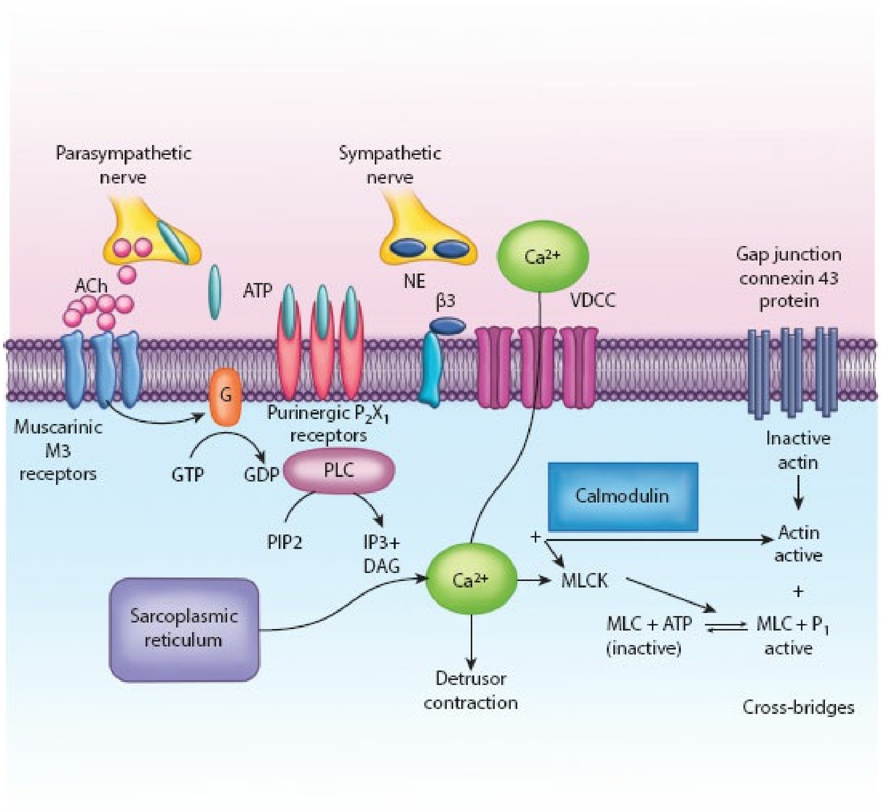


Figure 23.2 Biochemistry of detrusor contraction: Detrusor contraction during voiding is mediated by action of acetylcholine (ACh) released from the parasympathetic nerves together with adenosine triphosphate (ATP) at the detrusor neuromuscular synapse. ATP exerts mutually exclusive effects through the activation of excitatory purinergic $P2X_1$ receptors on the detrusor smooth muscle, and action on inhibitory $P2Y_1$ receptors controls ACh release from cholinergic nerve endings. The relaxation of detrusor required for storage phase is mediated by the action of norepinephrine (NE) released by the sympathetic nerves acting on β_3-receptors expressed in detrusor. Activation of afferents residing in the suburothelial layer during storage phase is maintained by ACh and ATP released by stretched urothelium. Afferent and efferent communication in the bladder is facilitated by gap junction proteins.

Intradetrusor Interstitial Cells

Interstitial cells are also found in the detrusor layer and shown to be spontaneously active [33]. These cells stain for c-Kit and are located along both boundaries of muscle bundles in the guinea pig bladder [34,48,49]. They can increase Ca^2 activity in response to cholinergic stimulation via M3 muscarinic receptor activation and can be spontaneously active. This suggests they could act as pacemakers or intermediaries in transmission of nerve signals to smooth muscle cells [48,50,51]. Hashitani and colleagues [49] suggested that interstitial cells in the detrusor may be more important for modulating the transmission of Ca^2 transients originating from smooth muscle cells rather than being the pacemaker of spontaneous activity because Ca^2 transients occur independently in smooth muscles and interstitial cells [34,49,52,53].

Potential Role of Phosphodiesterases and Prostaglandins

Interstitial cells throughout the bladder demonstrate immunoreactivity for cyclic nucleotide cyclic guanosine monophosphate (cGMP) [54,55]. The functional role of cGMP-dependent signaling was suggested by the attenuated increase in intracellular Ca^2 and current responses to ATP in guinea pig interstitial cells following the addition of sodium nitroprusside [56]. Thus, increased levels of cGMP in interstitial cells following inhibition of phosphodiesterase 5 may diminish the synchronicity between detrusor muscle bundles [34]. These cells are also a source of prostaglandin E_2 (PGE_2) because of their expression of cyclooxygenase, which is known to induce spontaneous activity independent of efferent nerve activity [57,58]. Expression of EP1 receptor in urothelium has recently been reported [42], which could be activated by PGE2 to release ATP and increase detrusor contractility. Reduced spontaneous activity of rabbit bladder muscle strips after exposure with PGE_2 receptor antagonists is consistent with the stated role of EPI receptor and its ligand [59] (Figure 23.2).

NEUROPHYSIOLOGY

Urine Storage

The bladder pressure remains low during storage or bladder filling phase till the bladder volume remains lower than the threshold for inducing voiding. Denny-Brown and Robertson showed that under normal conditions (i.e., in the absence of prior bladder distension) the rise in intravesical pressure is linear with rise in bladder volume until high volumes were reached [60]. The accommodation of the bladder to increasing volumes of urine is primarily a passive phenomenon dependent on the viscoelastic characteristics of bladder wall and the quiescence of the parasympathetic efferent pathway [61–63].

Bladder distension–induced afferent activity triggers spinal reflex pathways, which facilitate storage by directly enhancing thoracolumbar sympathetic outflow and somatomotor discharge [64]. Reflex activation of the sympathetic outflow inhibits any neurally mediated contractions of the bladder during filling phase of micturition [63,65,66]. Organization of this reflex response in the lumbosacral spinal cord is confirmed by its persistence even after transection of the spinal cord at the thoracic levels (Figure 23.3). However, this bladder to sympathetic mechanism to suppress detrusor contractions during urine storage may be weak in humans, given that bilateral retroperitoneal lymph node dissection (involves destruction of sympathetic chains) has no discernible alteration of filling or storage function in humans.

During filling, sympathetic and somatic spinal reflexes are responsible for the low intravesical pressure and high urethral pressure maintained by the tonic activity of smooth and striated urethral sphincters, respectively [65] (Figure 23.3). The rise in intra-abdominal pressure during filling is also resisted by sympathetic and somatic spinal reflexes. The increased efferent firing in the pudendal nerve and the higher outlet resistance during filling are responsible for the maintenance of urinary continence and the increased activity of sphincter electromyogram during storage (Figure 23.4).

The bladder afferent input during bladder filling activates pudendal motoneurons as a result of somatic spinal reflex (the guarding reflex) [67], whereas the motoneurons are reciprocally inhibited during voiding [1]. EUS motoneurons are also activated by urethral or perineal afferents in the pudendal nerve [68]. This reflex may represent, in part, a continence mechanism that is activated by proprioceptive afferent input from the urethra or pelvic floor to induce closure of the urethral outlet. These excitatory sphincter reflexes are organized in the spinal cord.

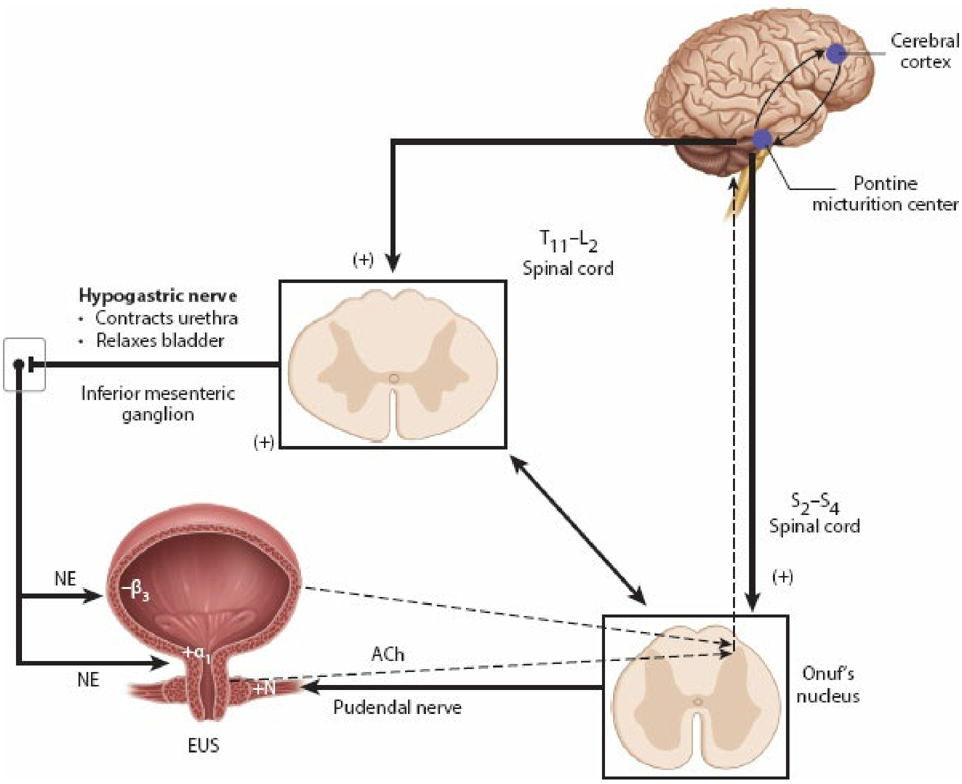


Figure 23.3 Storage reflexes. During the storage of urine, the distention of the bladder produces low-level bladder afferent firing. Afferent firing in turn stimulates the sympathetic outflow to the bladder outlet (base and urethra) and pudendal outflow to the external urethral sphincter (EUS). These responses occur by spinal reflex pathways and represent "guarding reflexes," which promote continence. Sympathetic firing also inhibits detrusor muscle and transmission in intramural ganglia. Afferent input (*dashed lines*) from the urethra and EUS can inhibit parasympathetic outflow to the detrusor through a spinal reflex circuit. ACh, acetylcholine; NE norepinephrine; excitatory (+) and inhibitory (−) mechanisms.

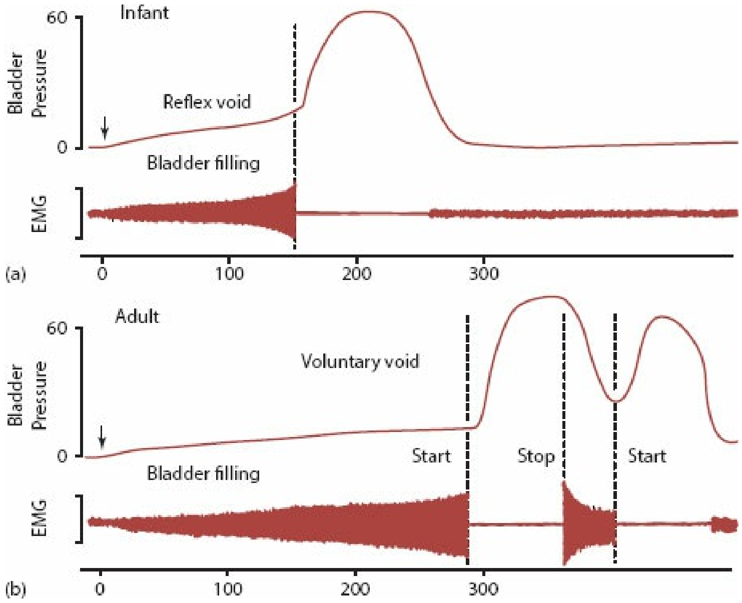


Figure 23.4 Combined cystometrogram and sphincter electromyogram (EMG) comparing reflex voiding responses in an infant (a) and a voluntary voiding response in an adult (b). The x-axis in all records represents bladder volume in milliliters, and the y-axis represents bladder pressure in centimeters of water and electrical activity of the electromyographic recording. On the left side of each trace, the arrows indicate the start of a slow infusion of fluid into the bladder (bladder filling). Vertical dashed lines indicate the start of sphincter

relaxation that precedes by a few seconds the bladder contraction in (a) and (b). In (b), note that a voluntary cessation of voiding (stop) is associated with an initial increase in sphincter electromyographic activity followed by a reciprocal relaxation of the bladder. A resumption of voiding is again associated with sphincter relaxation and a delayed increase in bladder pressure. (From de Groat WC, Basic neurophysiology and neuropharmacology, in P Abrams, S Khoury, and A Wein, eds., *Incontinence*, Health Publications, Plymouth, U.K., 1999, p. 112. With permission.)

Bladder Emptying

Bladder emptying requires sudden complete relaxation of striated sphincter followed immediately by increased intravesical pressure. The transition from storage phase to voiding phase can occur either involuntarily (reflexively) or voluntarily. The former is readily demonstrated in the human infant or in patients with neuropathic bladder when the bladder wall tension exceeds the micturition threshold due to increased urine volume. Voiding is initiated upon cessation of sympathetic and somatic input to the detrusor and sphincter, which causes sphincters to relax and the bladder neck to assume the shape of a funnel, and the concomitant increased parasympathetic activity causes the detrusor contraction to generate pressure for overcoming resistance generated by the collapsed urethra.

At this point, increased afferent firing from tension receptors in the bladder reverses the pattern of efferent outflow, producing firing in the sacral parasympathetic pathways and inhibition of sympathetic and somatic pathways. Reversal in efferent outflow in both sympathetic and somatic innervations to the urethra and sphincter causes a reflex relaxation followed in a few seconds by parasympathetic nerve–mediated detrusor contraction (Figure 23.5). As a result, the pressure inside bladder rises and the urethral pressure falls, which is a prerequisite for the urine expulsion.

ACh released from the parasympathetic nerves together with ATP [45] at the detrusor neuromuscular synapse mediates detrusor contraction. ATP exerts mutually exclusive effects through the activation of excitatory purinergic $P2X_1$ receptors on the detrusor smooth muscle, and action on inhibitory $P2Y_1$ receptors controls ACh release from cholinergic nerve endings [44]. Elimination of urine is also facilitated by noncholinergic/nonadrenergic nitric oxide release onto the internal urethral sphincter, resulting in a relaxation of the urethral outlet [69,70] and by removal of excitatory inputs to the urethra.

Secondary reflexes elicited by flow of urine through the urethra also facilitate bladder emptying [61,66,71]. These reflexes require the integrative action of neuronal populations at various levels of the neuraxis (Figure 23.6). The parasympathetic outflow to the detrusor and urethra has a more complicated central organization involving spinal and spinobulbospinal pathways passing through a micturition center in the PMC (pons) (Fib. 6B). Complete bladder emptying is facilitated by urethra to bladder reflex occurring while urine is flowing through urethra as demonstrated in anesthetized cat experiments by Barrington [72,73] (Figure 23.5). Barrington identified two components of this reflex. One component was activated by a somatic afferent pathway in the pudendal nerve, which facilitated voiding via the supraspinal pathway involving the PMC [73] (Figure 23.6). The other component was activated by a visceral afferent pathway in the pelvic nerve to facilitate voiding at the spinal micturition center [72]. Studies [71] in the anesthetized rat have further confirmed the seminal findings of Barrington [74].

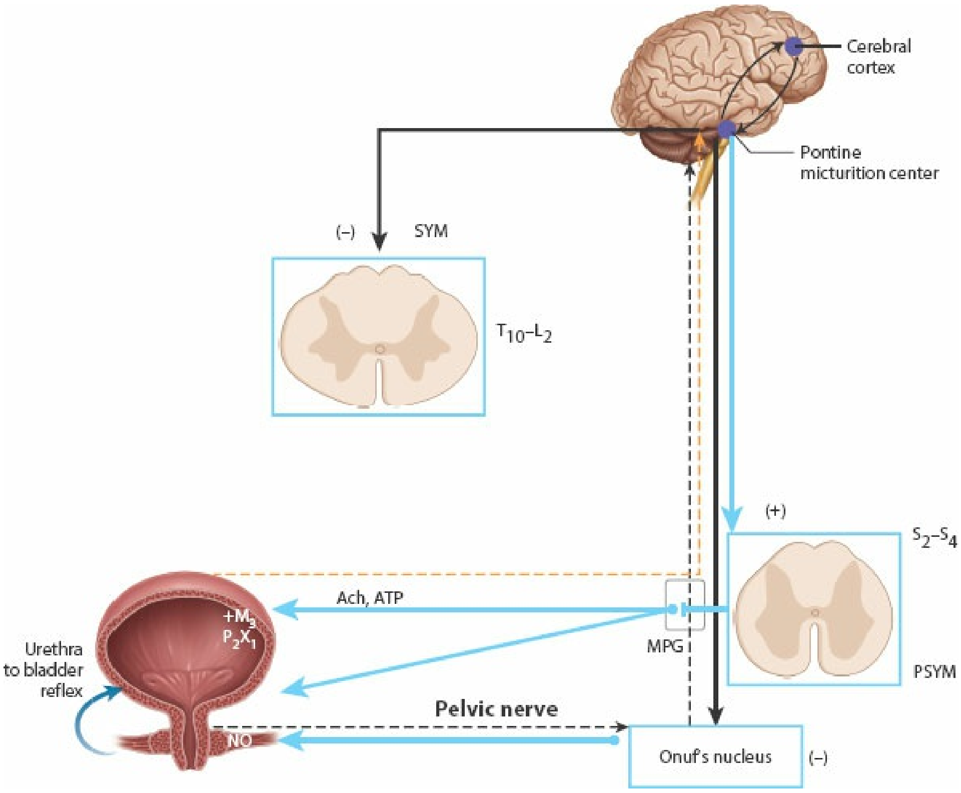


Figure 23.5 Voiding reflexes. At the initiation of micturition, intense vesical afferent activity activates the brainstem micturition center, which inhibits the spinal guarding reflexes (sympathetic and pudendal outflow to the urethra). The pontine micturition center (PMC) also stimulates the parasympathetic outflow to the bladder and internal sphincter smooth muscle. Maintenance of the voiding reflex is through ascending afferent input from the spinal cord, which may pass through the periaqueductal gray (PAG) matter before reaching the PMC. Afferent pathway (*colored dashed line*) from the detrusor activates spinal reflex mechanisms that induce firing in the somatic cholinergic nerves to the external urethral sphincter (EUS), sympathetic adrenergic nerves to the urethral smooth muscle, and cholinergic and nitrergic nerves to the urethral smooth muscle. Bulbospinal pathways from the brain can modulate these spinal reflex mechanisms. Urethral afferents (*black dashed line*) activated by urine flowing through urethra can further facilitate parasympathetic efferent outflow to the detrusor to complete voiding by means of a supraspinal pathway passing through the PMC as well as a spinal reflex pathway. ACh, acetylcholine; NEPI, norepinephrine; NO, nitric oxide; excitatory (+) and inhibitory (−) mechanisms.

Measurements of reflex bladder contractions under isovolumetric conditions during continuous urethral perfusion (0.075 mL/min) revealed that the frequency of micturition reflexes was significantly reduced when urethral perfusion was stopped or after urethral infusion of lidocaine (1%). Desensitization of the urethral afferent with intraurethral capsaicin also dramatically altered the micturition reflex. Intraurethral infusion of nitric oxide donors (S-nitroso-N-acetylpenicillamine [SNAP] or nitroprusside, 1–2 mM) markedly decreased the urethral perfusion pressure (approximately 30%) and decreased the frequency of reflex bladder contractions (45%–75%) but did not change the amplitude of bladder contractions.

The existence of this pudendal nerve–mediated reflex has been confirmed as low-frequency electrical stimulation of afferent axons in the human pudendal nerve and the deep perineal nerve, a caudal branch of the pudendal nerve in cats that can initiate reflex bladder contractions and voiding [75,76]. The existence of urethra to bladder reflex may explain why stress incontinence and urge incontinence are comorbidities in women. Women with mixed incontinence may have detrusor overactivity activated by leakage of urine into the urethra due to stress incontinence, which support the theory of stress incontinence inducing urge incontinence [77]. Interestingly, surgical cure of the stress incontinence of women with mixed incontinence has resolved the urge incontinence in up to half of the patients.

Micturition Control Circuitry

Volitional control over micturition is maintained by multiple reflex pathways organized in the brain and spinal cord to mediate the coordination between the urinary bladder and the urethra. Inputs from supraspinal, spinal, and peripheral nervous system are necessary to maintain "switch-like" patterns of filling and voiding activity (Figures 23.4 and 23.5), which maintain a reciprocal relationship between the urinary bladder and the urethral outlet [78,79]. The principal reflex components of these switching circuits are listed in Figures 23.4 and 23.6. Some reflexes promote urine storage, whereas others facilitate voiding. During the filling phase, there is an inhibitory discharge to PMC for relaxing the bladder and tightening the sphincter (guarding reflex).

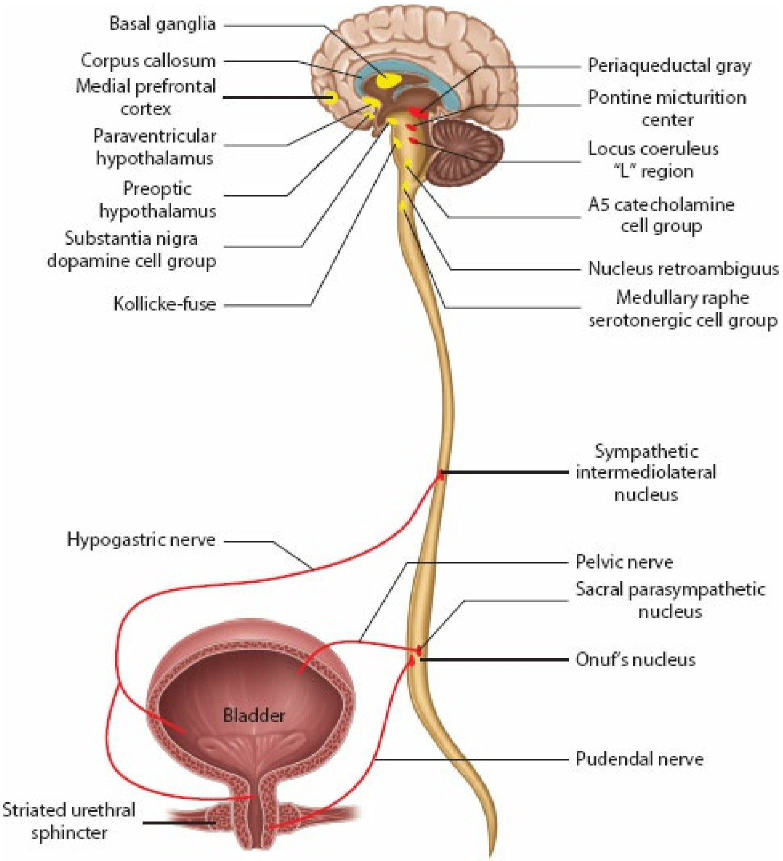

Basal ganglia
Corpus callosum
Medial prefrontal cortex
Paraventricular hypothalamus
Preoptic hypothalamus
Substantia nigra dopamine cell group
Kollicke-fuse
Periaqueductal gray
Pontine micturition center
Locus coeruleus "L" region
A5 catecholamine cell group
Nucleus retroambiguus
Medullary raphe serotonergic cell group
Sympathetic intermediolateral nucleus
Hypogastric nerve
Pelvic nerve
Sacral parasympathetic nucleus
Onuf's nucleus
Bladder
Pudendal nerve
Striated urethral sphincter

Figure 23.6 Schematic of micturition control circuitry: Sympathetic preganglionic pathways emerge from the lumbar spinal cord and pass to the sympathetic chain ganglia (SCG) and then through the inferior splanchnic nerves (ISNs) to the inferior mesenteric ganglia (IMG). Preganglionic and postganglionic sympathetic axons then travel in the hypogastric nerve (HGN) to the pelvic plexus and the urogenital organs. Parasympathetic preganglionic axons that originate in the sacral spinal cord pass in the pelvic nerve to ganglion cells in the pelvic plexus and to distal ganglia in the organs. Sacral somatic pathways are contained in the pudendal nerve, which provides an innervation to the external urethral sphincter (EUS) muscles. The pudendal and pelvic nerves also receive postganglionic axons from the caudal sympathetic chain ganglia. These three sets of nerves contain afferent axons from the lumbosacral dorsal root ganglia (DRG).

It is also possible that individual reflexes might be linked together in a serial manner to create complex feedback mechanisms. For example, the bladder to EUS guarding reflex that triggers sphincter contractions during bladder filling could, in turn, activate sphincter muscle afferents that initiate an inhibition of the parasympathetic excitatory pathway to the bladder. Thus, a bladder to sphincter to bladder reflex pathway could in theory contribute to the suppression of bladder activity during urine storage. Alterations in these primitive reflex mechanisms may contribute to neurogenic bladder dysfunction.

Afferent Pathways

An intact afferent system is crucial to physiological voiding and bladder filling. During the filling phase, mechanoreceptors in bladder wall initiate visceral afferent (Aδ-fibers) activity that is carried by afferent axons in the pelvic nerve that synapse on spinal interneurons in lumbosacral spinal cord [62,80,81]. The pelvic nerve afferents consist of myelinated (A) and unmyelinated (C) axons to monitor the volume of the bladder and the amplitude of the bladder contraction (Figure 23.5). The primary afferent neurons of the pelvic and pudendal nerves are contained in sacral dorsal root ganglia (DRG), whereas afferent innervation in the hypogastric nerves arises in the rostral lumbar DRG. The central axons of the DRG neurons carry the sensory information from the lower urinary tract to second-order neurons in the spinal cord [80,82–84] (Figure 23.6). Visceral afferent fibers of the pelvic [82] and pudendal [83] nerves enter the cord and travel rostrocaudally within Lissauer's tract.

During neuropathic conditions and possibly inflammatory conditions, there is recruitment of C fibers from a new functional afferent pathway that can cause urge incontinence and possibly bladder pain. The suppression of detrusor overactivity in patients by sacral root stimulation may reflect in part the activation of the afferent limb of these visceral-bladder and somatic-bladder inhibitory reflexes [85–89].

Spinal and Supraspinal Pathways Involved in the Micturition Reflex

In the spinal cord, afferent pathways terminate on second-order interneurons that relay information to the brain or to other regions of the spinal cord including the preganglionic sympathetic fibers from the intermediolateral cell column of the lower thoracic (T10) to upper lumbar (L2) spinal cord that form the thoracic and lumbar splanchnic nerves. The preganglionic fibers then synapse on the prevertebral inferior mesenteric ganglia (IMG) or paravertebral ganglia and travel along the hypogastric and pelvic nerves, respectively. Because polysynaptic pathways but not monosynaptic pathways mediate bladder, urethral, and sphincter reflex, interneuronal mechanisms play an essential role in the regulation of lower urinary tract function. Electrophysiological [90,91] and neuroanatomic [79,92–94] techniques have identified lower urinary tract interneurons in the same regions of the cord that receive afferent input from the bladder.

Pharmacological experiments revealed that glutamic acid is the excitatory transmitter in these pathways [84]. The inhibitory neurons release γ-aminobutyric acid (GABA) and glycine. Reflex pathways that control the external sphincter muscles also use glutamatergic excitatory and GABAergic and glycinergic inhibitory interneuronal mechanisms. Stimulation of afferent fibers from various regions (anus, colon–rectum, vagina, uterine cervix, penis, perineum, pudendal nerve) can inhibit the firing of sacral interneurons evoked by bladder distention [90]. This inhibition may be a result of presynaptic inhibition at primary afferent terminals or be due to direct postsynaptic inhibition of the second-order neurons. Direct postsynaptic inhibition of bladder preganglionic neurons can also be elicited by stimulation of somatic afferent axons in the pudendal nerve or visceral afferents from the distal bowel [95,96].

Peripheral Nervous System

The lower urinary tract is innervated by three sets of the peripheral nerves involving the parasympathetic, sympathetic, and somatic nervous systems (Figure 23.6). Pelvic parasympathetic nerves arise at the sacral level of the spinal cord, excite the bladder, and relax the urethra. Lumbar sympathetic nerves inhibit the bladder body and excite the bladder base and urethra. Pudendal nerves excite the EUS. These nerves contain afferent (sensory) and efferent axons [62,63,94,97].

Parasympathetic Pathways

The preganglionic parasympathetic fibers arise from the ventral roots in the lateral part of the sacral intermediate gray matter in a region termed the sacral parasympathetic nucleus (S2–S4) and spinal cord to form the pelvic splanchnic nerves [63,82,84,98,99]. Upon coursing through and exiting the hypogastric and pelvic plexus, the fibers join the pelvic and pudendal nerves to synapse on terminal ganglia [1] and innervate the detrusor smooth muscle and urethra. The parasympathetic postganglionic neurons in humans are located not only in the detrusor wall layer but also in the pelvic plexus. This dual location can allow the possibility of afferent and efferent neuron interconnection at the level of the intramural ganglia in cauda equina or pelvic plexus injury [66,84]. Such injury leaves patients neurologically decentralized but may not be completely denervated.

Sympathetic Pathways

Sympathetic outflow from the rostral lumbar spinal cord provides a noradrenergic excitatory and inhibitory input to the bladder and urethra [69]. The peripheral sympathetic pathways follow a complex route that passes through the sympathetic chain ganglia (SCG) to the IMG and then through the hypogastric nerves to the pelvic ganglia [100]. The activation of the sympathetic nerves induces relaxation of the bladder body and contraction of the bladder outlet and urethra, which contribute to filling phase in the bladder. Urine storage is facilitated by bladder wall relaxation and accommodation promoted by action of noradrenaline at β-adrenergic receptors in bladder [101] and activation of α-adrenergic receptors on the internal urethral sphincter resulting in contraction of the urethral outlet.

Somatic Pathways

The EUS motoneurons are located along the lateral border of the ventral horn of the sacral (S2–S4) spinal cord, commonly referred to as Onuf's nucleus [83]. Sphincter motoneurons also exhibit transversely oriented dendritic bundles that project laterally in the lateral funiculus, dorsally into the intermediate gray matter, and dorsomedially toward the central canal. Spinal reflex pathways not only enhance sympathetic outflow but also α-motoneuron discharge from Onuf's nucleus. Propagation of this signal along the pudendal nerve to the EUS elicits skeletal muscle contraction by activating nicotinic ACh receptors to provide voluntary control over urinary continence.

The inhibition can be induced by activation of afferent input from visceral organs including the penis, vagina, rectum, perineum, urethral sphincter, and anal sphincter [63,102,103]. Contractions of the EUS and possibly other pelvic floor striated muscles can stimulate firing in muscle proprioceptive afferents, which then activate central inhibitory mechanisms to suppress the micturition reflex (Figure 23.5). Electrical stimulation of somatic afferent pathways projecting in the pudendal nerve to the caudal lumbosacral spinal cord can also inhibit voiding function.

Electrophysiological studies in cats showed that the inhibition was mediated by suppression of interneuronal pathways in the sacral spinal cord and also by direct inhibitory input to the parasympathetic preganglionic neurons [104]. A similar inhibitory mechanism has been identified in monkeys by direct stimulation of the anal sphincter muscle [105]. The inhibition of EUS reflex activity during micturition is dependent, in part, on supraspinal mechanisms because it is weak or absent in chronic spinal animals and humans, resulting in simultaneous contractions of bladder and sphincter (i.e., detrusor sphincter dyssynergia) [106,107]. In the adult, the reflex loop passes through the pontine center.

Pontine Micturition Center and Brainstem Modulatory Mechanisms

Various studies indicate that the micturition reflex is normally mediated by a spinobulbospinal reflex pathway passing through relay centers in the brain [61,62,66,78]. The occurrence of voiding dysfunction following lower thoracic spinal cord injury highlights the crucial role of supraspinal circuitry in voiding relative to the filling phase. The experiments involving brain-lesioning techniques in animals have confirmed that neurons in the brainstem at the level of the inferior colliculus have an essential role in the control of the parasympathetic component of micturition [61,62,66,108].

Removal of brain areas above the colliculus by intercollicular decerebration usually facilitates micturition by elimination of inhibitory inputs from more rostral centers. However, transections at any point below the colliculi abolish micturition. In addition to providing axonal inputs to the locus coeruleus and the sacral spinal cord [109–111], neurons in the dorsolateral pontine tegmentum termed pontine micturition center (PMC) also send axon collaterals to the paraventricular thalamic nucleus, which is thought to be involved in the limbic system modulation of visceral behavior [110]. Some neurons in the PMC also project to the PAG region [112], which regulates many visceral activities as well as pain pathways [113]. Thus, neurons in the PMC communicate with multiple supraspinal neuronal populations that may coordinate micturition with other functions of the organism.

Although the circuitry in humans is uncertain, brain imaging studies have revealed increases in blood flow in this region of the pons during micturition [114]. This change presumably reflects increases in neuronal activity. Thus, the PMC appears critical for micturition across species. In the midbrain, recent evidence supports that mesencephalic PAG can directly receive information of bladder fullness bypassing the local spinal reflexes via ascending spinal tract neurons. After cortical processing, the

PAG sends excitatory input to PMC, which has descending cortical projections that synapse on preganglionic parasympathetic neurons and inhibitory interneurons in the sacral spinal cord to prevent excitatory input reaching the urethral sphincters. Efferent parasympathetic outflow is enhanced by PMC and the preganglionic sympathetic and α-motoneuron discharge to the sphincter is attenuated during voiding. The ascending excitation to the dorsolateral metencephalon is diminished by the reduced bladder distension as a consequence of voiding, which switches on storage phase once again. PMC plays an important role in the integration of the micturition reflex [112].

Central Pathways That Modulate the Micturition Reflex

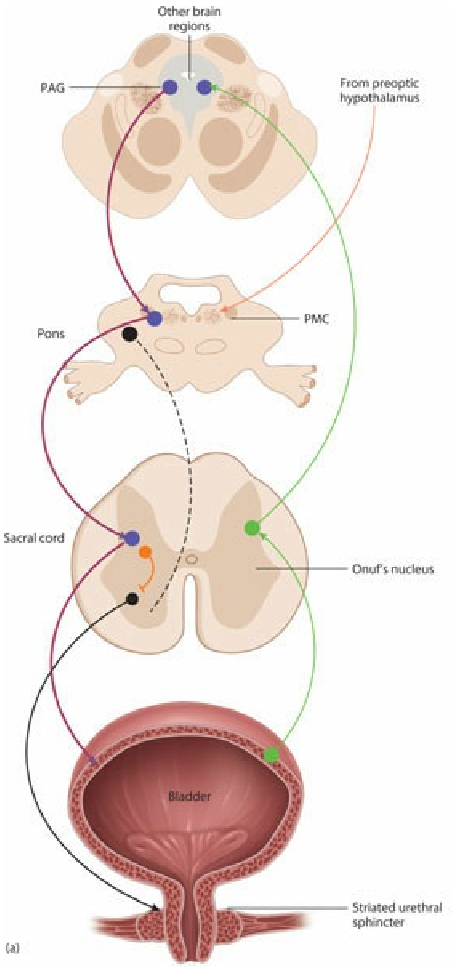
Transneuronal virus tracing methods have identified virus-infected cells in several regions of the hypothalamus and the cerebral cortex after injection of pseudorabies virus into the lower urinary tract in animals [92–94,115]. Neurons in the cortex were located primarily in the medial frontal cortex. Tracers injected into the paraventricular nucleus of the hypothalamus labeled terminals in the sacral parasympathetic nucleus as well as the sphincter motor nucleus [116]. The influence of the cortex on voiding function could be mediated by a number of pathways, including direct cortical projections from the prefrontal cortex (PFC) and insular cortex to the PMC or projections through the hypothalamus and the extrapyramidal system [1]. Studies in humans indicate that voluntary control of voiding is dependent on connections between the frontal cortex and the septal–preoptic region of the hypothalamus as well as on connections between the paracentral lobule and the brainstem. Lesions to these areas of cortex appear to directly increase bladder activity by removing cortical inhibitory control [1].

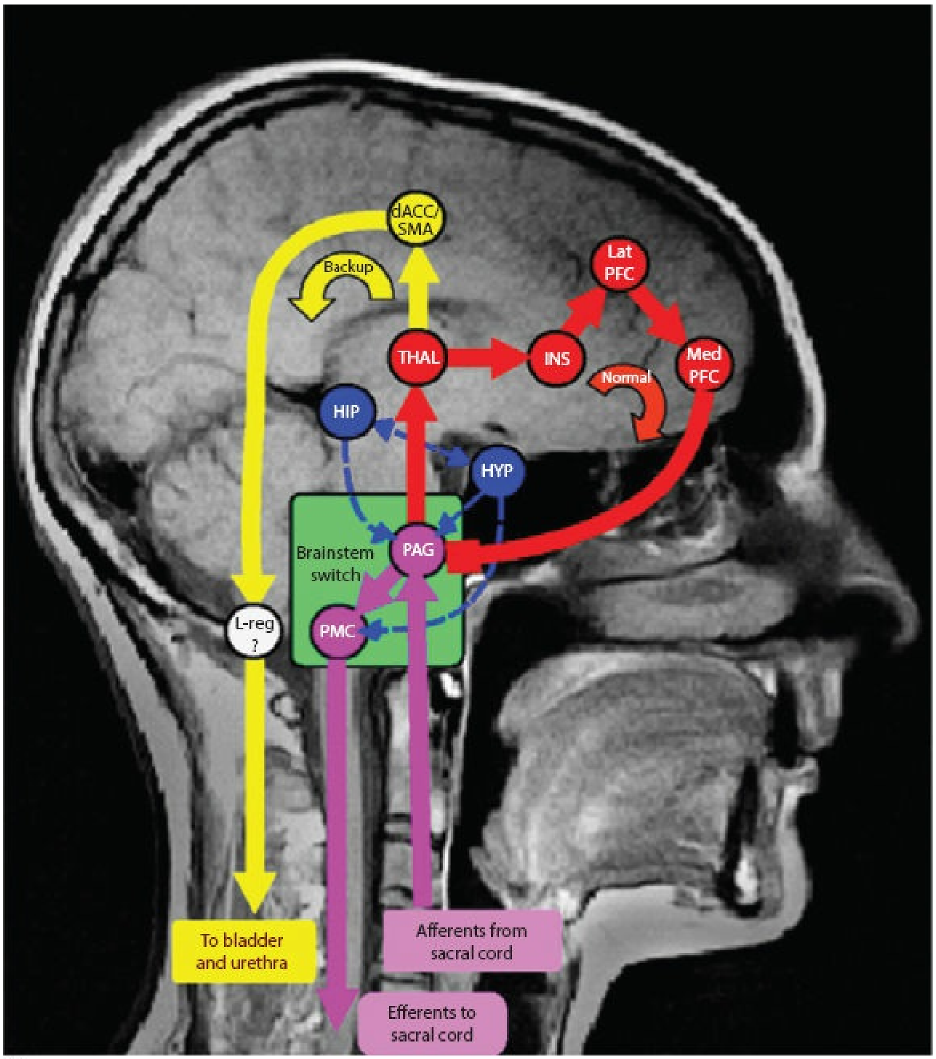
Human Brain Imaging Studies

Evidence from human imaging studies has supported findings from preclinical studies and demonstrated the active control of micturition by brain during filling and voiding [117]. Functional neuroimaging have been performed in normal volunteers using single-photon emission computed tomography, positron-emission tomography, functional magnetic resonance imaging, and near-infrared spectroscopy to observe activation in brain areas responsible for the perception of bladder fullness and the sensation of the desire to void during bladder filling, whereas others examined brain activity during micturition [118,119]. Brain is activated during bladder filling [120] particularly in the PAG, the midline pons, the anterior and the mid-cingulate gyrus, the anterior insula, and bilaterally the frontal lobes, supplementary motor area, referred to as the “frontal micturition center” [120,121] (Figure 23.7).

The constellation of these cortical areas seem to “switch on and off” the spino–bulbo–spinal micturition reflex. The results were consistent with the notion that the PAG receives information about bladder fullness and then relays this information to other brain areas involved in the control of bladder storage. In fMRI studies in men and women, activation during urinary storage is found in the supplementary motor area, mid-cingulate cortex, insula, and right PFC, and the right anterior insula and midbrain PAG were more active at higher rather than at lower bladder volumes [122,123].

PET scan studies in normal men and women revealed that during voiding, two cortical areas (the dorsolateral PFC and anterior cingulated gyrus) were active (i.e., exhibited increased blood flow). The hypothalamus including the preoptic area as well as the pons and the PAG also showed activity in concert with voluntary micturition [112,114,124]. Another PET study during voiding also confirmed that micturition was associated with increased activity in the pons, inferior frontal gyrus, hypothalamus, and PAG while also showing activity in several other cortical areas (postcentral gyrus, superior frontal gyrus, thalamus, insula, and globus pallidus) and the cerebellar vermis [125]. Neuroimaging fMRI studies also evaluated the effect of voluntary contractions of the pelvic floor during urine withholding or during cold stimulation on the activation of the parietal cortex, cerebellum, putamen, and supplementary motor area (SMA) [126] or the frontal cortex, basal ganglia, and cerebellum [127].


Other brain regions
PAG
From preoptic hypothalamus
Pons
PMC
Sacral cord
Onuf's nucleus
Bladder
Striated urethral sphincter
(a)



(b)

Figure 23.7 (a) Simplified model of supraspinal control over micturition. (b) Brain areas activated by storage and voiding involved in brainstem and spinal cord reflexes that act as "switch" (on-voiding; off-storage) identified by PET and fMRI. Brain areas activated during bladder filling are the PAG, the midline pons, the anterior and mid-cingulate gyrus, the anterior insula, and bilaterally the frontal lobes, supplementary motor area (SMA) referred to as the "frontal micturition center." Ascending afferent fibers (afferents) carry the information from the bladder synapse in the periaqueductal gray (PAG) and are relayed to the right insula (RI), forming the substrate for sensation. The anterior cingulate gyrus (ACG) is responsible for monitoring, arousal, and efferent output to the PAG and pontine micturition center (PMC). The prefrontal cortex (PFC) is involved in voluntary decision about voiding and generates efferent signals to control ACG and ultimately PMC. PMC then provides motor output to cause voiding. Impaired supraspinal control in cases of neurodegenerative disease leads to incontinence. (From Griffiths D and Tadic SD: Bladder control, urgency, and urge incontinence: Evidence from functional brain imaging. *Neurourol Urodyn*. 2008. 27(6). 466–474. Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.)

Based on the results, a simplified model of normal bladder filling is proposed, where the filling activates bladder and urethral afferents, which are received in the PAG, are mapped in the insula, and form the basis of the desire to void; the anterior cingulate gyrus (ACG) provides monitoring and control; the PFC makes voiding decisions. Voiding reflex is continuously inhibited at the PMC as the bladder fills until the decision to void is made in the PFC. The increasing desire to void corresponds to a gradual increase in insular response. Neuroimaging of patients with stroke, tumor, and multiple sclerosis has confirmed the role of these brain areas in micturition as the activated areas strikingly overlap the lesions described in patients.

Brain imaging studies have also been performed to identify changes in cerebral perception of detrusor overactivity. A PET study in patients with Parkinson's disease reported activation of the PAG, supplementary motor area, basal ganglia, and cerebellum during detrusor overactivity [128]. A fMRI study of subject with confirmed overactivity showed that infusion in the bladder is associated with activity in the PAG, thalamus, insula, and anterior cingulated gyrus; however, weak responses in the ACG at large bladder volumes are observed in urge-incontinent patients [129,130]. Cortical responses become exaggerated, especially in ACG. This may be both a learned reaction to previous incontinence episodes and a neural correlate of urgency [131]. Urge-incontinent subjects have weak responses or deactivation observed in the PFC or the limbic system, leading to a defect on supraspinal bladder control that may cause urge incontinence, and enhanced responses in the anterior cingulate gyrus, which may be due to abnormal bladder afferents or related to a loss of control in other brain areas and could be correlated with urge sensations [119]. Radiographic imaging of the CNS with control and dysregulation of the lower urinary tract is an exciting area of research, but the results are preliminary. Subjects are conscious and thinking about their bladder during the test and may have an indwelling catheter that may alter what parts of the brain are activated naturally or artificially.

CONCLUSIONS

Micturition is a function accomplished by unique biomechanics of bladder and urethral muscles as well as by a complex neural control system located in the brain and spinal cord. Storage of urine in the bladder till a socially acceptable moment arrives is mediated by increased sympathetic activity, which relaxes the urinary bladder via activation of postsynaptic β_3-receptors and contracts both urethral and prostatic smooth muscles via the α_1-adrenoceptor. The volitional control of micturition depends on an intact afferent system to relay the information on the state of bladder fullness to higher brain centers. Voiding in healthy adults happens after the PMC orders the sacral parasympathetic nucleus to increase parasympathetic activity, which activates postsynaptic muscarinic receptors to cause detrusor contraction and reciprocal relaxation of both urethral and prostatic smooth muscle by nitric oxide release. In addition, the rhabdosphincter is relaxed by inhibition of the pudendal nucleus at the sacral portion.

The neural control system performs like a switching circuit to maintain a reciprocal relationship between the reservoir (urinary bladder) and the outlet components (urethral sphincter) of the urinary tract. The switching circuit is modulated by various neurotransmitters and is sensitive to a variety of drugs. In infants, the switching circuits function in a purely reflex manner to produce involuntary voiding; however, in adults, urine storage and release are subject to volitional control. An understanding of the physiological events mediating micturition and continence provides a rational basis for the management of lower urinary tract dysfunction.

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Pharmacology of the Bladder

Karl-Erik Andersson

INTRODUCTION

The lower urinary tract (LUT) is controlled by a complex interplay between the central (CNS) and peripheral nervous systems and local regulatory factors [1]. Malfunction at various levels may result in micturition disorders, which roughly can be classified as disturbances of storage or emptying. Failure to store urine may lead to various forms of incontinence (mainly urgency and stress incontinence), and failure to empty to urinary retention. Lower urinary tract symptoms (LUTS) include storage, voiding, and postmicturition symptoms. Storage symptoms (urgency, frequency with and without incontinence, nocturia) form the overactive bladder (OAB) syndrome, which may or may not be associated with involuntary detrusor contractions demonstrated by cystometry (detrusor overactivity [DO]). Pharmacological treatment of urinary incontinence (UI) is a main option, and several drugs with different modes and sites of action have been tried [2–4]. However, to be able to optimize existing therapies and to identify suitable new targets for treatment, knowledge about the mechanisms of micturition is necessary.

In the following texts, a brief review is given of the normal nervous control of the LUT and of some therapeutic principles used for treatment of UI.

NERVOUS MECHANISMS FOR BLADDER EMPTYING AND URINE STORAGE

The nervous mechanisms for bladder emptying and urine storage involve a complex pattern of afferent and efferent signaling in *parasympathetic*, *sympathetic*, and *somatic* nerves. These nerves constitute reflex pathways, which either maintain the bladder in a relaxed state, enabling urine storage at low intravesical pressure, or initiate micturition by relaxing the outflow region and contracting the bladder smooth muscle. Under normal conditions, there is a reciprocal relationship between the activity in the detrusor and the activity in the outlet region. During voiding, contraction of the detrusor muscle is preceded by a relaxation of the outlet region, thereby facilitating the bladder emptying [5–7]. On the contrary, during the storage phase, the detrusor muscle is relaxed, and the outlet region is contracted to maintain continence.

Contraction of the detrusor smooth muscle and relaxation of the outflow region result from activation of *parasympathetic* neurons located in the sacral parasympathetic nucleus in the sacral spinal cord at the level of S2–S4 [8]. The axons pass through the pelvic nerve and synapse with the postganglionic nerves either in the pelvic plexus, in ganglia on the surface of the bladder (vesical ganglia), or within the walls of the bladder and urethra (intramural ganglia) [9]. The preganglionic neurotransmission is predominantly mediated by acetylcholine acting on nicotinic receptors, although the transmission can be modulated by adrenergic, muscarinic, purinergic, and peptidergic presynaptic receptors [10]. The postganglionic neurons in the pelvic nerve mediate the excitatory input to the normal human detrusor smooth muscle by releasing acetylcholine acting on muscarinic receptors. However, an atropine-resistant (nonadrenergic, noncholinergic [NANC]) contractile component is regularly found in the bladders of most animal species [11,12]. Such a component can also be demonstrated in functionally and morphologically altered human bladder tissue [13–15] but contributes only to a few percent to normal detrusor contraction [1]. ATP is one important mediator of the NANC contraction [16,17] although the involvement of other transmitters cannot be ruled out [1,18]. The pelvic nerve also conveys parasympathetic nerves to the outflow region and the urethra. These nerves exert an inhibitory effect on the smooth muscle by releasing nitric oxide [19] and other transmitters [20–22].

Most of the *sympathetic* innervation of the bladder and urethra originates from the intermediolateral nuclei in the thoracolumbar region (T10-L2) of the spinal cord. The axons leave the spinal cord via the splanchnic nerves and either travel through the inferior mesenteric ganglia (IMF) and the hypogastric nerve or pass through the paravertebral chain to the lumbosacral sympathetic chain ganglia and enter the pelvic nerve. Thus, sympathetic signals are conveyed in both the hypogastric nerve and the pelvic nerve [9]. The preganglionic sympathetic transmission is, like the parasympathetic preganglionic transmission, predominantly mediated by acetylcholine acting on nicotinic receptors. Some preganglionic terminals synapse with the postganglionic cells in the paravertebral ganglia or in the IMF, while others synapse closer to the pelvic organs, and short postganglionic neurons innervate the target organs. Thus, the hypogastric and pelvic nerves contain both pre- and postganglionic fibers [9]. The predominant effect of the sympathetic innervation is to contract the bladder base and the urethra. In addition, the sympathetic innervation inhibits the parasympathetic pathways at spinal and ganglionic levels. In humans, noradrenaline is released in response to electrical stimulation in vitro [23], and the normal response to released noradrenaline is relaxation [24,25]. However, the importance of the sympathetic innervation for relaxation of the human detrusor has never been established. In contrast, in several animal species, the adrenergic innervation has been demonstrated to mediate relaxation of the detrusor during filling.

Most of the *sensory* nerves to the bladder and urethra originate in the dorsal root ganglia at the lumbosacral level of the spinal cord and travel via the pelvic nerve to the periphery. In addition, some afferents originate in the dorsal root ganglia at the thoracolumbar level and travel in the hypogastric nerve. The sensory nerves to the striated muscle of the external urethral sphincter travel in the pudendal nerve to the sacral region of the spinal cord [9]. The most important afferents for the micturition process are myelinated Aδ-fibers and unmyelinated C-fibers travelling in the pelvic nerve to the sacral spinal cord [26–28], conveying information from receptors in the bladder wall. The Aδ-fibers respond to passive distension and active contraction, thus conveying information about bladder filling [29]. The activation threshold for Aδ-fibers is 5–15 mm H_2O. This is the intravesical pressure at which humans report the first sensation of bladder filling [10]. C-fibers have a high mechanical threshold and respond primarily to chemical irritation of the bladder urothelium/suburothelium [30] or cold [31]. Following chemical irritation, the C-fiber afferents exhibit spontaneous firing when the bladder is empty and increased firing during bladder distension [30]. These fibers are normally inactive and are therefore termed “silent fibers.”

The *somatic* innervation of the urethral rhabdosphincter and of some perineal muscles (for example, compressor urethrae and urethrovaginal sphincter) is provided by the pudendal nerve. These fibers originate from sphincter motor neurons located in the ventral horn of the sacral spinal cord (levels S2–S4) in a region called Onuf’s (Onufrowicz’s) nucleus [32].

STORAGE PHASE

During the storage phase, the bladder has to relax in order to maintain a low intravesical pressure. Urine storage is regulated by two separate storage reflexes, of which one is sympathetic (autonomic) and the other is somatic [32]. The sympathetic storage reflex (pelvic-to-hypogastric reflex) is initiated as the bladder distends (myelinated Aδ-fibers) and the generated afferent activity travels in the pelvic nerves to the spinal cord. Within the spinal cord, sympathetic firing from the lumbar region (L1–L3) is initiated, which, by effects at the ganglionic level, decreases excitatory parasympathetic inputs not only to the bladder but also through postganglionic neurons that releases noradrenaline, which facilitates urine storage by stimulating mainly β_3-adrenoceptors (ARs) in the detrusor smooth muscle (see the following texts). As mentioned previously, there is little evidence for a functionally important sympathetic innervation of the human detrusor, which is in contrast to what has been found in several animal species. The sympathetic innervation of the human bladder is found mainly in the outlet region, where it mediates contraction. During micturition, this sympathetic reflex pathway is markedly inhibited via supraspinal mechanisms to allow the bladder to contract and the urethra to relax. Thus, the Aδ afferents and the sympathetic efferent fibers constitute a vesico-spinal-vesical storage reflex, which maintains the bladder in a relaxed mode while the proximal urethra and bladder neck are contracted.

In response to a sudden increase in bladder pressure, such as during a cough, laugh, or sneeze, a more rapid somatic storage reflex (pelvic-to-pudendal reflex), also called the guarding or continence reflex, is initiated. The evoked afferent activity travels along myelinated Aδ afferent nerve fibers in the pelvic nerve to the sacral spinal cord, where efferent somatic urethral motor neurons, located in the nucleus of Onuf, are activated. Afferent information is also conveyed to the periaqueductal gray (PAG) and to the pontine storage center (the L-region). Axons from these motor neurons of the nucleus of Onuf travel in the pudendal nerve and release acetylcholine, which activates nicotinic cholinergic receptors on the rhabdosphincter, which contracts. This pathway is tonically active during urine storage. During sudden abdominal pressure increases, however, it becomes dynamically active to contract the rhabdosphincter. During micturition, this reflex is strongly inhibited via spinal and supraspinal mechanisms to allow the rhabdosphincter to relax and permit urine passage through the urethra. In addition to this spinal somatic storage reflex, there is also supraspinal input from the pons, which projects directly to the nucleus of Onuf and is of importance for volitional control of the rhabdosphincter [33].

EMPTYING PHASE

Vesico-Bulbo-Vesical Micturition Reflex

Electrophysiological experiments in cats and rats provide evidence for a voiding reflex mediated through a vesico-bulbo-vesical pathway involving neural circuits in the pons, which constitute the pontine micturition center (PMC). Other regions in the brain, important for micturition, include the hypothalamus and cerebral cortex [10,34,35]. Bladder filling leads to increased activation of tension receptors within the bladder wall and thus to increased afferent activity in Aδ-fibers. These fibers project on spinal tract neurons mediating increased sympathetic firing to maintain continence as discussed earlier (storage reflex). In addition, the spinal tract neurons convey the afferent activity to more rostral areas of the spinal cord and the brain. One important receiver of the afferent information from the bladder is the PAG in the rostral brain stem. The PAG receives information both from afferent neurons in the bladder and from more rostral areas in the brain, i.e., cerebral cortex and hypothalamus. This information is integrated in the PAG and the medial part of the PMC (the M-region), which also control the descending pathways in the micturition reflex. Thus, PMC can be seen as a switch in the micturition reflex, inhibiting parasympathetic activity in the descending pathways when there is low activity in the afferent fibers and activating the parasympathetic pathways when the afferent activity reaches a certain threshold [10,35]. The threshold is believed to be set by the inputs from more rostral regions in the brain. In cats, lesioning of regions above the inferior colliculus usually facilitates micturition by elimination of inhibitory inputs from more rostral areas of the brain. On the other hand, transections at a lower level inhibit micturition. Thus, the PMC seems to be under a tonic inhibitory control. A variation of the inhibitory input to PMC results in a variation of bladder capacity. Experiments on rats have shown that the micturition threshold is regulated by, e.g., GABAergic inhibitory mechanisms in the PMC neurons [36].

Vesico-Spinal-Vesical Micturition Reflex

Spinal lesion rostral to the lumbosacral level interrupts the vesico-bulbo-vesical pathway and abolishes the supraspinal and voluntary control of micturition. This results initially in an areflexic bladder accompanied by urinary retention [10]. An automatic vesico-spinal-vesical micturition reflex develops slowly, although voiding is generally insufficient due to bladder sphincter dyssynergia, i.e., simultaneous contraction of the bladder and urethra. It has been demonstrated in chronic spinal cats that the afferent limb of this reflex is conveyed through unmyelinated C-fibers, which usually do not respond to bladder distension [30], suggesting changed properties of the afferent receptors in the bladder. Accordingly, the micturition reflex in chronic spinal cats is blocked by capsaicin, a neurotoxin that is believed to block C-fiber-mediated neurotransmission [37,38].

TARGETS FOR PHARMACOLOGICAL INTERVENTION

CNS Targets

Anatomically, several CNS regions may be involved in micturition control: supraspinal structures, such as the cortex and diencephalon, midbrain, and medulla, and also spinal structures [35,39–43]. Several transmitters and their receptors are involved in the reflexes and sites described earlier and may be targets for drugs aimed for control of micturition. Although few drugs with a CNS site of action have been developed, several agents acting on the CNS may have effects on micturition.

OPIOID RECEPTORS

Endogenous opioid peptides and corresponding receptors are widely distributed in many regions in the CNS of importance for micturition control, e.g., the PAG, the PMC, the spinal parasympathetic nucleus, and the nucleus of Onuf [44–46].

It has been well established that morphine, given by various routes of administration to animals and humans, can increase bladder capacity and eventually cause urinary retention. Given intrathecally (i.t.) to anesthetized rats and intravenously (i.v.) to humans, the µ-opioid receptor antagonist, naloxone, has been shown to stimulate micturition [47,48], suggesting that a tonic activation of µ-opioid receptors has a depressant effect on the micturition reflex.

Morphine given i.t. was effective in patients with DO due to spinal cord lesions [49] but was associated with side effects, such as nausea and pruritus. Further side effects of opioid receptor agonists comprise respiratory depression, constipation, and abuse. Attempts have been made to reduce these side effects by increasing selectivity toward one of the different opioid receptor types [50]. At least three different opioid receptors—µ, δ, and κ—bind stereospecifically with morphine and have been shown to interfere with voiding mechanisms. Theoretically, selective receptor actions, or modifications of effects mediated by specific opioid receptors, may have useful therapeutic effects for micturition control.

Tramadol is a well-known analgesic drug [51]. By itself, it is a weak µ-receptor agonist, but it is metabolized to several different compounds, some of them almost as effective as morphine at the µ-receptor. However, the drug (metabolites) also inhibits serotonin (5-HT) and noradrenaline reuptake [51]. This profile is of particular interest since both µ-receptor agonism and amine reuptake inhibition may be useful principles for treatment of OAB/DO, as shown in a placebo-controlled study with duloxetine [50].

In rats, tramadol abolished experimentally induced DO caused by cerebral infarction [52]. Tramadol also inhibited DO induced by apomorphine in rats [53]—a crude model of bladder dysfunction in Parkinson’s disease. Singh et al. [54] gave tramadol epidurally and found the drug to increase bladder capacity and compliance and to delay filling sensations without ill effects on voiding. Safarinejad and Hosseini [55] evaluated, in a double-blind, placebo-controlled, randomized study, the efficacy and safety of tramadol in patients with idiopathic DO. A total of 76 patients 18 years or older were given 100 mg tramadol sustained release every 12 hours for 12 weeks. Clinical evaluation was performed at baseline and every 2 weeks during treatment. Tramadol significantly reduced the number of incontinence periods and induced significant improvements in urodynamic parameters. The main adverse event was nausea. It was concluded that in patients with nonneurogenic DO, tramadol provided beneficial clinical and urodynamic effects. However, the study was later retracted due to “statistical errors….which undermine confidence in the results presented” (Br J Clin Pharmacol, 2013;77:1). Even if tramadol could be shown to have positive effects on LUTS/DO/OAB, it may not be a suitable drug for treatment due to side effects (nausea, constipation, dependency).

Central stimulation of δ-opioid receptors in anesthetized cats and rats inhibited micturition [56,57] and parasympathetic neurotransmission in cat bladder ganglia [58]. In humans, nalbuphine, a µ-receptor antagonist, and κ-receptor agonist, increased bladder capacity [59]. Buprenorphine (a partial µ-receptor agonist and κ-receptor antagonist) decreased micturition pressure and increased bladder capacity more than morphine [59]. These effects should be considered when the drugs are used for, e.g., pain control. In addition, further exploration of these non-µ-opioid receptor mediated actions on micturition seems motivated.

SEROTONIN (5-HT) MECHANISMS

It is well established that the lumbosacral autonomic, as well as the somatic motor nuclei (Onuf’s nuclei), receive a dense serotonergic input from the raphe nuclei, an innervation that is not subjected to the general decline in lumbosacral spinal innervation found with increasing age [60]. Multiple 5-HT receptors have been found at sites where processing of afferent and efferent impulses from and to the LUT takes place [61]. Although, as pointed out by de Groat [62], there is some evidence in the rat for serotonergic facilitation of voiding, the descending pathway is essentially an inhibitory circuit, with 5-HT as a key neurotransmitter. Thus, electrical stimulation of 5-HT-containing neurons in the caudal raphe nucleus causes inhibition of bladder contractions [63,64]. Most experiments in rats and cats indicate that activation of the central serotonergic system by 5-HT reuptake inhibitors, as well as by 5-HT_{1A} and 5-HT_2 receptor agonists, depresses reflex bladder contractions and increases the bladder volume threshold for inducing micturition [62]. 5-HT$_{1A}$ receptors are involved in multiple inhibitory mechanisms controlling the spinobulbospinal micturition reflex pathway. The regulation of the frequency of bladder reflexes is presumably mediated by a suppression of afferent input to the micturition-switching circuitry in the pons, whereas the regulation of bladder contraction amplitude may be related to an inhibition of the output from the pons to the parasympathetic nuclei in the spinal cord.

It has been discussed whether or not there is a deficiency in 5-HT behind both depression and OAB [65–67]. If there is, the question is if selective serotonin reuptake inhibitors (SSRIs) are effective for micturition control only in depressed patients, or if selective 5-HT uptake inhibition is a general principle that can be used for treatment of OAB. There are no randomized controlled clinical trials (RCTs) showing that SSRIs are useful for the treatment of OAB/DO [4,68]. In contrast, there are reports suggesting that the SSRIs in patients without incontinence actually can cause incontinence, particularly in the elderly. Patients exposed to 5-HT uptake inhibitors had an increased risk (15 out of 1000 patients) for developing UI [69]. This causes doubts over the anecdotal reports that SSRIs may be used as a general treatment for OAB. On the other hand, in an RCT, the combined 5-HT and noradrenaline reuptake inhibitor, duloxetine, was shown to be effective in patients with OAB [70].

Γ-AMINOBUTYRIC ACID MECHANISMS

γ-Aminobutyric acid (GABA) has been identified as a main inhibitory transmitter in the brain and spinal cord. GABA functions appear to be triggered by binding of GABA to its ionotropic receptors, GABA$_A$ and GABA$_C$, which are ligand-gated chloride channels, and its metabotropic receptor, GABA$_B$ [71]. Since blockade of GABA$_A$ and GABA$_B$ receptors in the spinal cord–[72,73] and brain [73,74] stimulated rat micturition, an endogenous activation of GABA$_{A+B}$ receptors may be responsible for continuous inhibition of the micturition reflex within the CNS. In the spinal cord, GABA$_A$ receptors are more numerous than GABA$_B$ receptors, except for the dorsal horn where GABA$_B$ receptors predominate [75,76].

Experiments using conscious and anesthetized rats demonstrated that exogenous GABA, muscimol (GABA$_A$ receptor agonist) and baclofen (GABA$_B$ receptor agonist), given i.v., i.t., or intracerebroventricularly inhibit micturition [73,77]. Similar effects were obtained in nonanesthetized mice [78]. Baclofen given i.t. attenuated oxyhemoglobin-induced DO in rats, suggesting that the inhibitory actions of GABA$_B$ receptor agonists in the spinal cord may be useful for controlling micturition disorders caused by C-fiber activation in the urothelium and/or suburothelium [73]. In mice, where DO was produced by intravesical citric acid, baclofen given subcutaneously had an inhibitory effect, which was blocked by the selective GABA$_B$ receptor antagonist CGP55845 [78]. Beneficial effects of baclofen have also been documented in humans with DO [79].

Stimulation of the PMC results in an immediate relaxation of the external striated sphincter and a contraction of the detrusor muscle of the bladder. Blok et al. [33] demonstrated in cats a direct pathway from the PMC to the dorsal gray commissure of the sacral cord. It was suggested that the pathway produced relaxation of the external striated sphincter during micturition via inhibitory modulation by GABA neurons of the motoneurons in the sphincter of Onuf. In rats, i.t. baclofen and muscimol ultimately produced dribbling UI [72,73], and this was also found in conscious mice given muscimol and diazepam subcutaneously [78]. Thus, normal relaxation of the striated urethral sphincter is probably mediated via GABA$_A$ receptors [73], with GABA$_B$ receptors having a minor influence on motoneuron excitability [80].

Gabapentin

Gabapentin was originally designed as an anticonvulsant GABA mimetic capable of crossing the blood–brain barrier [81]. However, its effects do not appear to be mediated through interaction with GABA receptors, and its mechanism of action is still controversial [81]. Gabapentin is also widely used not only for seizures and neuropathic pain, but for many other indications such as anxiety and sleep disorders due to its apparent lack of toxicity.

In a pilot study, Carbone et al. [82] reported on the effect of gabapentin on neurogenic detrusor activity. They found a positive effect on symptoms and a significant improvement of urodynamic parameters after treatment and suggested that the effects of the drug should be explored in further controlled studies in both neurogenic and nonneurogenic DO. Kim et al. [83] found that fourteen of 31 patients with (OAB) and nocturia, refractory to antimuscarinic treatment, improved with oral gabapentin. The drug was generally well tolerated and was considered to be an option in selective patients when conventional treatment modalities have failed. Ansari et al. [84] treated children with refractory OAB symptoms (not responding to conventional antimuscarinics) with gabapentin as an add-on and found the drug to give modest positive results. The drug was well tolerated with few adverse effects.

NORADRENALINE AND A-ADRENOCEPTORS

Noradrenergic neurons in the brain stem project to the sympathetic, parasympathetic, and somatic nuclei in the lumbosacral spinal cord. Bladder activation through these bulbospinal noradrenergic pathways may involve excitatory α_1-ARs. In rats undergoing continuous cystometry, doxazosin, given i.t., decreased micturition pressure, both in normal rats and in animals with postobstruction bladder hypertrophy [85]. The effect was much more pronounced in the animals with hypertrophies/OABs. Doxazosin given i.t., but not intra-arterially, to spontaneously hypertensive rats exhibiting bladder overactivity, normalized bladder activity [86]. It was suggested that doxazosin has a site of action at the level of the spinal cord and ganglia. However, there are no RCTs documenting positive effects of α-AR antagonists in OAB/DO [4,68].

NK1-RECEPTOR ANTAGONISTS

The main endogenous tachykinins, substance P (SP), neurokinin (NK) A, and NKB, and their preferred receptors, NK1, NK2, and NK3, respectively, have been demonstrated in various CNS regions, including those involved in micturition control [87–89]. NK1 receptor expressing neurons in the dorsal horn of the spinal cord may play an important role in DO, and tachykinin involvement via NK1 receptors in the micturition reflex induced by bladder filling has been demonstrated [90] in normal and, more clearly, rats with bladder hypertrophy secondary to bladder outlet obstruction (BOO). Capsaicin-induced DO was reduced by blocking NK1 receptor–expressing neurons in the spinal cord, using i.t. administered SP–saponin conjugate [91]. Furthermore, blockade of spinal NK1 receptor could suppress detrusor activity induced by dopamine receptor (L-DOPA) stimulation [92].

In conscious rats undergoing continuous cystometry, antagonists of both NK1 and NK2 receptors inhibited micturition, decreasing micturition pressure and increasing bladder capacity at low doses and inducing dribbling incontinence at high doses. This was the most conspicuous in animals with outflow obstruction [93]. Intracerebroventricular administration of NK1- and NK2-receptor antagonists to awake rats' suppressed detrusor activity induced by dopamine receptor (L-DOPA) stimulation [94]. Taken together, available information suggests that spinal and supraspinal NK1 and NK2 receptors may be involved in micturition control.

Aprepitant, an NK1-receptor antagonist used for treatment of chemotherapy-induced nausea and vomiting [95], significantly improved symptoms of OAB in postmenopausal women with a history of urgency incontinence or mixed incontinence (with predominantly urgency UI), as shown in a well-designed pilot RCT [96]. The primary end point was percent change from baseline in average daily micturitions assessed by a voiding diary. Secondary end points included average daily total UI and urgency incontinence episodes and urgency episodes. Aprepitant significantly decreased the average daily number of micturitions compared with placebo at 8 weeks. The average daily number of urgency episodes was also significantly reduced compared to placebo and so were the average daily number of urgency incontinence and total UI episodes, although the difference was not statistically significant. Aprepitant was generally well tolerated and the incidence of side effects, including dry mouth, was low. The results of this initial proof of concept study suggest that NK1-receptor antagonism holds promise as a potential treatment approach for OAB. In another RCT including 476 patients with OAB, the effects of the selective NK1-receptor antagonist, serlopitant (several doses), were compared with those of tolterodine ER 4 mg [97]. Tolterodine was numerically superior to all doses of serlopitant in mean micturitions per day and secondary end points (urgency, total incontinence, urge incontinence episodes, and incidence of dry mouth), and the authors concluded that even NK1-receptor antagonists may have a role in the treatment of OAB, but serlopitant did not offer advantages in efficacy compared to tolterodine. In a phase II RCT, Haab et al. [98] assessed the efficacy and safety of the NK1-receptor antagonist, netupitant, in patients with OAB. The study failed to demonstrate superiority of netupitant versus placebo in decreasing OAB symptoms.

It seems as even if NK1-receptor antagonists may have a beneficial effect on OAB symptoms, none of the drugs tested have shown any efficacy advantages over standard therapy with antimuscarinics.

DOPAMINE AND DOPAMINE RECEPTORS

Many patients with Parkinson’s disease have neurogenic DO and other functional disturbances of detrusor function [99–101], possibly as a consequence of nigrostriatal dopamine depletion and failure to activate inhibitory D1 receptors [101,102]. Sillén et al. [103] showed that apomorphine, which activates both D1 and D2 receptors, induced bladder overactivity in anesthetized rats via stimulation of central dopaminergic receptors. The effects were abolished by infracollicular transection of the brain and by prior intraperitoneal administration of the centrally acting dopamine receptor blocker, spiroperidol. Kontani et al. [104,105] suggested that the bladder overactivity induced by apomorphine in anesthetized rats resulted from synchronous stimulation of the micturition centers in the brain stem and spinal cord and that the response was elicited by stimulation of both dopamine D1 and D2 receptors. Kitta et al. [106] tried to elucidate the role of extracellular dopamine, glutamate, and GABA by in vivo microdialysis in the PAG during cystometry, as well as to evaluate the dopaminergic system’s role in the micturition reflex of an animal model of Parkinson’s disease. Based on their results, they suggested that the micturition reflex is under tonic dopaminergic regulation through D1 receptors, in which a GABAergic mechanism is involved, and that the bladder overactivity observed in 6-OHDA-lesioned rats may be caused by dysfunction of GABAergic regulation underlying the micturition reflex.

The effect of dopaminergic drugs on micturition has produced conflicting results [101], and Winge et al. [107] found that the effect on micturition of treatment with dopaminergic drugs in Parkinson’s disease was unpredictable. Studies have shown that in early phases of Parkinson’s disease, a single dose of levodopa exacerbates DO [108]. In contrast, in advanced stages of the disease, the drug improved bladder storage function [109].

The effects on micturition of various dopamine receptor active drugs used for, e.g., different psychiatric conditions, should not be neglected.

Peripheral Targets

Possible peripheral targets for pharmacological intervention may be (1) the efferent neurotransmission, (2) the smooth muscle itself, including ion channels and intracellular second messenger systems, and (3) the afferent neurotransmission. Although many effective drugs are available for these target systems, most of them are less useful in the clinical situation due to the lack of selectivity for the LUT, which may result in intolerable side effects. Thus, a main task is to find systems or receptors, more or less specific for the LUT, which can be manipulated without disturbing other systems in the body, or alternatively, to design drugs in a way that results in higher tissue concentrations in the LUT than elsewhere in the body.

MUSCARINIC RECEPTORS

Muscarinic receptors comprise five subtypes, encoded by five distinct genes [110]. The five gene products correspond to pharmacologically defined receptors, and M_1–M_5 is used to describe both the molecular and pharmacological subtypes. In the human bladder, the mRNAs for all muscarinic receptor subtypes have been demonstrated [111,112], with a predominance of mRNAs encoding M_2 and M_3 receptors [111,113]. These receptors are also functionally coupled to G-proteins, but the signal transduction systems vary [114–119].

Detrusor smooth muscle contains muscarinic receptors of mainly the M_2 and M_3 subtypes [114–119]. The M_3 receptors in the human bladder are believed to be the most important for detrusor contraction. Jezior et al. [120] suggested that muscarinic receptor activation of detrusor muscle includes both nonselective cation channels and activation of Rhokinase. Supporting a role of Rho-kinase in the regulation of rat detrusor contraction and tone, Wibberley et al. [121] found that Rho-kinase inhibitors (Y-27632, HA 1077) inhibited contractions evoked by carbachol without affecting the contraction response to KCl. They also demonstrated high levels of Rho-kinase isoforms (I and II) in the bladder. Schneider et al. [119] concluded that carbachol-induced contraction of human urinary bladder is mediated via M_3 receptors and largely depends on Ca^{2+} entry through nifedipine-sensitive channels and activation of the Rho-kinase pathway. Thus, the main pathway for muscarinic receptor activation of the detrusor via M_3 receptors may be calcium influx via L-type calcium channels and increased sensitivity to calcium of the contractile machinery produced via inhibition of myosin light chain phosphatase through activation of Rho-kinase [122].

The functional role for the M_2 receptors has not been clarified, but it has been suggested that M_2 receptors may oppose sympathetically mediated smooth muscle relaxation, mediated by β-ARs [123]. M_2 receptor stimulation may also activate nonspecific cation channels [124] and inhibit ATP-sensitive K^+ (K_{ATP}) channels through activation of protein kinase C [125,126]. In certain disease states, M_2 receptors may contribute to contraction of the bladder. Thus, in the denervated rat bladder, M_2 receptors or a combination of M_2- and M_3-mediated contractile responses and the two types of receptor seemed to act in a facilitatory manner to mediate contraction [127–129]. In obstructed, hypertrophied rat bladders, there was an increase in total and M_2 receptor density, whereas there was a reduction in M_3 receptor density [130]. The functional significance of this change for voiding function has not been established. Pontari et al. [131] analyzed bladder muscle specimens from patients with neurogenic bladder dysfunction to determine whether the muscarinic receptor subtype mediating contraction shifts from M_3 to the M_2 receptor subtype, as found in the denervated, hypertrophied rat bladder. They concluded that whereas normal detrusor contractions are mediated by the M_3 receptor subtype, in patients with neurogenic bladder dysfunction, contractions can be mediated by the M_2 receptors.

Muscarinic receptors may also be located on the presynaptic nerve terminals and participate in the regulation of transmitter release. The inhibitory prejunctional muscarinic receptors have been classified as M_4 in the human bladder [132]. Prejunctional facilitatory muscarinic receptors appear to be of the M_1 [133]. The muscarinic facilitatory mechanism seems to be upregulated in hyperactive bladders from chronic spinal cord–transected rats. The facilitation in these preparations is primarily mediated by M_3 muscarinic receptors [133,134].

Muscarinic receptors have also been demonstrated on the urothelium/suburothelium. The porcine urothelium was found to express a high density of muscarinic receptors, even higher than the bladder smooth muscle [135], and, in the rat and human urothelium, the receptor proteins and mRNAs, respectively, for all muscarinic receptor subtypes (M_1–M_5), were demonstrated [136]. Mansfield et al. [137] found, using RT-PCR analysis, an abundant expression of muscarinic M_2 receptors in the human bladder mucosa. These receptors may occur at other locations than the urothelium, e.g., on suburothelial interstitial cells [138,139].

The suburothelial nerve plexus is close to the urothelium [140–142]. The urothelium, as mentioned previously, has been suggested to work as a mechanosensory conductor, and in response to, e.g., distension, it releases ATP affecting underlying afferent nerve fibers via purinoceptors [143,144]. This may consequently modify the afferent response of the bladder [145,146]. ACh is produced in the urothelium, but the mechanism behind its release does not seem to involve vesicular exocytosis [147,148]. The organic cation transporter 3 subtype has been demonstrated in and suggested to be involved in the nonneuronal release from rat urothelium [148].

ADRENERGIC RECEPTORS

α-Adrenoceptors

α-ARs may have effects on different locations in the bladder: the detrusor smooth muscle, the detrusor vasculature, the afferent and efferent nerve terminal and intramural ganglia. For some of these possible sites, only fragmentary information is available. Most investigators agree on that there is a low expression of these receptors in the detrusor muscle [149–152]. In the human bladder studies, Malloy et al. [149] found that 2/3 of the α-AR mRNA expressed was α_{1D}, there was no α_{1B}, and 1/3 was α_{1A}.

Nomiya and Yamaguchi [153] confirmed the low expression of α-AR mRNA in normal human bladder and further demonstrated that there was no upregulation of any of the adrenergic receptors with obstruction. In addition, in functional experiments, they found a small response to phenylephrine at high drug concentrations with no difference between normal and obstructed bladders. Thus, in the obstructed human bladder, there seemed to be no evidence for α-AR upregulation. This finding was challenged by Bouchelouche et al. [154] who found an increased response to α_1-AR stimulation in obstructed human bladders. If there is a change of sensitivity to α-AR stimulation in the obstructed bladder of clinical importance (influencing the response to α-AR blockers) remains to be established.

All subtypes of α-ARs can be found in different parts of the human vascular tree, and they all mediate contraction. The expression varies with vessel bed and increases with age. In the bladder, the function of the detrusor muscle is dependent on the vasculature and the perfusion. Hypoxia induced by partial outlet obstruction is believed to play a major role in both the hypertrophic and degenerative effects of partial outlet obstruction. Das et al. [155] investigated in rats whether doxazosin affected blood flow to the bladder and reduced the level of bladder dysfunction induced by partial outlet obstruction. They found that 4 weeks treatment with doxazosin increased bladder blood flow in both controlled and obstructed rats. Furthermore, doxazosin treatment reduced the severity of the detrusor response to partial outlet obstruction. Thus, doxazosin could reduce the increase in bladder weight in obstructed animals, which could be one of the mechanisms that contributed to a positive effect on DO caused by the obstruction.

It is well documented that α_1-AR antagonists can ameliorate LUTS in men [68,156,157]. Currently used α_1-AR antagonists are considered effective for treatment of both storage and voiding symptoms in men with LUTS associated with or suggestive of BPH [157]. However, in a study where tamsulosin was given alone, or together with tolterodine, to male patients with LUTS and OAB symptoms, monotherapy with the drug was not effective [158].

In females, treatment with OAB, α_1-AR antagonists seem to be ineffective. In an RCT, comprising 364 women with OAB, no effect of tamsulosin vs. placebo could be demonstrated [159]. On the other hand, voiding symptoms in women with functional outflow obstruction, or LUTS, were treated (with modest success) with an α_1-AR antagonist [160,161]. It should be remembered that in women these drugs may produce stress incontinence [162].

In patients with neurogenic DO, treatment with α_1-AR antagonists was moderately successful [163].

β-Adrenoceptors

It has been known for a long time that isoprenaline, a nonsubtype selective β-AR agonist, can relax the bladder smooth muscle [18]. Even if the importance of β-ARs for human bladder function still remains to be established [164], this does not exclude that they can be useful therapeutic targets. All three subtypes of β-ARs (β_1, β_2, and β_3) can be found in the detrusor muscle of most species, including humans [150,164] and also in the human urothelium [165]. However, the expression of β_3-AR mRNA [150,153] and functional evidence indicate a predominant role for this receptor in both normal and neurogenic bladders [150,166,167]. The human detrusor also contains β_2-ARs, and most probably, both receptors are involved in the physiological effects (relaxation) of noradrenaline in the bladder [150,164]. β_3-AR agonists have a pronounced effect on spontaneous contractions of isolated detrusor muscle [168], which may be the basis for their therapeutic effects in OAB/DO.

It is generally accepted that β-AR-induced detrusor relaxation is mediated by activation of adenylyl cyclase with the subsequent formation of cAMP [169]. However, there is evidence suggesting that in the bladder K^+ channels, particularly calcium-activated K^+ (BK_{ca}) channels, may be involved in β-AR-mediated relaxation independent of cAMP [170–173].

The in vivo effects of β_3-AR agonists on bladder function have been studied in several animal models. It has been shown that β_3-AR agonists increase bladder capacity with no change in micturition pressure and residual volume [174–177]. For example, Hicks et al. [178] studied the effects of the selective β_3-AR agonist, GW427353, in the anesthetized dog and found that the drug evoked an increase in bladder capacity under conditions of acid-evoked bladder hyperactivity, without affecting voiding. Aizawa et al. [179] showed that another selective β_3-AR agonist, mirabegron, could inhibit filling-induced activity in both mechanosensitive Aδ- and C-fiber primary bladder afferents of the rat bladder.

Mirabegron is the only β_3-AR selective agonist approved for treatment of OAB. Several pharmaceutical companies are developing β_3-AR selective agonists for treatment of this disorder [180,181]; however, so far, mirabegron is the only β_3-AR selective agonist approved for treatment of OAB.

Pharmacokinetics

Mirabegron is rapidly absorbed after oral administration, and maximum plasma concentration (T_{max}) is reached in about 2 hours [182,183]. The terminal elimination half-life ($t_1/2$) is approximately 23–25 hours. The drug circulates in the plasma as the unchanged active form and inactive metabolites. Most of an administered dose is excreted in urine, mainly as the unchanged form, and one-third is recovered in feces, almost entirely as the unchanged form [184]. Mirabegron is highly lipophilic and is metabolized in the liver via multiple pathways, mainly by cytochrome (CY) P450, CYP3A4, and CYP2D6 [185–187].

Mechanism(s) of Action

Filling of the bladder initiates activity in “in-series”-coupled, low-threshold mechanoreceptive (Aδ) afferents [188]. This implies that, if the compliance of the bladder is increased, the response to distension is decreased and, to recruit sufficient afferent activity needed to initiate micturition, greater filling volumes are needed—thus, bladder capacity increases. One determinant of bladder compliance is the spontaneous (autonomous) bladder activity during filling. Experimental studies of human [168,189,190], rat [191–193], and monkey [194] bladder have documented inhibitory effects of β3-AR agonists on autonomous activity in vitro and on “nonvoiding contractions” in vivo. Mirabegron inhibited only nonvoiding activity in rat, while tolterodine (antimuscarinic) inhibited nonvoiding activity as well as the amplitude of voiding contractions [191]. Since the voiding contraction is caused by a massive release of contractant transmitters (ACh and ATP), this may be the reason why bladder emptying does not seem to be impaired by β_3-AR agonists [195].

Clinical Use

Efficacy: Mirabegron has been evaluated in three pivotal phases, 12-week RCTs in patients with OAB symptoms of urgency UI, urgency, and urinary frequency [196–198]. These trials showed the drug to be effective and very well tolerated. In a urodynamic safety study on 200 male patients with BOO and LUTS, the effects of mirabegron 50 or 100 mg once daily for 12 weeks have been reported [199]. Mirabegron did not adversely affect flow rate, detrusor pressure at maximum flow rate, or bladder contractile index and was well tolerated.

The safety and efficacy of long-term administration of mirabegron 50 and 100 mg was compared to that of tolterodine in a 12-month, 3-armed, parallel group study (no placebo arm). A total of 812 (50 mg) and 820 (100 mg) patients were randomized to receive mirabegron, and 812 patients received tolterodine ER 4 mg. The primary variable was incidence and severity of treatment-emergent adverse effects, and secondary variables were change from baseline at months 1, 3, 6, 9, and 12 in key OAB symptoms. Both mirabegron and tolterodine improved key OAB symptoms from the first measured time point of 4 weeks, and efficacy was maintained throughout the 12-month treatment period [200].

Tolerability and Adverse Effects

In the clinical studies performed, the tolerability of mirabegron has been good as well as the adverse effect close to those of placebo [201]. For example, in the study of Khullar et al. [197], the incidence of adverse effects for the placebo and mirabegron 50 and 100 mg groups were 50.1%, 51.6%, and 46.9%, respectively. The most common (≥3%) adverse effects in any treatment group were hypertension (6.6%, 6.1%, and 4.9%, respectively), urinary tract infection (1.8%, 2.7%, and 3.7%), headache (2.0%, 3.2%, and 3.0%), and nasopharyngitis (2.9%, 3.4%, and 2.5%). The incidence of dry mouth was similar in the placebo and mirabegron groups (2.6% vs. 2.8%) and lower than observed in patients receiving tolterodine SR (10.1%). The incidence of constipation was similar in all treatment groups (placebo 1.4%, mirabegron 1.6%), including tolterodine (2.0%).

One concern with the use of β_3-AR agonists has been the possibility of negative cardiovascular effects. However, in the studies on OAB, patients referred to the mean increases (compared to placebo) in systolic/diastolic blood pressure after therapeutic doses of mirabegron once daily, which was approximately 0.5–1 mmHg and reversible upon discontinuation of treatment. In a study on healthy volunteers, mirabegron increased *heart rate* (HR) in a dose-dependent manner. Maximum mean increases in HR from baseline for the 50, 100, and 200 mg dose groups compared to placebo were 6.7 beats per minute (bpm), 11 bpm, and 17 bpm, respectively, in healthy volunteers [202]. However, in the clinical efficacy and safety studies, the change from baseline in mean pulse rate for mirabegron 50 mg was approximately 1 bpm and reversible upon discontinuation of treatment.

The cardiac safety of mirabegron was evaluated in a thorough QT/QTc (HR-corrected QT interval) study, including supratherapeutic dose. This was a randomized, placebo-, and active-controlled (moxifloxacin 400 mg), four-treatment-arm, parallel crossover study in 352 healthy subjects [202]. The effect of multiple doses of mirabegron 50, 100, and 200 mg once daily on QTc interval was studied; mirabegron did not cause QTcI prolongation at the 50 mg therapeutic and 100 mg supratherapeutic doses in either sex. The drug prolonged QTcI interval at the 200 mg supratherapeutic dose (upper one-sided 95% CI >10 ms) in females, but not in males.

Even if the cardiovascular effects of mirabegron observed in clinical studies have been minimal and clinically not relevant, effects on heart rate and blood pressure need to be monitored when the drug is generally prescribed and patients with cardiovascular morbidities are treated.

A combination of an antimuscarinic and mirabegron (or other β_3-AR agonists) seems rationale and theoretically attractive. Abrams et al. [203] evaluated the efficacy of combinations of solifenacin/mirabegron compared with solifenacin 5 mg monotherapy in a phase II, factorial design, randomized, double-blind, parallel-group, and placebo- and monotherapy-controlled trial including 1306 male and female (66.4%) patients with OAB aged ≥ 18 years. They were randomized to 12 weeks of treatment in 1 of 12 groups: 6 combination groups (solifenacin 2.5, 5, or 10 mg plus mirabegron 25 or 50 mg), 5 monotherapy groups (solifenacin 2.5, 5, or 10 mg or mirabegron 25 or 50 mg), or placebo. It was found that compared with solifenacin 5 mg monotherapy, all combinations with solifenacin 5 or 10 mg significantly improved mean volume voided per micturition (the primary end point), micturition frequency, and urgency. All combinations were well tolerated, with no important additional safety findings compared with monotherapy or placebo.

PHOSPHODIESTERASE INHIBITORS

Drugs stimulating the generation of cAMP are known to relax smooth muscles, including the detrusor [164,169]. It is also well established that drugs acting through the NO/cGMP system can relax the smooth muscle of the bladder outflow region [164]. Use of phosphodiesterase (PDE) inhibitors to enhance the presumed cAMP- and cGMP-mediated relaxation of LUT smooth muscles (detrusor prostate, urethra) should then be a logical approach [204]. There are presently 11 families of PDEs, some of which preferentially hydrolyze either cAMP or cGMP [204].

As a basis for PDE inhibitor treatment of LUTS, Uckert et al. [205] investigated human bladder tissue, revealing messenger RNA for PDEs 1A, 1B, 2A, 4A, 4B, 5A, 7A, 8A, and 9A; most of these PDEs preferably inhibit the breakdown of cAMP. In vitro, human detrusor muscle responded poorly to sodium nitroprusside and to agents acting via the cGMP system [206]. However, significant relaxation of human detrusor muscle, paralleled by increases in cyclic nucleotide levels, was induced by papaverine, vinpocetine (a low affinity inhibitor of PDE 1), and forskolin (stimulating the generation of cAMP), suggesting that the cAMP pathway and PDE 1 may be important in regulation of detrusor smooth muscle tone [207]. Significant dose-dependent relaxations were also induced by human cAMP analogs [207]. With these studies as a background, Truss et al. [206] presented preliminary clinical data with vinpocetine in patients with urgency/urgency incontinence or low compliance bladders and not responding to standard antimuscarinic therapy. This initial open pilot study suggested a possible role for vinpocetine in the treatment of OAB. However, the results of a larger RCT in patients with DO showed that vinpocetine only showed statistically significant results for one parameter [207]. Studies with other PDE 1 inhibitors than vinpocetine (which may not be an optimal drug for elucidation the principle) do not seem to have been performed.

PDE 4 (which also preferably hydrolyzes cAMP) has been implicated in the control of bladder smooth muscle tone. PDE 4 inhibitors reduced the in vitro contractile response of guinea pig [208] and rat [209,210] bladder strips and also suppressed rhythmic bladder contractions of the isolated guinea pig bladder [211]. Previous experiences with selective PDE 4 inhibitors showed emesis to be a dose-limiting effect [212]. If this side action can be avoided, PDE 4 inhibition seems to be a promising approach.

NO has been demonstrated to be an important inhibitory neurotransmitter in the smooth muscle of the urethra and its relaxant effect is associated with increased levels of cyclic GMP [1]. However, few investigations have addressed the cAMP- and cGMP-mediated signal transduction pathways and its key enzymes in the mammalian urethra. Morita et al. [213] examined the effects of isoproterenol, prostaglandin E_1 and E_2, and SNP on the contractile force and tissue content of cAMP and cGMP in the rabbit urethra. They concluded that both cyclic nucleotides can produce relaxation of the urethra. Werkström et al. [214] characterized the distribution of PDE 5, cGMP, and PKG1 in female pig and human urethra and evaluated the effect of pharmacological inhibition of PDE 5 in isolated smooth muscle preparations. After stimulation with the NO donor, DETA NONOate, the cGMP-immunoreactivity (IR) in urethral and vascular smooth muscles increased. There was a wide distribution of cGMP- and vimentin-positive interstitial cells between pig urethral smooth muscle bundles. PDE 5 IR could be demonstrated not only within the urethral and vascular smooth muscle cells but also in vascular endothelial cells that expressed cGMP-IR. Nerve-induced relaxations of urethral preparations were enhanced at low concentrations of sildenafil, vardenafil, and tadalafil, whereas there were direct smooth muscle relaxant actions of the PDE 5 inhibitors at high concentrations.

The observation that patients treated for erectile dysfunction with PDE 5 inhibitors had an improvement of their LUTS has sparked a new interest in using these drugs also for treatment of LUTS and OAB. After the report in an open study [215] that treatment with sildenafil appeared to improve urinary symptom scores in men with ED and LUTS, this observation has been confirmed in several well-designed and conducted RCTs [216–218].

The effects of PDE 5 inhibitors for treatment of male LUTS have been well summarized in several previous reviews [219,220].

The mechanism of action of tadalafil in relieving LUTS has not been established, even if improvement of the bladder blood flow to the LUT has been suggested [221,222]. In an RCT, Pinggera et al. [223], using transrectal ultrasonography, compared the effects of tadalafil 5 mg/day and placebo given for 8 weeks to men with moderate to severe LUTS/BPH. They found no differences between the treatments but did not exclude that changes in blood flow may have occurred, which for several reasons could not be detected. Interestingly, previously, Pinggera et al. [224], using transrectal color Doppler ultrasound, quite convincingly showed that tamsulosin could increase perfusion to the LUT.

ION CHANNELS

Ion channels are important regulators of the cell function. Located within the plasma membrane, they control the permeability of different ions. The two most thoroughly investigated classes of ion channels are calcium channels and potassium channels [164].

Calcium Channels

Calcium is a key component for cell function in many cells. In smooth muscle, increased intracellular calcium concentrations activate the contractile mechanisms, and in nerve terminals, calcium influx in response to action potentials is an important mechanism for neurotransmitter release. Calcium channels can be divided into at least four different subtypes: L, N, P, and Q channels. The calcium channels present in smooth muscles are L-type (dihydropyridine sensitive) calcium channels and seem to be involved in contraction of the human bladder irrespective of the mode of activation [225]. A decrease of the membrane potential (depolarization) increases the open probability for calcium channels, thereby increasing the calcium influx. Thus, the channels are dependent on the membrane potential and are termed voltage-operated calcium channels (VOCC). Elevated intracellular calcium levels are also believed to initiate release of calcium from intracellular stores, a mechanism called calcium-induced calcium release [226,227]. Thus, regulation of the intracellular calcium concentration in smooth muscle cells is one conceivable way to modulate bladder contraction. Dihydropyridines, e.g., nifedipine, have a potent inhibitory effect on isolated detrusor muscle. Inhibitory effects have also been demonstrated on experimentally induced contractions under in vivo conditions in rats and clinically in patients with DO [18]. However, therapeutically, there is no evidence that calcium antagonists have any useful effects in the treatment of OAB/DO [4,68].

Potassium Channels

Potassium channels represent another mechanism to modulate the excitability of the smooth muscle cells. Under normal conditions, the resting membrane potential in smooth muscle cells is determined predominantly by the membrane conductivity for potassium ions. Increased potassium conductivity will lower the membrane potential by increasing the potassium efflux. As a consequence, this will increase the threshold for opening of VOCC and initiation of contraction. There are several different types of K^+ channels, and at least two subtypes have been found in the human detrusor, K_{ATP} and large conductance BK_{Ca}. Studies on the isolated human detrusor muscle and on the bladder tissue from several animal species have demonstrated that K^+-channel openers reduce spontaneous contractions as well as contractions induced by carbachol and electrical stimulation [164]. However, the lack of selectivity of presently available K^+-channel blockers for the bladder versus the vasculature has thus far limited the use of these drugs. No effects of cromakalim or pinacidil on the bladder were found in studies on patients with spinal cord lesions or detrusor instability secondary to outflow obstruction [228,229]. Some new K^+-channel openers have been developed and claimed to have selectivity toward the bladder [164]. However, so far there is no evidence that K^+-channel openers is an option for treatment of OAB/DO [4,68].

AFFERENT SIGNALING MECHANISMS

Urothelium

Recent evidence suggests that the urothelium may serve as a mechanosensor, which, by producing NO, ATP, ACh, and other mediators, can control the activity in afferent nerves and thereby the initiation of the micturition reflex [230–232]. Low pH, high K^+, increased osmolality, and low temperatures can all influence afferent nerves, possibly via effects on the "vanilloid" (TRPV1) receptor, which is expressed both in afferent nerve terminals and in the epithelial cells that line the bladder lumen [233,234]. A network of interstitial cells (interstitial cells of Cajal [ICCs]), extensively linked by Cx43-containing gap junctions, was found to be located beneath the urothelium in the human bladder [235,236]. This interstitial cellular network was suggested to operate as a functional syncytium, integrating signals and responses in the bladder wall. The firing of suburothelial afferent nerves and the threshold for bladder activation may be modified by both inhibitory (e.g., NO) and stimulatory (e.g., ATP, ACh, tachykinins, prostanoids) mediators. ATP, generated by the urothelium, has been suggested as an important mediator of urothelial signaling [230,231]. Supporting such a view, intravesical ATP induces DO in conscious rats [237]. Furthermore, mice lacking the $P2X_3$ receptor were shown to have hypoactive bladders [144,238].

There seem to be other, thus far unidentified, factors in the urothelium that could influence bladder function [1]. Fovaeus et al. [239] found a previously unrecognized nonadrenergic, nonnitrergic, nonprostanoid inhibitory mediator is released from the rat urinary bladder by muscarinic receptor stimulation. However, it was not clear whether this factor came from the detrusor muscle or from both the bladder and the urothelium. Data have been presented suggesting the presence of a diffusible, urothelium-derived inhibitory factor, which could not be identified, but appeared to be neither nitric oxide, a cyclooxygenase product, a catecholamine, adenosine, GABA nor any substance sensitive to apamin. The identity and possible physiological role of the unknown factor remains to be established and should offer an interesting field for further research [135,240]. This mechanism can be involved in the pathophysiology of the OAB syndrome and DO and thus seem to be interesting targets for pharmacological intervention.

Myocytes

Myogenic activity can be defined as the ability of a smooth muscle cell to generate mechanical activity independent of external stimuli [164,241]. In the individual myocyte, contractile activity is preceded and initiated by an action potential, which is calcium driven [242]. It has been suggested that the detrusor muscle is arranged into units (modules), which are circumscribed areas of the muscle [243]. These modules show contractile activity during the filling phase of the micturition cycle and might be controlled by several factors including a peripheral myovesical plexus, consisting of intramural ganglia and ICC [244,245]. Intercellular connections may contribute to not only module control but also locally generated mediators. Kinder and Mundy [246] found that spontaneous contractile activity developed more often in muscle strips from overactive than normal bladders, a finding underlined by Brading [247] and confirmed by Mills et al. [248]. Turner and Brading [249] discussed the occurrence of "patchy denervation" in cases of DO with subsequent changes of the smooth muscle cells, e.g., supersensitivity to ACh. Such an increased sensitivity has been demonstrated in smooth muscle preparations from patients with idiopathic and neurogenic DO [250]. It has been reported that suburothelial ICC respond to purinergic stimulation by firing Ca^{2+} transients [251]. Interestingly, these suburothelial ICC may be able to affect the activity of the detrusor myocytes [252–254]. The frequency of the spontaneous rhythmic contractions of isolated detrusor smooth muscle preparations seems to vary between species and is probably also dependent on experimental factors [164,244]. Characteristically, these contractions are resistant to the Na-channel blocker (TTX) and cannot be blocked by hexamethonium, atropine, α-AR blockers, β-AR blockers, or suramin, apparently excluding direct involvement of nerves and nerve-released transmitters [164]. Contractions can be effectively inhibited by L-type Ca^{2+}-channel blockers and K^+-channel openers, supporting the important role of L-type Ca^{2+} channels for the activity. It cannot be excluded that these spontaneous contractions generate part of the afferent activity ("afferent noise") during filling of the bladder [255].

SENSORY NERVES AND VANILLOID RECEPTORS

Intravesical administration of capsaicin or resiniferatoxin (RTX) has been shown to increase bladder capacity and decrease urge incontinence in patients with neurogenic, as well as nonneurogenic forms of DO [4,68,256]. Vanilloids are exogenous ligands of vanilloid receptor type 1 (TRPV1 or VR1), an ion channel present in the membrane of type C primary afferent nerve fibers innervating the bladder wall and the periurethral zone of the prostate gland [257]. This receptor, which plays a key role in inflammatory pain perception and control of the micturition reflex [257,258], may be upregulated by nerve growth factor (NGF), a neurotrophic molecule detected in high concentrations in overactive detrusors generated by chronic BOO [259]. Vanilloids, by reducing uptake of NGF through sensory neurons, may counteract TRPV1 upregulation. In addition, vanilloids decrease the response of already expressed TRPV1 receptors (desensitization) [258].

Important sensory information from the prostate and bladder is conveyed by C-fibers. Local anesthesia of the prostatic urethra was shown to increase bladder volume to first sensation to urinate and maximal bladder capacity and also to reduce or abolish DO, in patients with benign prostatic enlargement [260]. Likewise, intravesical lidocaine was shown to reduce involuntary detrusor contractions in patients with DO [261]. Lidocaine is more effective to anesthetize C- than Aδ-fibers supporting the contribution of prostate and bladder C-fiber input to abnormal detrusor activity.

The ice water test triggers a capsaicin-sensitive spinal micturition reflex mediated by unmyelinated C-fibers in the bladder and urethra [262]. Chai et al. [263] demonstrated a positive ice water test in 71% of subjects with BOO (12 of 17), which was significantly higher than the 7% positive ice water test rate in nonobstructed subjects (3 of 44). The authors suggested this to be caused by an enhanced spinal micturition reflex, possibly due to plasticity of bladder afferents after BOO. If this is the case, intravesical treatment of patients with LUTS associated with BOO with intravesical vanilloids, by desensitizing C-fibers, would be an interesting approach. Two preliminary studies with intravesical RTX suggested that this may be the case [264,265]. In a controlled study on neurogenic DO, Silva et al. [266] concluded that the drug was effective for treatment of this disorder. Several other studies have arrived at divergent results, some claiming good effects and others not demonstrating any superiority of RTX over placebo [4,68].

Despite some evidence of efficacy in LUTS/OAB/DO, capsaicin and RTX are no longer widely used [4,68]. Side effects (pain) and the lack of stable RTX preparations, available for easy bladder instillation, will make further investigation of the compound difficult. Different origins of the vanilloid and different ways for preparation and storage of the solutions might have caused substantial differences in the amount of active compound effectively administered to the patients. In addition, RTX adheres to plastics, another reason to the discrepancies that have been observed among RTX studies.

BOTULINUM TOXIN

Botulinum toxin (BoNT) is a neurotoxin produced by *Clostridium botulinum*. BoNT comprises seven subtypes, of which subtype A (BoNT-A), which has the longest duration of action, is clinically the most important. BoNT-A is available in three different commercial forms: onabotulinumtoxinA, abobotulinumtoxinA, and incobotulinumtoxinA. Although there are differences in potency between the forms, there are no reasons to believe that their basic mechanism of action is different. The potency of each one is usually expressed in units (U); however, the doses are not interchangeable. Unfortunately, clinical dose conversion studies for the LUT are not available. Most of the intravesical experience reported on BoNT-A deals with Botox®.

BoNT consists of a heavy and a light chain linked by a disulphide bond. In the synaptic cleft, the toxin binds to synaptic vesicle protein [267] through its heavy chain and is internalized by the nerve terminal. Upon cleavage, the light chain is released in the cytosol, where it impedes binding of neurotransmitter-containing synaptic vesicles to the plasma membrane. The rationale for using botulinum toxin to treat human DO is based on the assumption that effects of the toxin on skeletal muscle would be replicated in bladder smooth muscle [268,269] and that detrusor muscle paralysis would reduce the symptoms of bladder overactivity [270]. BoNT has been currently developed as a second-line treatment option (following failure of, or intolerance to, appropriate antimuscarinic therapy) for patients with NDO with UI or other neurogenic OAB symptoms and who are able and willing to perform CIC. Efficacy has also been demonstrated in spinal cord injury patients with detrusor-sphincter dyssynergia [270–273].

The first report of the application of BoNT-A in NDO appeared in 2000 [268]. Since then, several RCTs have documented the clinical effects of onabotulinumtoxinA in neurogenic and idiopathic DO, where the drug decreases incontinence episodes, frequency, and urgency and improves quality of life [274–277]. The drug was also shown to be effective in patients with idiopathic OAB [278]. Successful treatment of OAB symptoms with BoNT-A does not appear to be related to the existence of DO. No differences in outcomes were found between those with and those without baseline DO [279,280].

Nitti et al. [278] reported results of the first large (n = 557) phase III placebo-controlled trial of onabotulinumtoxinA in patients with OAB. To be included, patients should have ≥3 urgency UI episodes in 3 days and ≥8 micturitions/day. They were randomized 1:1 to receive intradetrusor injection of onabotulinumtoxinA 100U or placebo (saline). Coprimary end points were changed from baseline in UI episodes/day and proportion of patients with a positive response on the treatment benefit scale at week 12 posttreatment. Secondary end points included other OAB symptoms and health-related quality of life. OnabotulinumtoxinA significantly reduced the daily frequency of UI episodes versus placebo (−2.65 vs. −0.87, $p < 0.001$) and 22.9% vs. 6.5% of patients became completely continent. A larger proportion of onabotulinumtoxinA-treated patients than placebo reported a positive response on the TBS (60.8% vs. 29.2%, $p < 0.001$). All other OAB symptoms improved versus placebo ($p \leq 0.05$). OnabotulinumtoxinA improved patients' health-related quality of life across multiple measures ($p < 0.001$).

The finding that onabotulinumtoxinA 100U was consistently effective with a two- to fourfold improvement over placebo in all symptoms of OAB is important: an effect of this magnitude versus placebo does not seem to have been reported previously with antimuscarinics or β_3-AR agonists.

Adverse Effects

In the study by Nitti et al. [278], the majority of adverse effects occurred in the first 12 weeks (15.5% with onabotulinumtoxinA vs. 5.9% with placebo). The most frequently reported adverse effect was uncomplicated urinary tract infection with no upper urinary tract involvement. Other adverse effects were dysuria (12.2%), bacteriuria (5.0%), and urinary retention (5.4%). Postvoid residual (PVR) urine volume significantly increased with onabotulinumtoxinA versus placebo, with the highest volume at week 2 posttreatment, and 8.7% of patients had an increase from baseline of ≥200 mL in PVR urine volume at any time following the initial toxin treatment (none with placebo). The proportion of patients who initiated clean intermittent catheterization (CIC) at any time during treatment cycle 1 was 6.1% versus none in the placebo group; for over half the patients who initiated CIC (10/17), the duration of CIC was ≤6 weeks. This value is lower than those reported in previous studies on idiopathic DO [274–277,281]. In the study of Nitti et al. [278] discontinuation rates due to adverse effects were low both in the onabotulinumtoxinA (1.8%) and in the placebo (1.4%) groups.

DRUGS IN DEVELOPMENT

Among many potential targets for future treatment of LUTS/OAB [282], the most promising seems to be the purinergic [17,283] and cannabinoid [284,285] systems and the different members of the transient receptor potential (TRP) channel family [286,287]. P2X receptors are considered to be important in LUTS/OAB pathophysiology, and the use of $P2X_3$ receptor antagonists for treatment of these conditions has a good preclinical rationale, but clinical experiences are so far lacking. Clinical observations have indicated that different cannabinoid receptor agonists offer a promising therapeutic approach. In addition, inhibition of the degradation of endocannabinoids (inhibitors of fatty acid amide hydrolase) may be of therapeutic interest. Several members of the TRP channel superfamily, including TRPV1, TRPV2, TRPV4, TRPM8, and TRPA1, are expressed in the bladder. They may act as sensors of stretch and/or chemical irritation. However, even if the TRPV1 agonists, capsaicin, and RTX have shown clinical efficacy [282], the roles of TRP channels for LUT function/dysfunction and their potential as therapeutic targets have not been established.

CONCLUSION

To effectively LUTS/OAB and to treat UI caused by DO, identification of suitable targets for pharmacological intervention is necessary. Such targets may be found in the CNS or peripherally. Since in most cases the causes underlying LUTS/DO are unknown, pharmacotherapy is mainly directed against symptoms. Several drugs alternatives are available, but none of them suitable for all patients. Since LUTS and OAB symptoms can have multifactorial pathophysiology, individually designed treatments are required for optimal effect, and combination therapy may be needed.

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25 Uropathogens and the Lower Urinary Tract

Leslie Rickey

Urinary tract infections (UTIs) are a major cause of individual morbidity as well as societal cost. Between 40% and 60% of women will experience a UTI at some point during their lifetime [1]. According to the 2006 National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey, there are 8.1 million cases of UTIs a year in the United States and an estimated cost of 1.6 billion dollars annually [1,2]. Our understanding of the pathophysiology and bacterial factors related to UTIs has been greatly advanced over the last decade with the goal of identifying novel therapeutic targets and gaining better understanding of the host response. Researchers investigating the urinary microbiome have also begun to explore the relationship between the bacterial milieu of the bladder and lower urinary tract symptoms, which may represent an alternative treatment pathway for patients with overactive bladder symptoms. This chapter will review the current understanding of bacterial pathogenesis and host factors that play a role in UTIs as well as highlight relevant research developments regarding the urinary microbiome.

BACTERIAL PATHOGENESIS

Escherichia coli is the primary cause of community- and hospital-acquired UTIs [3] and has been the subject of the majority of uropathogen research. *E. coli* are generally referred to as intestinal or extraintestinal and can be either pathogenic or nonpathogenic depending on their genomic makeup that allows expression of certain virulence traits. There is a subset of extraintestinal *E. coli* associated with UTI, referred to as uropathogenic *E. coli* (UPEC). Current understanding implicates both bacterial and host factors that affect pathogenesis. Isolates from the urinary tract and rectal samples are often the same, suggesting that the intestinal tract is the primary source of UPEC [4]. Pathogenesis is conferred by virulence factors encoded in UPEC including adhesins that facilitate entry into urothelial cells, iron acquisition systems, and toxin secretion.

The first event that must occur in order for UPEC to colonize the lower urinary tract is attachment or binding to the urothelial cell. The presence of bacterial surface adherence factors called pili or fimbriae facilitates UPEC adhesion to host cells, and type 1 pili are common in *E. coli* isolates [5]. Interestingly, UPEC genomes can carry multiple gene clusters encoding for fimbria; therefore, similar strains of UPEC can have subpopulations with distinct pili, which increases the chances of adhesion [6]. Type 1 pili contain FimH subunits, an adhesin that is able to mediate urothelial cell invasion via uroplakin receptors on the urothelial cell surface [7]. In animal studies, a FimH-specific antibody was able to block urothelial adhesion and thus decrease bacterial counts in the urine [8]. Additionally, a FimH null mutant in a mouse UTI model resulted in decreased bacterial survival and decreased inflammatory response compared to *E. coli* expressing normal type 1 fimbria [9]. The Tamm–Horsfall protein (THP) is synthesized in the kidney and is an important host defense against the critical first step of bacterial adherence to the urothelium. THP binds to type 1-fimbriated *E. coli* and prevents bacterial adherence to the uroplakin receptors [10], and THP knockout mice are more prone to UTI. The THP-deficient mice carried higher bacterial loads and cleared bacteria more slowly than their wild-type counterparts [11].

Integrins are also surface adhesion molecules, and certain subtypes are bound by FimH. This attachment appears to facilitate bacterial uptake into host cells by communication with and reorganization of the actin cytoskeleton, a process that may be mediated by tyrosine kinase signaling pathways [12]. The bacteria then rapidly multiply within the superficial urothelial cells, and these infected cells are eventually exfoliated via an apoptosis-like pathway (Figure 25.1) [13]. While this mechanism allows the host to clear large numbers of bacteria, urothelial integrity is disrupted in the process. UPEC may in fact facilitate this response via proaptotic effects mediated by interactions with inflammatory cascade transcription factors such as NF-KB [14]. During exfoliation, some bacteria are released from the cell and are able to invade into deeper immature urothelial layers that are exposed during the exfoliation process [15,16]. At this stage, bacterial replication seems to be restricted by actin filaments [17] and thus these intracellular bacterial colonies (IBCs) confer a survival advantage by evading host defenses. In fact, it is thought that these quiescent bacterial communities may provide a reservoir for recurrent infections [15]. In addition, some bacteria take on a filamentous morphology and are able to avoid neutrophil phagocytosis [18], which provides a survival advantage and may contribute to sustained infection. In a mouse model, bacteria persisted in bladder tissue despite being cleared from the urine after gentamicin therapy [19], and although certain antibiotics reduced IBCs, UPEC reservoirs were not completely eradicated despite multiple antibiotic regimens [20].

Although it is known that bacterial invasion leads to epithelial cytokine production, the exact mechanism by which the inflammatory cascade is initiated is not well understood. The lipopolysaccharide (LPS) complex associated with the bacterial cell surface is recognized by CD14 and Toll-like receptors (TLR) on the urothelial cell surface, resulting in production of inflammatory mediators including interleukin-6 (IL-6) and IL-8, which in turn activates neutrophil recruitment to aid in bacterial clearance [21,22]. Polymorphisms in TLR can affect response to LPS; therefore, genetic variations may lead to alterations in host response to pathogens [23]. In the urinary tract, several TLR polymorphisms are associated with either increased susceptibility to or greater protection from UTI as well as number of UTI episodes [24]. There are several known toxins that modulate the host inflammatory response, induce cytopathic effects, and cause tissue damage. Alpha-hemolysin promotes cell lysis, appears to attenuate the host inflammatory response, and is associated with clinical severity [25,26]. Cytotoxic necrotizing factor 1 (CNF1) has been shown to cause membrane changes that facilitate bacterial internalization into host cells [27] and inhibit neutrophil activity in animal models [28].

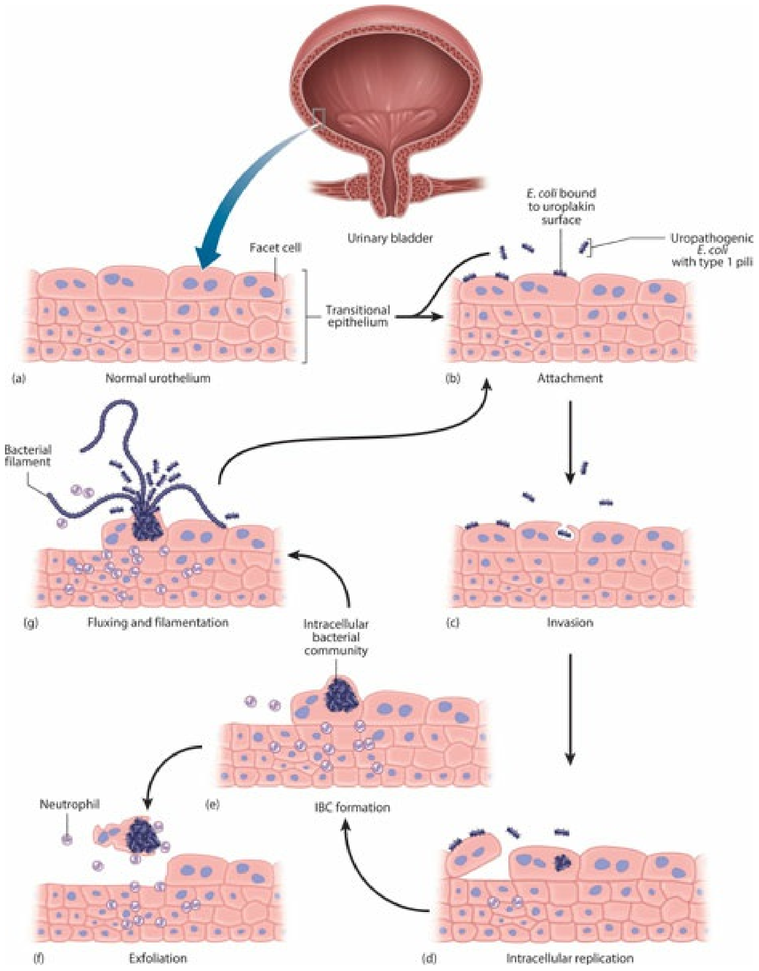

Figure 25.1 Uropathogenic *E. coli* (UPEC) intracellular bacterial colony (IBC) pathogenic pathway observed in the murine cystitis model. The bladder urothelium (a) is a pseudostratified transitional epithelium lined by large facet cells. These cells have an apical asymmetric unit membrane containing uroplakins that help form

the impermeable bladder barrier and also serve as receptors for UPEC. Bacteria introduced into the bladder adhere to the bladder surface via type 1 pili (b). Upon attachment, bacteria are able to invade (c) and replicate (d) within the facet cell cytoplasm. UPEC form large biofilm-like IBCs within these cells (e). Ultimately, the bacteria flux out of their intracellular niche (g), some adopting a filamentous morphology; they then adhere to other host cells and reenter the infectious cycle. During this process, infected urothelial cells are sloughed into the urine (f) and neutrophils are recruited to the site of infection. (Reproduced from Klumpp DJ et al., *Infect Immun*, 69, 6689, 2001.)

Iron is required for bacterial cellular processes and survival, and the competition for available iron stores highlights the impressive ability of UPEC to evade host defenses. One host defense is to limit iron availability via transferrin, an iron carrier protein that can move iron stores in and out of cells. However, UPEC can utilize enterobactin, which has a higher affinity for iron than transferrin and can therefore scavenge iron from the environment [29]. An additional host protein called lipocalin 2 specifically binds enterobactin and is upregulated in urothelial cells containing UPEC [30,31]; however, UPEC have yet additional iron acquisition systems that are not recognized by lipocalin and can therefore work around this host defense as well [32].

RELATIONSHIP OF BACTERIA AND LOWER URINARY TRACT SYMPTOMS

The relationship between bacteriuria and lower urinary tract symptoms has traditionally been restricted to symptoms related to UTIs. However, our understanding of “significant bacteriuria” has been challenged by recent advances in microbiology and more accurate descriptions of the type and number of bacteria present in the bladder.

The concept of significant bacteriuria defined as $>10^5$ CFU/mL was originally described by Kass in the 1950s [33] in an attempt to distinguish bacterial infection of the urinary tract from contamination as a risk factor for pyelonephritis. However, the effect of lower urinary tract bacteria on lower urinary tract symptoms is not likely isolated to what we currently term a “urinary tract infection.” It has been established that acute urinary tract symptoms can be associated with lower quantitative bacterial counts and that the presence of pyuria should be considered as well. Expert guidelines support that bacterial counts of $\geq 10^3$ CFU/mL associated with acute onset of dysuria should be considered a UTI as well [34,35]. In a study comparing young women with acute urinary symptoms were compared to asymptomatic controls, only 33% of the symptomatic women had bacterial counts $>10^5$; however, 70% had bacterial counts $>10^3$ (compared to 7% asymptomatic controls) [36]. In addition, when a cutoff of 20 leukocytes/mm^2 was used, pyuria was present in 77% of symptomatic women compared to 19.6% of controls. These results demonstrate not only the use of bacterial counts less than 10^5 when diagnosing a UTI in a symptomatic patient, but also the difficulty in establishing a clear cutoff that relates bacterial counts and pyuria to a true infection.

The significance of “low count bacteriuria” and how the urinary microbiome may contribute to LUTS is a topic of current investigation. When $\geq 10^4$ CFU/mL is used as a cutoff, bacteriuria is independently associated with nocturia (OR 3.21, CI: 1.02–10.14, $p = 0.046$), urgency (OR 7.02, CI: 1.49–33.05, $p = 0.01$), and bladder pain (OR 3.28, CI: 1.13–9.54, $p = 0.03$) in women without acute UTI symptoms [37]. Although the noninfected bladder has long been assumed to be a sterile environment, bacterial communities have been identified in a majority of culture-proven UTI-free female subjects using 16S rRNA gene sequencing [38]. Another group of investigators considered not only pyuria and urine culture, but also the presence of intracellular bacteria in epithelial cells shed in the urine. They found a significant difference in positive urine cultures in subjects with chronic LUTS compared to controls (17% vs. 2%, $p = 0.004$). Perhaps more striking, however, was the finding that 94% of symptomatic subjects had evidence of intracellular bacteria compared to 29% of controls ($p = 0.006$) [39], raising the possibility that cellular colonization may play a role in the development of LUTS. Interestingly, between-group differences in bacterial species were demonstrated in both urine culture and 16S rRNA ribotyping of intracellular bacteria. Finally difference in bacterial community have been shown in the urine of women [40]. The investigators also observed a decreased bacterial diversity in the urine from subjects vs. controls, which they note has been reported in the microbiota studies of chronic inflammatory states of the gastrointestinal tract as well.

In conclusion, advances in the science of bacterial pathogenesis as well as identification of host factors that may predispose an individual to colonization or altered immune response are increasing our understanding of the host–pathogen relationship in the urinary tract. Ongoing work in this area will not only allow clinicians to more accurately and effectively treat affected patients, but eventually inform preventative strategies for the millions of women suffering from UTI and other inflammatory disorders of the lower urinary tract.

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26 Classification of Lower Urinary Tract Dysfunction in the Female Patient

David Staskin and Alan J. Wein

INTRODUCTION

Devising a Classification System

The purpose of a classification system is communication. The value of grouping and interrelating concepts and facts into an organizational structure can be measured by the ability of the final product to provide a logical framework for introducing new theories, scientific findings, and clinical observations into the existing knowledge. In addition, the system should act as a useful clinical tool for diagnosing and treating disease. Rather than create new areas of contention, a classification system that is proposed for general use should ideally incorporate ideas and resolve conflicts. The attempt to devise an all inclusive system that completely describes lower urinary tract (LUT) function and dysfunction and the decision to adopt this single classification system would certainly be ideal, but is confounded by difficulties in agreement concerning construct and the standardization of terminology.

Complex interrelationships create difficulty in maintaining the simplicity of such systems. Filling (storage) and voiding (emptying) dysfunction may be classified by multiple methods.

Classification can be done by symptoms (patient interview eliciting LUT symptoms), the precipitating LUT activity from those symptoms, and the anticipated condition as in Table 26.1; by bladder activity or outlet activity (overactive or underactive) as in Table 26.2; by neurological activity (neurogenic) as in Table 26.3; by objective LUT testing (urodynamic studies) as in Table 26.4; or descriptively in a more complex system that combines the aspects of structure (anatomy) function (physiology), disease states (clinical diagnosis and the expected effect on LUT function), and observed LUT behavior (LUT dysfunction associated with a specific lesion or disease) as in Table 26.5.

The standardization of terminology is vital to ensure that the meaning of a "common language" employed by the users of the system reflects the same symptoms and signs and methods and measurements. The reader is directed to the ICS Standardization of Terminology (Appendices I through V) for a review of ICS "standards" [1–5]. As with classification systems that must undergo constant evolution, the ICS terminology has been revised and terms have been added, modified, and even subtracted without substitution [6,7].

When devising and presenting these classification systems, ICS terminology has generally been preserved, but the reader will note some differences between the ICS terms and the utilization of descriptors in the expanded descriptive classification (e.g., "sensory" terminology) included in Table 26.5.

The following classification systems are oriented to LUT symptoms with or without incontinence. In the case of incontinence, the presumption is that the "wetness" experienced by the patient is urine and that the source of egress is the urethra.

The clinical assessment should rule out wetness secondary to perspiration, inflammation or discharge, or from vaginal and/or rectal sources. For example, specific to the differential diagnosis of "wetness" is the importance of ruling out vesicovaginal or ureterovaginal fistula. The extended descriptive classification attempts to provide a complex but illustrative functional model.

This chapter does not include an in-depth review of LUT pathophysiology, diagnosis, or therapy, but these are reviewed exhaustively elsewhere within this textbook. In addition, this chapter is not intended to be a review of the historical development of the various methods of classification, although prior historical models are selectively referenced. However, the readers are strongly encouraged to utilize these models to "organize their thoughts" and facilitate the development of a logical approach to care.

Proposing Simple and More Complex Classification Systems: Symptomatic and Functional

Classifications

A symptomatic classification system is presented in Table 26.1. It is based on the concept that symptoms may suggest inclusively the underlying abnormal activity, pathophysiology, and condition. Since the patient's symptoms may be extremely useful or misleading due to overlapping findings in LUT conditions [8–10], an illustrative differential diagnosis of common conditions is also presented.

A classification system that is specifically oriented toward the description of LUT function and activity should divide the LUT into its two anatomical areas—the "bladder" (detrusor) and "bladder outlet" (sphincter) during the physiological functions of "storage" (filling) and "emptying" (voiding). A simple functional classification is presented in Table 26.2. The bladder or outlet activity is described as "overactive," "normal," or "underactive." An overactive bladder (OAB) represents an unwanted increase in detrusor activity ("pressure," episode(s) of undesired contractility or a decrease in bladder compliance, or the "sensation of filing," an increase in afferent activity) during urinary storage; an underactive bladder represents insufficient detrusor activity/pressure during bladder emptying (absent or poorly sustained contraction). An overactive outlet describes increased activity or resistance/obstruction during emptying (anatomic blockage, deficient voluntary sphincter coordination, neurogenic sphincter dyssynergia), and an underactive outlet represents insufficient activity/resistance during storage (inadequate intrinsic function or altered anatomical support relationships). These abnormalities in function/activity can occur alone, or in combination [11–17].

Table 26.1 Classification by Symptoms

Stress urinary incontinence (SUI)
Symptom—The involuntary loss of urine on effort or exertion (lift, strain, cough, sneeze).
Activity—Underactive outlet.
Condition—Urodynamic stress incontinence: the involuntary loss of urine resulting from an increase in intra-abdominal pressure that overcomes the resistance of the bladder outlet in the absence of a true bladder contraction. The decrease in bladder outlet or urethral resistance may result from poor anatomical support of the bladder neck (urethral hypermobility/SUI-A) or a loss of urethral function (intrinsic sphincter deficiency SUI-ISD) or, most commonly, a mixture.
Clinical confusion—The patient describes the symptom of urinary loss with "activity" but the etiology of involuntary leakage is actually an uninhibited bladder contraction: SUI should have urinary loss synchronous with "effort"; similarly, many patients will describe SUI as a sensation, which is confused with "urgency"; finally, stress and urgency incontinence may coexist.

Urgency urinary incontinence (UUI)
Symptom—The loss of urine with the sensation of urgency, voiding before the ability to toilet.
Activity—Overactive bladder (OAB-wet): detrusor overactivity.
Condition—Urinary urgency incontinence (urodynamic): the involuntary loss of urine resulting from an increase in bladder pressure secondary to detrusor overactivity (an uninhibited bladder contraction or unstable bladder). Detrusor overactivity may be the result of a suprasacral spinal or intracranial neurological lesion that results in uncontrolled reflex contractions (detrusor hyperreflexia) or may be idiopathic. Patients may demonstrate other symptoms associated with "urgency" (frequency, urgency, nocturia) without urinary loss (OAB-dry).
Clinical confusion—The patient has decreased sensation and loses urine from motor activity of the detrusor without the feeling of "urgency." OAB is a syndrome consisting of the symptoms "urgency, with or without urgency incontinence, usually with frequency and nocturia" suggestive of urodynamic bladder overactivity but inclusive of "urgency and frequency without incontinence" OAB-dry (vida infra) or the sensation of urgency (desire to void in the absence of a detectable rise in detrusor pressure–sensory urgency).

Mixed urinary incontinence
Symptom—Mixed symptoms of UUI and SUI, urinary loss with effort and with urgency.
Activity—OAB-wet detrusor overactivity and underactive sphincter.
Condition—A mixture of the conditions described earlier as SUI and UUI.
Clinical confusion—Urinary loss may be from SUI or UUI but the predominance and bother resulting from one condition or the other may not be discernable from the history and physical exam alone, thus creating difficulty in choosing treatment for the "primary" symptom.

Urgency and frequency without incontinence
Symptom—Urgency and frequency without urinary loss.
Activity—Detrusor overactivity with compensatory sphincter activity or no detrusor activity or abnormal afferent activity or processing (sensory).
Condition—Urgency is the complaint of a sudden compelling desire to pass urine that is difficult to defer, and frequency is the complaint by the patient who considers that she voids too often by day or at night (going to bed and arising), whereas

nocturia is waking at night one or more times to void preceded by and followed by sleep. “Sensory urgency,” a term that has been removed from the ICS lexicon and was used to describe the sensation of urinary urgency without a detectable rise in detrusor pressure.

Clinical confusion—The classification of a moderate or strong “desire to void” without true “urgency” is unresolved. “Sensory urgency–desire to void” is not in the current ICS lexicon.

Overflow incontinence

Symptom—The involuntary loss of urine resulting from urinary retention with bladder overdistention. The retention (failure to empty) may result from inadequate bladder contractility or outlet obstruction (or both).

Activity—Underactive bladder (retention)/overactive outlet (obstruction).

Condition—Urinary loss occurs when the intravesical pressure overcomes the urethral resistance as a result of bladder contractility, increases in intra-abdominal pressure and/or urethral relaxation.

Clinical confusion—The symptoms that are described may be a mixture of stress (SUI) and urgency (OAB) complaints.

Altered bladder sensation and pain

Symptom—Frequent voiding with or without pain; conversely a loss of sensation.

Activity—No detrusor contraction/alteration in afferent input or processing.

Condition—Bladder pain, discomfort, and pressure can be characterized by type, frequency, duration, location, and precipitating and relieving factors. Bladder sensation can be described as increased, normal, reduced, absent, or nonspecific (neurologic). Increased or decreased voiding may be correlated with the sensation.

Clinical confusion—Urinary urgency and frequency without incontinence may be a product of abnormal sensation or bladder contractile activity. The source of pelvic pain may not be the lower urinary tract. Interstitial cystitis or chronic urethritis remain diagnoses of exclusion.

Functional incontinence

Symptom—The involuntary loss of urine resulting from a deficit in the ability to perform toileting functions secondary to physical or mental limitations.

Activity—Abnormal lower urinary tract function usually coexists with functional issues.

Clinical confusion—The underlying pathophysiology of stress, urge, or overflow incontinence may coexist, as well as difficulty in eliciting an accurate history. The patient’s primary “functional” issue may be dementia, delirium, or other forms of altered cognition; physical disability preventing easy and rapid toilet access. These conditions often exist alone or in combination with lower urinary tract dysfunction.

Table 26.2 Classification by Bladder and Outlet Activitya

Bladder	**Outlet**
Overactive (urgency)	Overactive (obstruction)
Normoactive	Normoactive
Underactive (retention)	Underactive (stress incontinence)

[a] Symptoms in parentheses.

The classification of neurogenic voiding dysfunction may also be adapted to a similar functional system based on the nature of the lesion and the expected behavior of the detrusor and sphincter and similarly can be correlated with symptoms as in Table 26.3 [18–23]. The neurological terms of detrusor hyperreflexia, normoreflexia, and areflexia and the outlet descriptive of dyssynergic, normal, or denervated are utilized and correlate with the type of function/activity.

The interrelationship between the LUT and the outlet, including the pelvic floor, requires a classification system that recognizes the individual contributions and the combined effects of the efferent systems (anatomy and function/activity), and the afferent systems from the bladder musculature and mucosa, the bladder neck, urethral mechanisms, and the pelvic floor structures [24–29]. It is simplistic to combine the effects of the bladder musculature and mucosa, the outlet/sphincter, and the levator complex on bladder activity without acknowledging the complex integration and interrelationship of these areas on LUT behavior. In addition, combining them into one functional area should not limit investigation into their individual contributions. The complex interrelationship of the bladder outlet and pelvic floor structures with voiding behavior are apparent in several common clinical conditions. For example, in the case of “urodynamic stress incontinence” or stress urinary incontinence (SUI), the ability to preserve or augment urethral basal tone, urethral sphincter function, and anatomical support from levator anatomy or contraction is critical for understanding the ability to maintain continence during “effort” [30–37]. Conversely, the initiation of voiding requires both pelvic floor and urethral sphincter relaxation in the absence of anatomical obstruction [23–28]. Conversely, symptoms of decreased emptying or urinary retention may result from the inhibition of detrusor contractility, secondary to increased pelvic floor or sphincter afferents, decreased afferent detrusor muscular or mucosal input, or voluntary contraction of the striated sphincter (psuedo-dyssynergia) during voiding. Similarly, an understanding of urgency incontinence and OAB syndrome symptoms require an appreciation of the relationship between afferent and efferent neurological pathways to the LUT, the bladder neck, and the pelvic floor on the detrusor, although definitive reflex arcs in the human may not have been identified [38–43].

Table 26.3 Classification by Neurological Activity

Neurogenic classification[a]			
Bladder/detrusor		Outlet/sphincter	
Hyperreflexic (overactive—urgency)		Uncoordinated (overactive—obstruction) Coordinated	
Normoreflexic		Denervated (underactive—stress inc.)	
Areflexic (underactive—retention)			
Expected behavior of the bladder, internal sphincter, and external sphincter based on location of the lesion			
	Bladder	Internal (smooth muscle) sphincter	External (skeletal) sphincter
Peripheral	Hypo-areflexic, underactive	Dernevated (+/−)	Denervated (+/−)
Infrasacral	Areflexic, underactive	Innervated	Denervated, underactive
Spinal	Hyperreflexic, overactive	Uncoordinated if T6 or above	Dyssynergic, overactive
Suprapontine	Hyperreflexic	Coordinated	Coordinated

Sources: Adapted from Krane RJ and Siroky MB, Classification of neuro-urologic disorders, in Krane RJ and Siroky MB, eds., *Clinical Neuro-Urology*, Little Brown, Boston, MA, 1979, pp. 419–421; Staskin D, Classification of voiding dysfunction, in Krane R and Siroky MB, eds., *Clinical Neurourology*, 2nd ed., Little Brown, Boston, MA, 1991, pp. 411–426.

[a] Underlining denotes function; italic type denotes symptoms.

Table 26.4 Classification by Urodynamics (Bladder and Outlet)

	Storage	**Emptying**
Bladder	Cystometrogram–F[a] DLPP[b]	Cystometrogram–V[f] Pdet-flow[f] Residual urine[f]
Outlet	UPP[c] VLPP[d] Fluoroscopy[e]	Pdet-flow[i] EMG[j] MUPP[k] Fluoroscopy[l] Residual urine[m]

Source: Adapted from Wein AJ, Pathophysiology and classification of voiding dysfunction, in Wein AJ, Kavoussi LR, Novick AC et al., eds., *Campbell-Walsh Urology*, 9th ed., Elsevier Science (Saunders), Philadelphia, PA, 2007, pp. 1973–1985.

[a] Filling cystometrogram (filling pressure).

[b] Detrusor leak point pressure (bladder compliance).

[c] Urethral pressure profile (urethral closure).

[d] Valsalva leak point pressure (pressure to leak).

[e] Fluoroscopy (anatomy of outlet closure mechanism).

[f] Voiding cystometrogram (emptying pressure).

[g] Pressure flow (detrusor contractility/flow/calculated resistance).

[h] Residual urine (after void).

[i] Pressure flow (detrusor contractility/flow/calculated resistance).

[j] Electromyography (striated sphincter activity).

[k] Micturition urethral pressure profile (localized urethral pressure).

[l] Fluoroscopy (anatomy of outlet opening).

[b] Residual urine (after void).

EXPANDED CLASSIFICATION OF VOIDING DYSFUNCTION: INCLUDING PELVIC FLOOR ACTIVITY

Outlet Dysfunction: Bladder Outlet and Pelvic Floor

The underactive outlet: The bladder outlet (sphincteric mechanism) is responsible for "outlet resistance" during urinary storage. The bladder outlet remains closed at rest. Resistance to leakage is provided by the intrinsic closure pressure along the length of the urethra. The urethra can be divided into two functional areas: these are (1) the "proximal" sphincteric mechanism—a product of mucosa, submucosa, and smooth muscle incorporating the bladder neck and proximal urethra—and (2) the distal mechanism or "external" sphincteric mechanism located in the middle of the "anatomical urethra" and intimately related anatomically and physiologically to the levator ani complex. Anatomical support facilitates transmission of intra-abdominal pressure to both areas and is provided by both the anterior vaginal wall and its attachments to the pelvis, and by the constant tone (slow-twitch fibers). Active contraction (fast-twitch fibers) of the levator complex can increase this support, but is usually seen only after pelvic muscle training and is not a "normal" reflex.

SUI is the involuntary loss of urine per urethra—which occurs when intravesical pressure overcomes the urethral resistance owing to an increase in intra-abdominal pressure in the absence of a true bladder contraction. Urethral closure pressure is maintained by preserving or augmenting anatomical support and by increasing the intrinsic activity of the external sphincter complex. The preservation or enhancement of the anatomical backboard facilitates pressure transmission in the proximal and distal sphincteric mechanism and preserves the anatomical relationships of the sphincteric components to maintain or increase closure pressure. Proper anatomical support provides an obvious mechanical advantage and, just as importantly, allows efficient action of the individual structures. Type I or type II SUI is classified as "poor anatomical support," associated with bladder neck and urethral motion. However, an understanding of the contribution of pelvic floor activity and dysfunction allows one to appreciate that the etiology of urinary leakage is probably multifactorial. Classically, an important event in maintaining continence is the preservation of intra-abdominal pressure transmission to the bladder neck and proximal urethra with respect to the bladder during stress maneuvers. In addition, inhibiting the rotational motion of the urethra prevents a relative differential in the movement of the posterior urethra with relation to the anterior urethra and the development of a shearing force between the anterior and posterior urethral walls that decreases urethral coaptation and compression.

The most fixed point, and the area of maximal pressure transmission during increases in intra-abdominal pressure, is the external sphincter–levator complex in the midanatomical urethra. Transmission forces as well as active sphincteric contraction provide urethral resistance during stress maneuvers.

The combination of defects at many levels of the sphincteric mechanism may combine to decrease urethral resistance. Type III SUI, intrinsic sphincter deficiency or low urethral closure pressure, describes a deficiency in any of the intrinsic urethral functions through atrophy, denervation, devascularization, or scarring, as detailed earlier. The degree of pudendal nerve denervation during childbirth may contribute to deficiencies in anatomical support both by affecting levator support and by decreasing intrinsic sphincter function.

It is reasonable to assume that the complex etiology of SUI is a mixture of anatomical support abnormalities and intrinsic sphincter abnormalities. The pathophysiology is related to the relative loss of mechanical (ligament) support of functioning (innervated) intrinsic (urethral) and extrinsic musculature (slow- and fast-twitch fibers of the levator complex). Therapy may be directed at correcting the defect, or compensating for the deficiency, by increasing the function of another component that contributes to urethral resistance. In fact, the most common operation for SUI is a midurethral sling. The mechanism of action has been described as a "kinking" or "backboard" effect, which in fact does not correct the common finding of bladder neck hypermobility but does increase urethral resistance to leakage and compensates for defects in anatomical support and intrinsic urethral deficiency.

Table 26.5 Expanded Functional Classification of Voiding Dysfunction Including Bladder Afferents and Pelvic Floor Activity

I. Outlet dysfunction: bladder outlet and pelvic floor

A. Underactive outlet (decreased urethral resistance)

Symptomatic: SUI

1. Anatomical support defects (SUI-A) (types I and II SUI): pathophysiology—anatomical motion creates inequities in transmission pressures to bladder and outlet, overcoming urethral resistance, and/or and conformational changes caused by vaginal wall motion disrupt outlet integrity.
    - a. Anatomical defects of fascia, muscles, ligaments, and bony pelvis.
    - b. Functioning support: muscular contraction—denervation or the loss of identification, strength, or coordination of levator musculature.
    - c. A degree of ISD (see 2) that in combination with SUI-A I or II contributes to critical decreases in resistance during effort to permit urinary leakage.
2. ISD (SUI-ISD) (type III) (LUCP)
   Pathophysiology: deficiency of the urethral closure mechanism secondary to decreased innervation, vascularization or trauma to mucosa, submucosa, or smooth, nonstriated skeletal or skeletal musculature of the urethra—intrinsic deficiency of the closure mechanism.
    - a. Proximal urethral sphincter: bladder neck (smooth muscle) and proximal urethra (SUI-ISD-p).
    - b. External sphincter: denervation or loss of resting tone, voluntary or reflex contraction (SUI-ISD-d).
    - c. Combined or total proximal and external sphincter deficiency (SUI-ISD-t).
3. Combined SUI (SUI-A-ISD)
   Pathophysiology: a degree of both anatomical motion and sphincter dysfunction.
    - a. Leakage from ISD may exist without hypermobility.
    - b. Hypermobility alone without a degree of ISD is not sufficient to result in urinary loss.
4. Failure to inhibit the detrusor: decreased pelvic floor inhibitory activity of bladder (etiology for OAB—see C).
   Pathophysiology: failure to contract pelvic floor releases detrusor reflex and decreases ability to inhibit active contraction.
    - a. Neurological: (infrasacral) denervation (areflexia of pelvic floor).
    - b. Behavioral: failure to contract pelvic floor (lack of identification/strength/coordination).
    - c. Mechanical: damage to pelvic floor structures with intact innervation.

B. Overactive outlet (increased urethral resistance)

Symptomatic: overflow incontinence/retention; frequency–urgency.

1. Anatomical obstruction (physical blockage) Pathophysiology: increased outlet resistance secondary to compression or narrowing.
    - a. Iatrogenic: surgical (e.g., for urinary incontinence).
    - b. Other: congenital, inflammatory, neoplastic, traumatic.
2. Functional obstruction (failure of relaxation)
   Pathophysiology: increased outlet resistance—inappropriate contraction or failure of normal relaxation.
    - a. Neurogenic: detrusor sphincter dyssynergia (skeletal musculature).
    - b. Behavioral: failure to relax pelvic floor musculature or external sphincter.
3. Combined anatomical and functional obstruction
4. Inhibition of detrusor activity: increased pelvic floor activity
   Pathophysiology: failure to relax pelvic floor inhibits initiation of detrusor activity and inhibits ability to develop or continue a sustained detrusor contraction.
    - a. Neurological: (suprasacral) overactivity/hyperreflexia (dyssynergic pelvic floor activity).
    - b. Behavioral: failure to relax pelvic floor (learned, acquired, maladaptive, psychogenic).
    - c. Situational: “voluntary” inhibition secondary to environment or pain.

II. Bladder dysfunction

A. Detrusor overactivity (increased intravesical pressure)

Symptomatic: urgency incontinence (with or without sensation)—OAB-wet.

1. Involuntary detrusor contractions: detrusor overactivity (motor urgency). Pathophysiology: increased detrusor (intravesical) pressure overcomes urethral resistance or causes sensation of urinary urgency
    - a. Detrusor overactivity (DO): primary = idiopathic, subclinical neurological, or symptomatic phasic detrusor activity; secondary = obstruction, reflex urethral relaxation, increased detrusor/mucosal afferent activity. OAB-urgency, with (OAB-wet) or without (OAB-dry) incontinence, usually with frequency and nocturia (absence of other pathology).
    - b. Detrusor overactivity (hyperreflexia): suprapontine (intracranial) neurological lesion (with or without sphincter control); spinal (suprasacral) neurological lesion (with or without sphincteric dyssynergia).
2. Decreased compliance

Pathophysiology: increased intravesical pressure secondary to decreased accommodation of detrusor.
  a. Fibrosis: radiation, inflammation, immune response.
  b. Neurological: loss/reversal of accommodation reflex—conus medullaris or peripheral.
3. Combined detrusor contractions and decreased compliance
4. Pelvic floor underactivity (see I.A.4)—decreased pelvic floor inhibition

B. Underactive bladder (decreased intravesical pressure)
Symptomatic: overflow incontinence/retention
1. Peripheral denervation or neuropathy. Pathophysiology: decreased contractility—neural efferent or myogenic/decreased afferent stimulation.
  a. Congenital, inflammatory, neoplastic, or trauma lesion to peripheral nerves.
  b. Diabetes or other metabolic cause.
2. Detrusor myopathy
Pathophysiology: decreased contractility secondary to smooth muscle damage.
  a. Fibrosis/collagen deposition.
  b. Inflammation/obstruction/overdistension.
3. Pharmacological inhibition
Pathophysiology: decreased contractility secondary to receptor blockade of neural efferents or afferents.
  a. Antimuscarinics.
  b. Smooth muscle relaxants/spasmolytics/membrane stabilizers.
4. Pelvic floor overactivity (see I.B.4)

III. Combined outlet and bladder dysfunction (I and II)

IV. Disorders of sensation

A. Decreased sensation
1. Decreased bladder sensation. Pathophysiology: denervation, myopathy, behavioral, pharmacological.
  a. Decreased sense of fullness and normal urge response.
  b. Loss of sense of fullness/urge warning only with active contraction.
  c. Loss of sense of fullness/urge incontinence without appreciation of “desire to void.”
  d. Urinary retention without appreciation of distension.
2. Decreased bladder outlet and pelvic floor sensation
Pathophysiology: denervation, myopathy, behavioral, pharmacological causing decreased ability to identify/contract/coordinate.
  a. Bladder overactivity (I.A.4): failure to inhibit?
  b. Bladder underactivity (myogenic or mucosal) (II.B.4): failure to initiate?
  c. Contributory to decreased bladder sensation? (IV.A.1.a through d).
  d. Sexual dysfunction—anorgasmia.

B. Increased sensation
1. Increased sensation of the bladder/bladder outlet Pathophysiology: neuropathic, inflammatory, mucosal permeability defect, psychogenic, afferent amplification.
  a. Frequency–urgency symptoms.
  b. Suprapubic and pelvic pain syndromes.
2. Increased sensation of the pelvic floor/bladder outlet
Pathophysiology: neuromuscular myalgia, neuropathic, inflammatory, psychogenic.
  a. Levator myalgia.
  b. Frequency–urgency and pelvic pain syndromes.
3. Combined deficit

*Abbreviations:*LUCP, low urethral closure pressure; ISD, intrinsic sphincter deficiency; OAB, overactive bladder; Pelvic floor activity, in italics; SUI, stress urinary incontinence.

The overactive outlet: Failure to empty the bladder may be due to elevated outlet resistance or to impaired contractility of the bladder. The most commonly observed clinical etiology of elevated outlet resistance is iatrogenic, obstruction following incontinence surgery. Other forms of anatomic urethral obstruction are less common. Neurogenic outlet obstruction, commonly seen following injury to the suprasacral spinal cord, is due to a loss of coordination between the bladder and sphincter (detrusor sphincter dyssynergia). The paradoxical failure of the outlet to relax during voiding may result in anatomical obstruction to flow or to inhibition of the initiation or completion of the detrusor contraction. Contraction of the pelvic floor or sphincter is a normal response for bladder inhibition but, when pathological, may be classified as pseudodyssynergia (voluntary or behavioral) or true dyssynergia (neurogenic). The relaxation of the urethral sphincter during voiding and dyssynergic activity in spinal cord injury has been documented. It is not known whether the specific anatomical areas of the urethra or pelvic floor (sphincter urethra, compressor urethra, urethrovaginal sphincter, bulbocavernosus, anal sphincter, levator complex) act in unison, individually, or at all in detrusor inhibition in normal subjects.

The OAB: The symptoms of OAB syndrome are urgency, with or without urge incontinence, usually with frequency and nocturia. Multiple etiologies have been proposed including reduced suprapontine inhibition, damaged axonal paths in spinal cord, increased LUT afferent input, loss of peripheral inhibition, and enhancement of excitatory neurotransmission in the micturition reflex pathway. Therefore, the central and peripheral nervous systems mediate bladder control through complex voluntary pathways and reflex arcs. Central efferent control of the bladder smooth musculature is mediated by afferent activity from the detrusor musculature and bladder mucosa (facilitatory) and the reflex and voluntary contractions of the pelvic floor and sphincter musculature (inhibitory).

The underactive bladder: Traditional concepts of detrusor underactivity have focused on either efferent innervation or myogenic dysfunction. By contrast, contemporary views emphasize the importance of the neural control mechanisms, particularly the afferent system, which can fail to potentiate detrusor contraction, leading to premature termination of the voiding reflex. To void efficiently, a feedforward mechanism by which urinary flow in the urethra helps to enhance and maintain adequate contractile function of the bladder until the bladder is empty is required. Sensory information is fed back to the motor system at several levels of control between the end organ and brain cortex. These sensors themselves can be damaged, for example, through an effect of ageing or ischemia. In addition, impairment of innervation can lead to decreased information transfer via either the sensory or motor nerves. A functional disruption of higher central nervous regulatory systems can lead to functional abnormal voiding [44].

During the initial phase of bladder emptying, the pelvic floor and external sphincter relax in order to decrease urethral resistance and facilitate low pressure flow. In addition, this relaxation decreases the reflex inhibition of bladder contractility. Relaxation is followed by a detrusor contraction, which continues until voiding is completed. When emptying failure is secondary to bladder dysfunction, it may be a result of either detrusor smooth muscle pathology or insufficient neural stimulation of the detrusor. Insufficient neural stimulation may occur at the neuromuscular level (pharmacological), with nerve impairment (neuropathy), or with alterations in central control of micturition (conus medullaris, spinal column, or brain). The impairment of detrusor contractility by the absence of pelvic floor relaxation is evident in spinal cord disease (failure to empty following adequate sphincterotomy in the spinal cord patient due to incomplete detrusor contractions) and Parkinsonism (failure to empty secondary to pelvic floor bradykinesia).

Mixed–combined disorders: Disorders of the bladder and outlet during storage and emptying may occur alone and in combination. The most common in the female patient is underactive outlet (SUI) and OAB. In addition, the elderly females or patients with neurological diseases may demonstrate detrusor overactivity (hyperreflexia) with impaired contractility (poorly sustained contraction).

Sensory disorders: Afferent neurons from the bladder and urethra are of major importance during both the storage and emptying phases, both initiating the voiding reflex and sustaining the voiding drive during bladder emptying. Somatic activity may inhibit the emptying reflex by voluntary contraction of the external sphincter or pelvic floor—and although not established in humans, may provide inhibitory activity during bladder filling. Traditional classification systems have focused on motor rather than sensory activity. Disorders of bladder and bladder outlet sensation may result from central or peripheral denervation, from psychological causes, or from pharmacological agents such as pain medications. The role of decreased sensation in the function of the pelvic floor and the interaction between the pelvic floor and bladder with relation to the sensory pathway on the micturition reflexes await further investigation. The pudendal nerve is responsible for the innervation of pelvic floor structures as well as of the genital skin, urethral mucosa, and anal canal. Proprioceptive information of the periurethral musculature and sensory innervation of the levator ani muscles are also mediated by the pudendal branches. Increased sensation or pain attributed to the bladder is a major clinical challenge.

The symptoms of urinary frequency, urinary urgency, and suprapubic pressure often result in diagnostic evaluations and therapy for bladder disorders, even in the absence of definitive findings of mucosal or smooth muscle abnormality. Pain that may originate from fascial, muscular, or neurological etiologies within the pelvic floor should be included in the differential diagnosis of the patient with urethral or bladder syndromes.

Traditionally, sensory signaling in the urinary bladder has been largely attributed to direct activation of bladder afferents. There is substantive evidence that sensory systems can be influenced by nonneuronal cells, such as the urothelium, which are able to respond to various types of stimuli that can include physiological, psychological, and disease-related factors. The corresponding release of chemical mediators (through activation of a number of receptors/ion channels) can initiate signaling mechanisms between and within urothelial cells, as well as other cell types within the bladder wall including bladder nerves. However, the mechanisms underlying how various cell types in the bladder wall respond to normal filling and emptying and are challenged by a variety of stressors (physical and chemical) are still not well understood. Alterations or defects in signaling mechanisms are likely to contribute to the pathophysiology of bladder disease with symptoms including urinary urgency, increased voiding frequency, and pain [45].

In addition, pelvic floor or bladder pain and OAB should not be considered mutually exclusive in spite of the fact that each is usually exclusion criteria when studying the other during studies involving pharmacotherapy.

Summary: The classification of voiding dysfunction has been presented with the major focus incorporating the division of the LUT into the bladder and the bladder outlet and the “activity” during storage/filling and emptying/voiding. These systems can be clearly illustrated with the functional areas of the bladder and outlet on the vertical and axis the functions of filling/storage and voiding/emptying on the horizontal. These graphic representations can be utilized to correlate functional anatomy, LUT function, urodynamic testing, etiology, and therapy.

Classification systems will continue to evolve as our understanding of LUT functions expands and our understanding of the complex interactions of storage/filling and emptying, efferent/motor and afferent/sensory, bladder and outlet, LUT, and surrounding pelvic floor structures must assimilate this knowledge into the categorical constructs. The reader is encouraged to incorporate these systems into their own clinical algorithms and critique and modify them based on additional evidence or “opinion.”

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27 Tissue Engineering and Regenerative Medicine for the Female Genitourinary System

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INTRODUCTION

Patients suffering from various congenital and acquired disorders of the reproductive tract are currently treated with surgical and hormonal therapies. These techniques are not ideal and do not routinely lead to physiological recovery of the affected organ or organs. This has led scientists in the field of regenerative medicine to apply the principles of cell transplantation, materials science, and bioengineering to construct biological substitutes that may eventually improve the quality of life for these patients.

The field of regenerative medicine encompasses various areas of technology such as tissue engineering and cloning. Tissue engineering combines the principles of cell transplantation, materials science, and bioengineering to develop new biological substitutes that may restore and maintain normal organ function. Tissue engineering strategies generally fall into two categories: the use of acellular matrices that allow the body's own regenerative systems and serve as scaffolds on which to direct new tissue growth and the use of matrices with cells. This chapter will discuss some of the principles of regenerative medicine as well as discuss some of the current research in the field of regenerative medicine for female genitourinary organs [1–4].

BIOMATERIALS IN TISSUE ENGINEERING

In many cell-based tissue engineering methods, cells are obtained from a tissue, expanded in vitro, and then seeded onto a scaffold composed of an appropriate biomaterial. These biomaterials replicate the biological and mechanical function of the native extracellular matrix (ECM) found in tissues in the body by serving as an artificial ECM. Biomaterials also provide a 3D scaffold for the cells to adhere forming new tissues with appropriate structure and function. They also allow for the delivery of cells and appropriate bioactive factors to desired sites in the body [5]. Bioactive factors, such as cell adhesion peptides and growth factors, can be seeded along with cells to help regulate and direct growth. Biomaterials can also provide mechanical support against in vivo forces and ensure that the predefined 3D structure of an organ is maintained during tissue development.

The ideal biomaterial should be biodegradable and bioresorbable to support the replacement of normal tissue without inducing inflammation. If the biomaterial is incompatible with the recipient, it may induce an inflammatory effect or immune response, which will lead to damage, necrosis, and cell death [6]. The biomaterial should also provide an environment in which appropriate regulation of cell behavior (adhesion, proliferation, migration, and differentiation) can occur so that functional tissue can form. Since biomaterials provide temporary mechanical support while the cells undergo spatial reorganization into tissue, the properly chosen biomaterial should allow the engineered tissue to maintain sufficient mechanical integrity to support itself in early development, while in late development, it should begin to degrade so that it does not hinder further tissue growth [5].

Three broad classes of biomaterials have been utilized in tissue engineering studies: naturally derived materials (e.g., collagen and alginate), acellular tissue matrices (e.g., bladder submucosa [BSM] and small intestinal submucosa [SIS]), and synthetic polymers such as polyglycolic acid (PGA), polylactic acid (PLA), and poly(lactic-co-glycolic acid) (PLGA). Collagen is the most abundant and ubiquitous structural protein in the body and may be readily purified from both animal and human tissues with an enzyme treatment and salt/acid extraction. Acellular tissue matrices are collagen-rich matrices prepared by removing cellular components from tissues. The matrices are often prepared by mechanical and chemical manipulation of a segment of tissue [1–4]. These matrices slowly degrade upon implantation and are replaced and remodeled by new ECM proteins synthesized and secreted by transplanted or ingrowing host cells. Commonly used acellular tissue matrices include BSM and SIS.

Polyesters of naturally occurring a-hydroxy acids, including PGA, PLA, and PLGA, are also widely used in tissue engineering. These polymers have gained FDA approval for human use in a variety of applications, including sutures. Because these polymers are thermoplastics, they can be easily formed into a 3D scaffold with a desired microstructure, gross shape, and dimension [7]. Other biodegradable synthetic polymers, including poly(anhydrides) and poly(ortho esters), can also be used to fabricate scaffolds for tissue engineering with controlled properties [8].

CELLS FOR TISSUE ENGINEERING

Human Embryonic Stem Cells

Human embryonic stem cells (hESCs) exhibit two remarkable properties: the ability to proliferate in an undifferentiated but pluripotent state (self-renewal) and the ability to differentiate into almost all of the specialized cell types in the body [9]. These cells are isolated by aspirating the inner cell mass from the embryo during the blastocyst stage (5 days after fertilization). hESCs have been shown to differentiate into cells from all three embryonic germ layers in vitro. Skin and neurons have been demonstrated, indicating ectodermal differentiation [10–13]. Blood, cardiac cells, cartilage, endothelial cells, and muscle have also been shown, indicating mesodermal differentiation [14–16]. Pancreatic cells have been formed, indicating endodermal differentiation [17]. The tendency, however, to form teratomas in vivo is a limitation to widespread usage of hESCs in cell therapy and tissue engineering as it is difficult if not impossible to control the tumorigenicity of these cells in vivo leading to a number of safety concerns surrounding the usage of these cells for therapeutic benefit. In addition, the ethical considerations surrounding the destruction of human embryos to obtain hESCs are yet to be resolved. Finally, the use of hESCs is banned in some countries, including the United States, and so their use in tissue engineering is infrequent in those countries at this time.

Laboratory-Generated Stem Cells

In addition to hESCs, stem cells for tissue engineering can be generated through “cloning” procedures. Somatic cell nuclear transfer (SCNT) is used to generate early-stage embryos that are explanted in culture to produce embryonic stem cell lines whose genetic material is identical to that of its source. These autologous stem cells have the potential to become almost any type of cell in the adult body and thus would be useful in tissue and organ replacement applications [18]. Therefore, SCNT may provide an alternative source of transplantable cells. There are, however, a number of limitations that require further study before this technique can be applied widely in tissue or organ replacement therapy. First, the efficiency of the cloning process is very low as evidenced by the fact that the majority of embryos derived from the cloning process do not survive [19–21]. In addition, cell cycle synchronization between donor cells and recipient oocytes must be accomplished [22]. Other barriers to the frequent use of SCNT in human applications are the requirement for human oocytes, which are difficult to obtain in the quantities required, and, as with hESCs, there are ethical considerations surrounding the production and destruction of human embryonic tissue that remain to be resolved.

Transformation of adult cells into pluripotent stem cells through a type of genetic “reprogramming” has also been described. Reprogramming is a technique that involves dedifferentiation of adult somatic cells to produce patient-specific pluripotent stem cells, without the use of embryos. Cells generated by reprogramming would be genetically identical to the somatic cells (and thus the patient who donated these cells) and would not be rejected. Takahashi and Yamanaka [23] were the first to discover that mouse embryonic fibroblasts and adult mouse fibroblasts could be reprogrammed into an “induced pluripotent state” (iPS). The resultant iPS cells possessed the immortal growth characteristics of self-renewing embryonic stem cells, expressed genes specific for ES cells, and generated embryoid bodies in vitro and teratomas in vivo. When iPS cells were injected into mouse blastocysts, they contributed to a variety of cell types. However, although iPS cells selected in this way were pluripotent, they were not identical to ES cells. Unlike ES cells, chimeras made from iPS cells did not result in full-term pregnancies. The epigenetic state of the iPS cells was found to be somewhere between that found in somatic cells and that found in ES cells, suggesting that the reprogramming was incomplete.

These results were improved significantly by Wernig et al. [24]. They observed that the number of reprogrammed colonies increased when drug selection was initiated later (day 20 rather than day 3 posttransduction). This suggests that reprogramming is a slow and gradual process and may explain why previous attempts resulted in incomplete reprogramming. Takahashi et al. [25] showed that retrovirus-mediated transfection of OCT3/4, SOX2, KLF4, and c-Myc generates human iPS cells that are similar to hES cells in terms of morphology, proliferation, gene expression, surface markers, and teratoma formation. Yu et al. [26] showed that retroviral transduction of OCT4, SOX2, NANOG, and LIN28 could generate pluripotent stem cells without introducing any oncogenes (c-MYC). Both studies showed that human iPS were similar but not identical to hES cells.

Another concern is that these iPS cells contain three to six retroviral integrations (one for each factor) that may increase the risk of tumorigenesis. Okita et al. [27] studied the tumor formation in chimeric mice generated from Nanog iPS cells and found 20% of the offspring developed tumors due to the retroviral expression of c-Myc. An alternative approach would be to use a transient expression method, such as adenovirus-mediated system, since both Okita et al. and Meissner et al. [28] showed strong silencing of the viral-controlled transcripts in iPS cells. This indicates that these viral genes are only required for the induction, not the maintenance, of pluripotency.

Amniotic Fluid Stem Cells

An alternate source of stem cells is from amniotic fluid. Amniotic fluid is known to contain multiple partially differentiated cell types derived from the developing fetus. Stem cell populations were isolated from these sources, called amniotic fluid stem cells (AFSCs), that express embryonic and adult stem cell markers [29]. The undifferentiated stem cells expand extensively without a feeder layer, and the population doubles every 36 hours. Lines were maintained for over 250 population doublings retaining long telomeres and a normal karyotype. The AFS cells are broadly multipotent. Clonal human lines verified by retroviral marking can be induced to differentiate into cell types representing each embryonic germ layer, including cells of adipogenic, osteogenic, myogenic, endothelial, neuronal, and hepatic lineages. In this respect, they meet a commonly accepted criterion for pluripotent stem cells, without implying that they can generate every adult tissue. However, unlike hESCs, AFSCs do not form tumors in vivo, which would be advantageous in clinical applications. The cells could be obtained either from amniocentesis or chorionic villous sampling in the developing fetus or from the placenta at the time of birth. The cells could be preserved for self-use, could be used without rejection, or could be banked.

Adult Stem Cells and Native Progenitor Cells

One of the limitations of applying cell-based regenerative medicine techniques to organ replacement has been the inherent difficulty of growing specific cell types in large quantities. Even when some organs such as the liver have a high regenerative capacity in vivo, cell growth and expansion in vitro may be difficult. By studying the privileged sites for committed precursor cells in specific organs as well as exploring the conditions that promote differentiation, one may be able to overcome the factors that limit cell expansion in vitro. For example, though urothelial cells could be grown in the laboratory setting, these types of cultures had only limited expansion capability. Several protocols have been developed over the past two decades that have overcome this difficulty. Studies have identified the undifferentiated cells in a urothelial culture, and culture techniques to keep them undifferentiated during their growth phase have been developed [30–32]. Using these cell culture methods, it is now possible to expand a urothelial strain from a single specimen that initially covers a surface area of 1 cm^2 to one covering a surface area of 3202 m^2 (the equivalent of one football field) within 8 weeks [30]. These studies have indicated that it should be possible to collect autologous bladder cells from human patients, expand them in culture, and return them to the donor in sufficient quantities for reconstructive purposes. In fact, expanded urothelial cells have been used in several clinical studies, including an important study that showed that a tissue-engineered bladder could be implanted into select patients [33]. Major advances have been achieved within the past decade on the possible expansion of a variety of primary human cells, with specific techniques that make the use of autologous cells possible for clinical application.

TISSUE ENGINEERING OF SPECIFIC ORGANS OF THE GENITOURINARY TRACT

Lower Urinary Tract

Bladder

Regenerative medicine with selective cell transplantation may provide a means to create functional new bladder segments. The success of cell transplantation strategies for bladder reconstruction depends on the ability to use donor tissue efficiently and to provide the right conditions for long-term survival, differentiation, and growth. Various cell sources have been explored for bladder regeneration. Native cells are currently preferable due to their autologous source, wherein they can be used without rejection [30]. It has been shown experimentally that the bladder neck and trigone area has a higher propensity of urothelial progenitor cells [34], and these cells are localized in the basal region [35]. Amniotic fluid– and bone marrow–derived stem cells can also be used in an autologous manner and have the potential to differentiate into bladder muscle [36] and urothelium [37]. ES cells as described earlier also have the potential to differentiate into bladder tissue [38].

Human urothelial and muscle cells can be expanded in vitro, seeded onto polymer scaffolds, and allowed to attach and form sheets of cells. The cell–polymer scaffold can then be implanted in vivo. Histological analysis indicated that viable cells were able to self-assemble back into their respective tissue types and would retain their native phenotype [39]. It has been well established for decades that portions of the bladder are able to regenerate generously over free grafts, most likely because the urothelium is associated with a high reparative capacity [40]. However, bladder muscle tissue is less likely to regenerate in a normal fashion. Both urothelial and muscle ingrowth are believed to be initiated at the edges of the injury, from the normal bladder tissue in toward the region of the free graft. Usually, however, contracture or resorption of the graft has been evident. Inflammation in response to the matrix may contribute to the resorption of the free graft (Figures 27.1 and 27.2).

As a result of this discovery, it was hypothesized that building the 3D bladder constructs in vitro, before implantation, would facilitate the eventual terminal differentiation of the cells after in vivo implantation. Further, this could minimize the inflammatory response, thus avoiding graft contracture and shrinkage. In a dog model [2], matrices that were seeded with cells and then used for bladder augmentation retained most of their preimplantation diameter, as opposed to matrices implanted without cells, in which significant graft contraction and shrinkage occurred. In addition, histological analysis demonstrated a marked paucity of muscle cells and a more aggressive inflammatory reaction in the matrices implanted without cells. The results of these initial studies showed that the creation of artificial bladders may be achieved in vivo; however, it could not be determined whether the functional parameters noted were created by the augmented segment or by the remaining native bladder tissue.

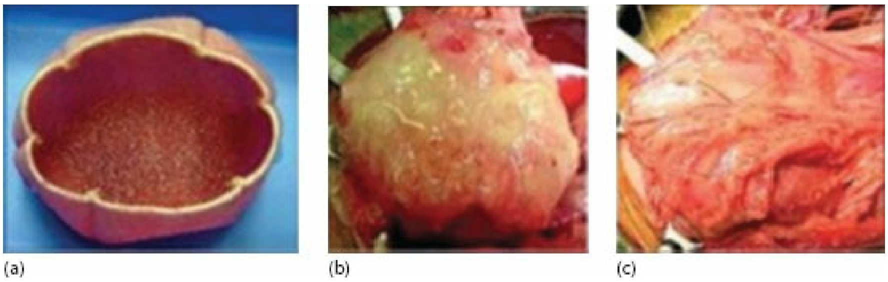

Figure 27.1 Scaffold seeded with cells (a) and engineered bladder anastomosed to native bladder with running 4-0 polyglycolic sutures (b). Implant covered with fibrin glue and omentum (c). (From Atala A et al., *Lancet*, 367(9518), 1241, April 15, 2006. With permission.)

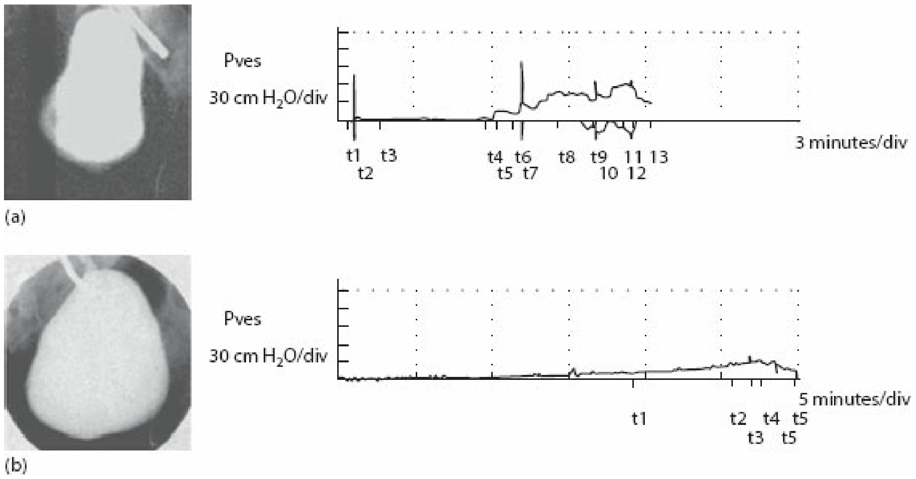

Figure 27.2 Preoperative (a) and 10-month postoperative (b) cystograms and urodynamic findings in a patient *i*th collagen–polyglycolic acid scaffold engineered bladder. (From Atala A et al., *Lancet*, 367(9518), 1241, April 15, 2006. With permission.)

Not all scaffold materials perform well if a large portion of the bladder must be replaced. In a study using SIS for subtotal bladder replacement in dogs, both the unseeded and cell-seeded experimental groups showed graft shrinkage and poor results [41]. This confirms that the type of scaffold used in the construction of tissue-engineered bladders is critical for the success of these technologies. The use of bioreactors, which provide mechanical stimulation for the growing organ in vitro, has also been proposed as an important parameter for success [42]. Bioreactors provide mechanical stimulation such as periodic stretching of the tissue, which has been shown to assist in in vitro muscle development, and exposure to flow conditions, which is important for the development of endothelial layers in blood vessels and hollow organs such as the bladder. In fact, Farhat and Yeger [42] have developed bioreactor systems specifically for bladder development. These systems provide simulated filling/emptying functions to the engineered tissue, and this may lead to a bladder construct with more functionality. A clinical experience involving engineered bladder tissue for cystoplasty was conducted starting in 1998. A small pilot study of seven patients reported the use of either collagen scaffolds seeded with cells or a combined PGA–collagen scaffold seeded with cells for bladder replacement. These engineered tissues were implanted with or without omental coverage. Patients reconstructed with engineered bladder tissue created with cell-seeded PGA–collagen scaffolds and omental coverage showed increased compliance, decreased end-filling pressures, increased capacities, and longer dry periods over time [33].

Although the experience to date is promising and shows that engineered tissues can be implanted safely, it is just a first step toward the goal of engineering fully functional bladders. Only a limited clinical experience exists to date, and the technology is not yet ready for wide dissemination, as further experimental and clinical studies are required.

Urethra

Various strategies have been proposed over the years for the regeneration of urethral tissue. Woven meshes of PGA without cells [43,44] or with cells [45] were used to regenerate urethras in various animal models. Naturally derived collagen-based materials such as decellularized BSM [4] and acellular urethral submucosa [46] have also been tested in various animal models for urethral reconstruction. The BSM matrix [4] proved to be a suitable graft for repair of urethral defects in rabbits. The grafts demonstrated a normal urothelial luminal lining and organized muscle bundles on the outer portion of the graft. These results were confirmed clinically in a series of men with a history of failed hypospadias reconstruction. The urethral defects in these patients were repaired with human bladder acellular collagen matrices [47]. The neourethral tissue was created by anastomosing the matrix to the urethral plate in an onlay fashion. The size of the created neourethra ranged from 5 to 15 cm. After a 3-year follow-up, three of the four patients had a successful outcome in regard to cosmetic appearance and function. One patient who had a 15 cm neourethra created developed a subglandular fistula (Figure 27.3).

Similar results were obtained in pediatric and adult patients with primary urethral stricture disease using the same collagen matrices [48]. Another study in 30 patients with recurrent stricture disease showed that a healthy urethral bed (two or fewer prior urethral surgeries) was needed for successful urethral reconstruction using the acellular collagen-based grafts [49]. More than 200 pediatric and adult patients with urethral disease have been successfully treated in an onlay manner with a bladder-derived collagen-based matrix. One advantage of this matrix over the traditional nongenital tissue grafts that have been used for urethroplasty is that the matrix material is “off the shelf.” This eliminates the necessity of additional surgical procedures for graft harvesting, which may decrease operative time as well as the potential morbidity due to the harvest procedure.

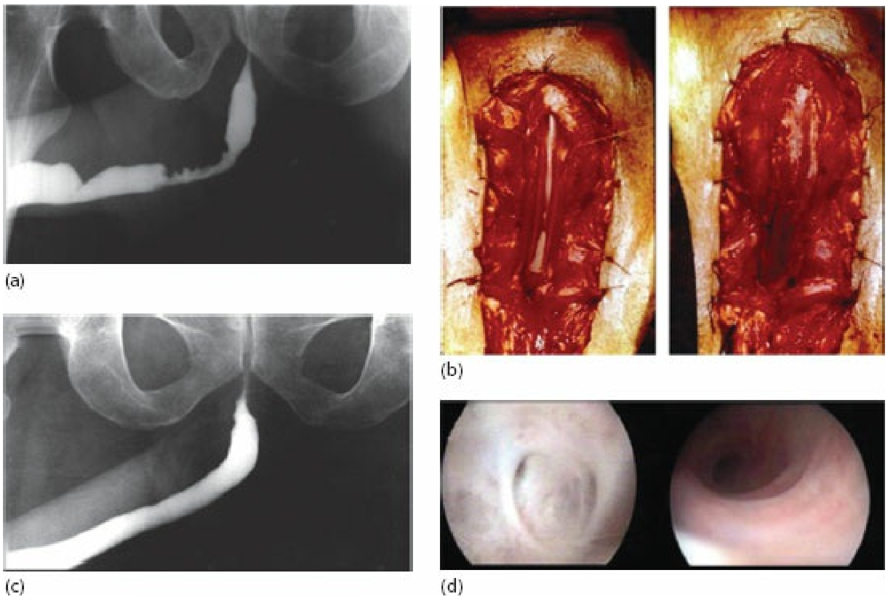

Figure 27.3 Representative case of bulbar stricture. Preoperative urethrogram (a). Urethral repair (b). Strictured tissue is excised, preserving the urethral plate on left side and matrix is anastomosed to urethral plate in an onlay fashion on right side. Urethrogram 6 months after repair (c). Cystoscopic view of urethra preoperatively on left side and 4 months after repair on right side (d). (From El-Kassaby AW et al., *J Urol*, 169(1), 170, January 2003. With permission.)

These techniques, which employed acellular matrices that had not been reseeded with cells, were applied experimentally and clinically in a successful manner for onlay urethral repairs. However, further study indicated that when tubularized urethral repairs with unseeded matrices were attempted experimentally, adequate urethral tissue regeneration was not achieved, and complications such as graft contracture and stricture formation occurred [50]. To determine if seeding the matrix with cells from the urinary tract could improve the results of tubularized urethral repairs, autologous rabbit bladder epithelial and smooth muscle cells were grown and seeded onto preconfigured tubular matrices. Entire urethral segments were then resected and urethroplasties were performed with tubularized collagen matrices either seeded with cells or without cells. The tubularized collagen matrices seeded with autologous cells formed new tissue that was histologically similar to native urethra. The tubularized collagen matrices without cells lead to poor tissue development, fibrosis, and stricture formation. These findings were confirmed clinically when a trial using tubularized nonseeded SIS for urethral stricture repair was performed in eight evaluable patients. Two patients with short inflammatory strictures maintained urethral patency. Stricture recurrence developed in the other six patients within 3 months of surgery [51].

Female Reproductive Organs

Uterus

Congenital malformations of the uterus may have profound implications clinically. Patients with cloacal exstrophy or intersex disorders may not have sufficient uterine tissue present for future reproduction. In addition, acquired causes including hysterectomy due to malignant or benign diseases or due to uterine adhesions are clinically important as the effect approximately 3%–5% of the population. For this group of patients, the only option of having genetic offspring is gestational surrogacy. The possibility of engineering functional uterine tissue using autologous cells has been investigated. Campbell et al. [52] performed a study in which the peritoneal cavity of rats and rabbits were used as in vivo bioreactors to produce uterine tissue grafts. In this study, biomaterial templates of the appropriate shape were implanted in the peritoneal cavities of rats or rabbits. After 2–3 weeks, the templates were removed, and the encapsulating myofibroblast-rich tissue that resulted from the foreign body response to the biomaterial was harvested. This tissue was then used to replace resected segments of the uterus in the same animals in which the tissue was grown. They reported that at 12 weeks after grafting, this novel uterine graft tissue thickened and developed the morphology of normal uterus. This structure included a lumen lined with endometrium, which was surrounded by several layers of smooth muscle cells (myometrium-like) interspersed with collagen. Importantly, these grafted uterine horns supported embryos to the late stages of gestation.

In another study by Li et al. [53], a collagen-targeting basic fibroblast growth factor (bFGF) delivery system was constructed. This bFGF delivery system was tested in a rat model of severe uterine damage. In this model, partial uterine horn excision was performed, and then the excised horn was reconstructed using the collagen-based delivery system. This study showed improved regeneration of both the endometrium and muscular cells, improved vascularization, and better pregnancy outcomes in the rats reconstructed with the system.

Uterine Cervix

The dysfunctional uterine cervix may also benefit from tissue engineering strategies. Spontaneous preterm birth is a frequent complication of pregnancy, and in some cases, abnormalities of the cervix have been implicated in this issue. House et al. [54] have shown that tissue engineering techniques can be used to create 3D cervical-like tissue constructs. Cervical cells were isolated from two premenopausal women and seeded on porous silk scaffolds. These constructs were cultured under dynamic or static culture conditions. After an 8-week culture interval, cervical cells had proliferated in all three dimensions and had synthesized an ECM with biochemical constituents and morphology similar to native tissue, but this matrix was better formed under dynamic culture conditions. This study suggested that it may be possible to engineer cervical tissue for a variety of conditions.

Vagina

Similarly, several pathological conditions, including congenital malformations like Mayer–Rokitansky–Kuster–Hauser (MRKH) syndrome, cloaca or thick transverse vaginal septum, obstetric trauma, and malignancy, can adversely affect normal vaginal development or anatomy. Vaginal reconstruction has traditionally been challenging due to the paucity of available native tissue. The feasibility of engineering vaginal tissue in vivo has been investigated [55]. Vaginal epithelial and smooth muscle cells of female rabbits were harvested, grown, and expanded in culture. These cells were seeded onto biodegradable polymer scaffolds, and the cell-seeded constructs were then implanted into nude mice for up to 6 weeks. Immunocytochemical, histological, and Western blot analyses confirmed the presence of vaginal tissue phenotypes. Electrical field stimulation studies in the tissue-engineered constructs showed similar functional properties to those of normal vaginal tissue. When these constructs were used for autologous total vaginal replacement, patent vaginal structures were noted in the tissue-engineered specimens, while the non-cell-seeded structures were noted to be stenotic [55]. The first case of creation of a human vagina using autologous in vitro cultured vaginal tissue has also been reported [56]. The patient had MRKH syndrome and tissue was grown from a 1 cm^2 biopsy of vaginal vestibular mucosa. Autologous reconstructed vaginal tissue reached 314 cm^2 in 2 weeks. A McIndoe–Reed–type procedure was then performed to create a vaginal space to allow inlay of cultured tissue. Clinical exam demonstrated a vaginal vestibular mucosa with normal length and depth with normal vaginal tissue on biopsy [57] (Figures 27.4 and 27.5).

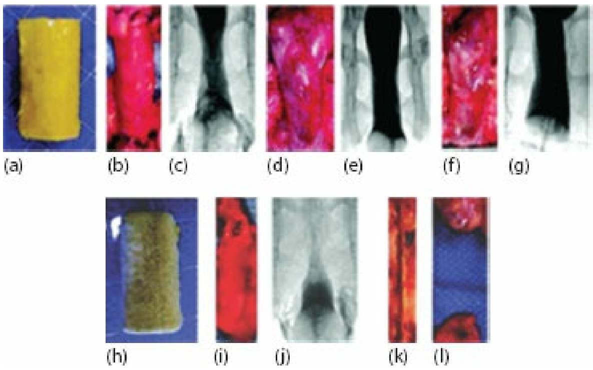

Figure 27.4 Appearance of tissue-engineered neovaginas. (a) Tubular polymer scaffold after cell seeding and 1-week in vitro culture, before implantation in vivo. (b, d, f) Gross appearance and (c, e, g) vaginography of cell-seeded constructs 1, 3, and 6 months, postimplantation, respectively. (h) Unseeded control scaffold before implantation. (i, k, l) Gross appearance of unseeded construct at 1, 3, and 6 months postimplantation. (j) Vaginography of unseeded graft at 1 month. (From De Filippo RE et al., *Transplantation*, 86(2), 208, July 27, 2008. With permission.)

Ovary

The fundamental role of the ovary is to produce oocytes capable of fertilization as well as to secrete hormones that will prepare the uterus for successful implantation. Ovarian sex steroids also play a major role in breast development, bone health, and sexual function in the female. A number of pathological conditions such as premature ovarian failure and cancer chemotherapy may severely compromise reproductive function. In addition, with the decline of sex steroid hormones around natural menopause, significant pathology, such as vasomotor symptoms, genital atrophy, and bone loss, ensues. In the attempt to restore a functional ovary, several approaches have been employed at the experimental level. Some of the significant approaches include regenerating ovarian tissues from stem cells, transplanting ovarian tissues, and use of tissue engineering tools.

Regenerating Ovarian Tissues from Stem Cells

It was previously considered that the germ cell renewal (formation of oocyte and follicle) is restricted to fetal life. A decade ago, Johnson et al. [60], during their investigation of follicular atresia in adult mouse, identified a group of cells in the ovarian surface epithelium immunostained positive for germ cell–specific marker, mouse vasa homologue, and showed BrdU (5-bromodeoxyuridine) incorporation. These germ-line stem cells (GSCs) were reported to maintain the oocyte and follicle production in the postnatal ovary. Even though there existed a debate on the existence of these stem cells in adult mammalian ovaries and their potential significance, a report by Zou et al. [61] provided concrete evidence that they are capable of producing offspring. The existence of these GSCs in an adult mammalian (mouse) ovary was reported to be exceedingly rare (0.014%) [62], and they seemed to decline with age [63]. As an alternative, extraovarian stem cells such as bone marrow–derived stem cells [64], ES, and iPS have been used to produce oocyte-like cells [63]. The differentiating ES were reported to have various limitations including their heterogeneity, which makes the in vitro oogenesis from these stem cells challenging.

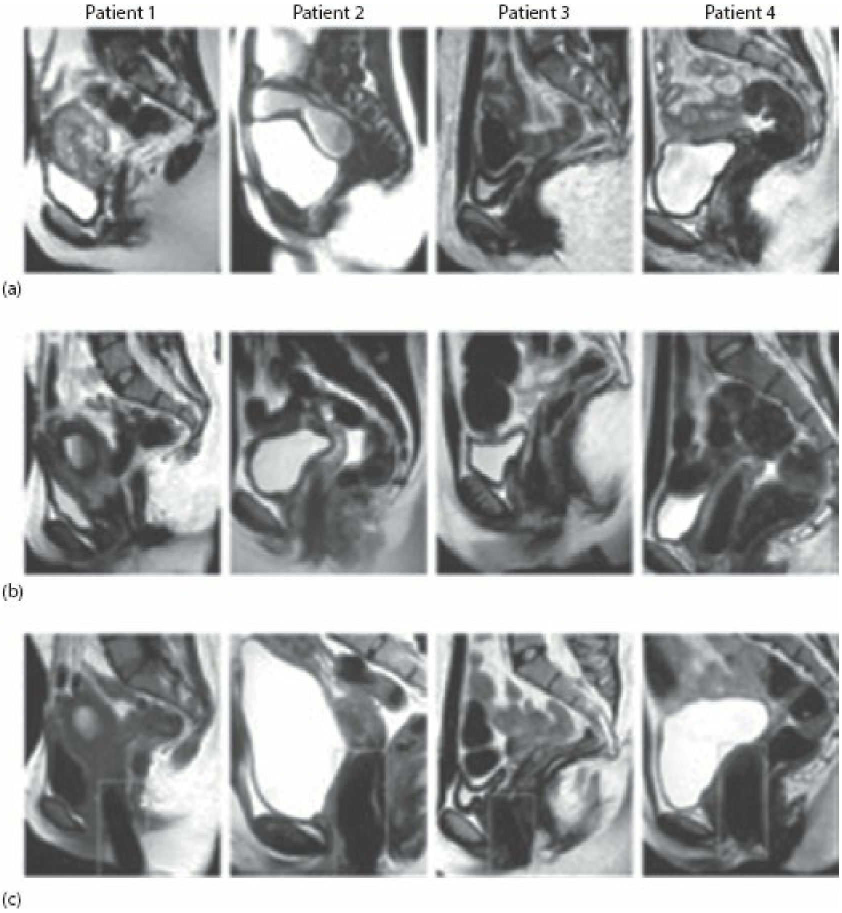

Figure 27.5 Preoperative and postoperative MRI images. Preoperative MRI images show absence of vaginal organs (a). MRIs 1 year after surgery show engineered vaginal organs (b). Latest MRI images up to 8 years after surgery (c) (boxes within the MRIs show engineered vaginal organs). (From Raya-Rivera AM et al., *Lancet*, 384(9940), 329, July 26, 2014. With permission.)

Autologous Transplantation of Ovarian Tissues after Cryopreservation or In Vitro Activation

Cryopreservation of ovarian tissues retrieved from both donors and autologous sources is another feasible approach to restore lost ovarian function. Autologous transplantations of cryopreserved whole ovary or partial ovarian tissues into rabbits [65], sheep [66,67], and monkeys [68] were reported to exhibit functions of the ovary including follicle development, resumption of regular cycles, and ovulation with corresponding hormone patterns. Kawamura et al. [69] reported a promising technique for autologous transplantation that recapitulates the fertility in a murine ovarian failure model, where follicular growth was induced through disruption of the Hippo signaling. When it comes to heterologous (allogenic or xenogenic) transplantation, the graft tissue has to be protected from the host immune system either by immune suppression or by immunoisolation. As discussed later, the use of tissue engineering tools is considered as a viable approach to overcome the immune hurdles. Since the functional unit of the ovary (follicle) is comprised of three major cells types, namely, oocyte, granulosa, and theca cells, and are extremely interdependent on each other for function, it has been a challenge to come up with a tissue design to accommodate all these cells in the same construct.

Tissue Engineering Approaches in Ovarian Biology

Recently, new in vitro culture methods involving tissue-engineered matrices have been developed to study the maturation of ovarian follicles [70,71]. The 2D culture systems support the production of immature mouse follicles or granulosa cell–oocyte complexes where the granulosa cell is attached to the culture substrate and migrates away from the oocyte [72]. In contrast, Shikanov et al. [73] have developed hydrogels to mimic the native ovarian environment by maintaining the 3D follicular architecture, cell–cell interactions, and paracrine signaling that direct follicular development. In this system, fibrin and alginate are gelled simultaneously and make up an interpenetrating network (FA-IPN). The degradable component of this FA-IPN may be particularly critical for clinical translation in order to support the greater than millionfold increase in volume that human follicles normally undergo in vivo. Krotz et al. [74] developed a design that they claimed as prefabricated self-assembled artificial human ovary. In this design, theca cells were cultured to form a honeycomb structure using agarose molds and later cumulus–oophorus complexes (COCs) were seeded in the luminae (multiple openings of the honeycomb structure). After 72 hours, theca cells surrounded the COCs and formed self-assembled complex microtissues reported to support the development of the oocyte, which was evident from the polar body extrusion. These kinds of artificial ovarian tissues serve as useful tools for in vitro maturation. On the other hand, for the purpose of cell-based hormone replacement therapy, Sittadjody et al. [75] have developed an engineered multilayer ovarian tissue model that secretes sex steroids and peptide hormones in response to gonadotropins in vitro. Theca and granulosa cells placed in different layers of multilayer alginate microcapsules that mimic the architecture of native follicles, their endocrine functions were found to be more potent than two other possible combinations. Similarly, encapsulated endocrine cells implanted into the peritoneum of rodents have been reported to deliver hormones in ovariectomized animals [76].

CONCLUSION

Regenerative medicine technologies for virtually every type of tissue and organ are currently being developed. Various tissues are at different stages of development. Some tissues have been used clinically such as bladder, urethral, and vaginal tissue, while others are still in preclinical development. The recent explosion in research in this field suggests that engineered tissues will likely represent a viable therapeutic option for patients in the future.

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Section IV

Diagnostic Evaluation of Incontinence and Urogenital Prolapse

28 History and Examination

Vik Khullar and Rhiannon Bray

INTRODUCTION

A precise history and examination are integral to the management of women with bladder or pelvic floor dysfunction. An accurate history is required to determine a woman's symptoms; a thorough examination ascertains the woman's signs. While this chapter deals with salient aspects of history and examination, it should be remembered that this information alone is not sufficient in the assessment of a woman. Other tools are employed to supplement the information obtained from taking a history and examining a woman. These include bladder diary and questionnaires to determine the impact of symptoms on her quality of life, expectations, and goals.

The most recent standardization document produced jointly by the International Continence Society (ICS) and International Urogynecology Association (IUGA) defines symptoms as any morbid phenomenon or departure from the normal in structure, function, or sensation experienced by the woman and indicative of disease or a health problem [1]. Symptoms are either volunteered by or elicited from the individual or may be described by the individual's caregiver. The environment, the activities of daily living, and a woman's ability to cope with her disease can profoundly alter her quality of life. A woman who is always close to a toilet may not notice her urinary frequency, but the same woman with no access to a toilet may have urinary incontinence, wear protective pads, and be severely incapacitated.

Can the severity of urinary symptoms be modified by behavior? Lifestyle changes are first-line treatments in the management of women with lower urinary tract symptoms (LUTS). Reduction of fluid intake improves symptoms of urgency and frequency [2]. Women with severe detrusor overactivity may restrict their fluid intake to less than 200 mL per day. On direct questioning, the urinary problem may not appear severe, with a normal diurnal urinary frequency, and it is only with a frequency/volume chart that a complete picture of the severity of symptoms can be determined. The volume of urine excreted relies not only on fluid intake but also on the secretion of antidiuretic hormone, which is impaired in diabetes insipidus. The circadian secretion of this hormone may be affected in women suffering nocturia and nocturnal polyuria [3].

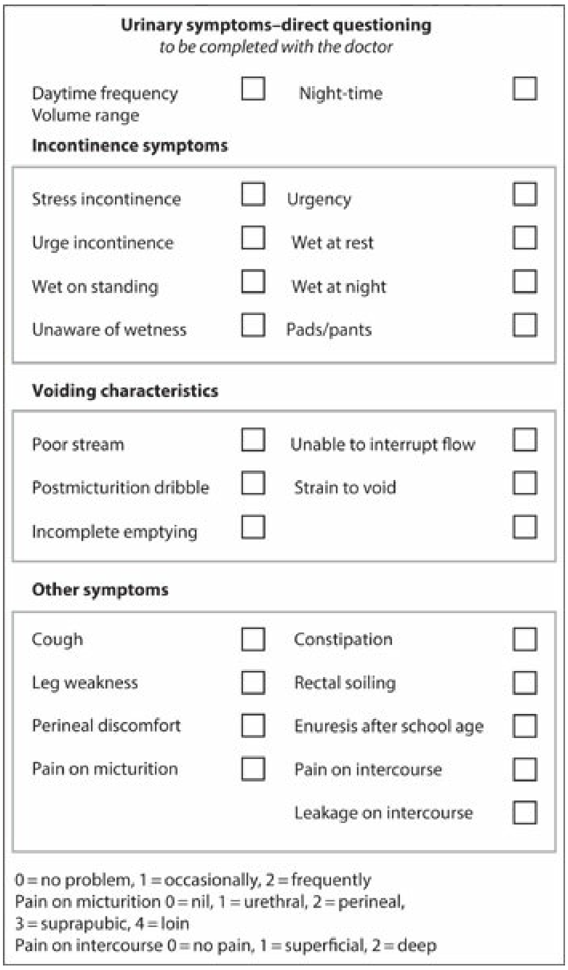
The most recently published ICS/IUGA standardization report on lower urinary tract terminology was published in 2010 [1], and the definitions used in this chapter are according to the terminology used in the report. The use of standardized terminology during the taking of the history is essential as it ensures accurate characterization of symptoms.

History

History taking must take place using the woman's own words. Women often fail to understand terms such as stress incontinence with a majority thinking that this relates to being mentally stressed and then leaking [4]. Therefore, symptomatic women may misclassify their urgency incontinence as stress incontinence due to this misunderstanding. This is then clarified into an easily understandable list of graded symptoms using a standard questionnaire (Figure 28.1). In a large study of women in five countries, the overall prevalence of urinary incontinence was 13.1%, with stress urinary incontinence the most common subtype (6.4%), followed by mixed urinary incontinence (2.4%) and urgency incontinence (1.5%) [5]. Across all countries surveyed, this trend is consistent. In another large cross-sectional web-based survey of over 15,000 women, the prevalence of stress urinary incontinence at least "sometimes" was found to be as high as 31.8% and urgency incontinence 24.4% [6]. Current data describe a wide variation in prevalence rates of incontinence in women, but the latest International Consultation on Incontinence reports that 10% of all adult women report leakage at least weekly and 25%–45% experience occasional leakage [7]. In general, the prevalence of all types of incontinence increases with age.

When comparing the symptoms and final urodynamic diagnosis, there is a marked overlap between diagnostic groups. A diagnosis based on history corresponds to urodynamic diagnosis in only up to 55% of women [8]. However, the use of a self-completed symptom questionnaire does produce a better relationship between urinary symptoms and urodynamic diagnosis [9]. Symptom complexes have been used in an attempt to improve diagnostic accuracy. The use of a bladder diary to enable patients to record fluid intake, output, and incontinence episodes for at least 24 hours can be extremely helpful in the initial assessment of urinary incontinence. It may also be therapeutic as it provides insight into bladder behavior, and it can be utilized to monitor the effectiveness of treatment during follow-up.

If symptoms are not of diagnostic value, why record them? Symptoms are valuable as a guide in determining treatment. In addition, symptoms should be taken into consideration during the urodynamic test as the provocative maneuvers should mimic conditions encountered by the woman in her normal daily activities and lead to her urinary symptoms. A 90-year-old woman with urgency and no stress incontinence is an inappropriate candidate for performing “star jumps” with a full bladder!



Urinary symptoms–direct questioning
to be completed with the doctor

Daytime frequency ☐
Volume range
Night-time ☐

Incontinence symptoms

Stress incontinence ☐
Urge incontinence ☐
Wet on standing ☐
Unaware of wetness ☐
Urgency ☐
Wet at rest ☐
Wet at night ☐
Pads/pants ☐

Voiding characteristics

Poor stream ☐
Postmicturition dribble ☐
Incomplete emptying ☐
Unable to interrupt flow ☐
Strain to void ☐
☐

Other symptoms

Cough ☐
Leg weakness ☐
Perineal discomfort ☐
Pain on micturition ☐
Constipation ☐
Rectal soiling ☐
Enuresis after school age ☐
Pain on intercourse ☐
Leakage on intercourse ☐

0 = no problem, 1 = occasionally, 2 = frequently
Pain on micturition 0 = nil, 1 = urethral, 2 = perineal,
3 = suprapubic, 4 = loin
Pain on intercourse 0 = no pain, 1 = superficial, 2 = deep

Figure 28.1 Standard questionnaire for urinary symptoms.

When questioning women complaining of urinary symptoms, all symptoms complained of should be explained in a woman’s own words. Stress incontinence is the term used to describe the symptom of urinary leakage that occurs with effort or exertion or on coughing or sneezing.

The severity of each symptom and its effect on the woman’s quality of life are noted, as improvement can be achieved through directing treatment to relieve the troublesome symptoms. The length of time that the symptoms have been present discriminates between transient and established incontinence and whether this has changed over time. General enquiry should be made of all urinary symptoms as the woman may not be able to describe them or may be too embarrassed to mention them. For this reason, a questionnaire is a useful guide as it ensures that all symptoms are enquired about.

The questionnaire should be validated in the language in which it is to be used and often the symptom questionnaire will be attached to a quality-of-life questionnaire [10,11]. The method used to obtain the symptoms will alter the answers. Questionnaires postally administered appear to produce higher severity responses from patients than the same questions used in an interview; this is particularly the case with questions of an embarrassing nature such as those relating to incontinence with sexual activity [12].

Table 28.1 Classification of Symptoms into Groups

- Abnormal storage
  - Incontinence: urge, stress
  - Frequency/nocturia
  - Nocturnal enuresis
- Abnormal voiding
  - Straining to void
  - Hesitancy
  - Incomplete emptying
  - Poor stream
  - Postmicturition dribble
- Abnormal sensation
  - Urgency
  - Dysuria
  - Absent sensation
  - Painful bladder

Symptoms can be grouped into storage LUTS, voiding LUTS, or postmicturition LUTS (Table 28.1). However, this classification of symptoms does not help in diagnosis as the same symptom can be produced by different mechanisms. For example, overflow incontinence can produce symptoms similar to those of detrusor overactivity: urinary frequency in overflow incontinence is caused by incomplete bladder emptying resulting in a reduced bladder capacity, whereas detrusor overactivity causes urinary frequency due to an overactive detrusor.

URINARY SYMPTOMS

Urinary Incontinence

Urinary incontinence is a failure of urinary storage and requires careful evaluation; it is defined as the complaint of any involuntary loss of urine [1]. It is important that incontinence is regarded as a symptom or a sign and not a diagnosis. Severe urinary incontinence of any origin has overlapping symptoms associated with urethral sphincter incompetence and detrusor overactivity. There are many causes of urinary incontinence (Table 28.2). It is important to determine whether the urine loss is continuous or intermittent.

Continuous urine loss is rare. It is usually seen when there is an ectopic ureter or fistula, and the woman will often complain of nocturnal incontinence as opposed to nocturnal enuresis. This occurs most often following pelvic surgery or as a result of malignancy or radiotherapy. Obstetric fistulae are more commonly seen in developing countries. Some women complain that they are “never dry” and suffer from severe intermittent urinary incontinence rather than a continuous loss of urine. This occurs in women who have had multiple previous operations and have a fixed and fibrosed “drainpipe” (type 3) urethra [13]. Otherwise, women who complain of urinary loss “all the time” have severe detrusor overactivity.

Table 28.2 Causes of Urinary Incontinence

- Urethral sphincter incompetence
  - Sphincter dysfunction
  - Abnormal bladder neck support
- Detrusor overactivity
  - Idiopathic detrusor overactivity
  - Neurogenic detrusor overactivity (e.g., multiple sclerosis, spinal trauma)

- Mixed incontinence
- Urethral diverticula
- Congenital abnormalities (e.g., epispadias, ectopic ureter, bladder exstrophy, spina bifida occulta)
- Transient incontinence
  - Urinary tract infection
  - Restricted mobility
  - Constipation
  - Excessive urine production
    - Diuretic therapy
    - Diabetes mellitus
    - Diabetes insipidus
    - Cardiac failure
    - Hypercalcemia
  - Confusion (e.g., dementia, acute illness)
  - Atrophic urethritis and vaginitis
- Pharmacological causes (e.g., diuretics, tranquilizers, cholinergic agents, prazosin)
- Fistulae (e.g., urethral, vesical, ureteral)
- Overflow incontinence
  - Hypotonic detrusor
  - Rarely urethral obstruction
- Urethral instability
- Functional

The pattern of intermittent urinary incontinence should be linked with associated activity such as physical exercise, laughing, putting the key in the front door, sexual intercourse, or orgasm. The severity of the incontinence can be quantified not only by volume but also by the type and number of pads or changes of underwear required in 24 hours and the magnitude of the provoking stimulus. There is often little relationship between the findings of urodynamic tests and the symptoms described by the woman in her daily life, and this may reflect modifications in behavior and lifestyle that she has made to ameliorate the effect of lower urinary tract dysfunction. It does not, however, reduce the importance of the urinary symptoms as they may still be impairing her quality of life. Often, women will not admit to urinary incontinence but state that they leak when a history is taken.

Urgency and Urgency Incontinence

Urgency is the sudden compelling desire to pass urine that is difficult to defer [1]. Urgency incontinence is the involuntary leakage of urine that is accompanied or immediately preceded by urgency [1]. Often, women will describe getting the sensation of the desire to void and not getting to the toilet in time. The quantity of urine lost can be anything from a few drops on lowering the undergarments prior to voiding to quite a large volume, and it is not uncommon for the patient to describe at least one occasion where the urine has poured down both legs uncontrollably.

This may be triggered by changes in temperature, opening the front door, hearing running water, and occasionally during sexual intercourse or orgasm. As the main coping strategy for this symptom is increasing voiding frequency, pad usage or incontinent episodes are not useful in assessing the severity of the condition.

The overactive bladder syndrome is defined as urgency, usually accompanied by increased daytime frequency and nocturia, with or without urgency urinary incontinence, in the absence of urinary tract infection or other obvious pathology [1].

Increased Daytime Frequency

Daytime frequency is the number of times a woman voids during waking hours; normal diurnal frequency is considered to be between four to seven voids per day. In a symptomatic population, the range may be greater. Increased daytime frequency is defined as the complaint by the patient that she voids more frequently during waking hours then previously deemed normal by the woman [1]. Accordingly, this is a subjective definition dependent on each individual rather than a numerical cutoff. Increased daytime frequency is not diagnostic for detrusor overactivity or for urodynamic stress incontinence although women with detrusor overactivity do void more frequently overall. Clustering of voids during the day may suggest a cause such as diuretics prescribed for congestive cardiac failure, drinking large volumes of fluid, or bad habit. Increased daytime urinary frequency may occur for a number of reasons (Table 28.3). The diurnal frequency does not increase with age in the symptomatic population seen in a urodynamic clinic (Table 28.4). The 95% upper limit of normal for urinary frequency in an asymptomatic population has been reported as being 13 voids per day, and this suggests a wide variation in the normal population as the median and mean values in this test–retest study was eight and seven, respectively [14].

Nocturia

Nocturia is defined as the complaint that the patient has to wake one or more times during the night to void; each void is preceded and followed by sleep [1]. It is important to discriminate between nocturia and a woman voiding because she is awake. It is difficult to be precise about the prevalence of nocturia, but approximately 50% of adults report waking once at night and 24% waking twice [5]. Waking twice or more has been associated decreased quality of life and increased bother [15]. Nocturia can be extremely disruptive and affect quality of life as well as being associated with other comorbidities such as hip fractures in the elderly [16]. The normal upper limit to the number of voids alters with age. If a woman passes urine more than once a night up to the age of 70 years, this is abnormal; voiding at night increases on average once every decade after the age of 70 in normal women (Table 28.5). This change is probably due to changing sleep patterns in the elderly. There may also be an effect of comorbidity—for example, postural effects resulting from daytime pooling of extracellular fluid in the lower limbs returning to the vascular compartment at night, as a result of subclinical heart failure.

Table 28.3 Causes of Abnormal Urinary Frequency

- Increased fluid intake and urine output; normal bladder capacity
  - Osmotic diuresis (e.g., diabetes mellitus).
  - Abnormal antidiuretic hormone production (e.g., diabetes insipidus).
  - Polydipsia; often the woman enjoys drinking a favorite beverage and only rarely is the behavior psychotic.
- Reduced functional bladder capacity
  - Inflamed bladder, increasing bladder sensation (e.g., acute bacterial cystitis, interstitial cystitis)
  - Detrusor overactivity
  - Habit or fear of urinary incontinence
  - Urinary residual secondary to detrusor hypotonia or outlet obstruction (rare)
  - Increased bladder sensation, normal bladder (e.g., anxiety)
- Reduced structural bladder capacity
  - Fibrosis after infection (e.g., tuberculosis)
  - Noninfective cystitis (e.g., interstitial cystitis, carcinoma)
  - Irradiation fibrosis (e.g., for bladder or cervical carcinoma)
  - Postsurgery (e.g., partial cystectomy)
  - Detrusor hypertrophy
- Decreased urinary frequency
  - Detrusor hypotonia
  - Impaired bladder sensation (e.g., diabetic neuropathy)
  - Reduced fluid intake

Table 28.4 Diurnal Frequency in a Symptomatic Populationa

Age (years)	**Mean frequency**	***n***
5–14	6.00	5
15–24	4.48	41
25–34	5.47	176
35–44	6.31	364
45–54	6.05	513
55–64	5.87	361
65–74	5.63	263
75–84	5.04	137
85–94	5.93	33

Total: 1893

[a] Patients seen in the urodynamic clinic, King’s College Hospital, London, between January 1993 and September 1994.

Table 28.5 Nocturnal Voids and Nocturia with Agea

Age (years)	**Mean voids per night**	**Nocturia (%)**	***n***
5.14	0.8	0	5
15–24	1.24	17	41
25–34	1.79	27	176
35–44	1.83	38	364
45–54	1.53	30	513
55–64	1.94	31	361
65–74	2.2	47	263
75–84	2.55	46	137
85–94	2.69	58	33

[a] Patients seen in the urodynamic clinic, King’s College Hospital, London, between January 1993 and September 1994.

It is important to discriminate between the woman who is awake and therefore voids and the woman who is woken by the desire to void; the first group of women often have no increase in their diurnal urinary frequency.

Nocturnal Enuresis

Nocturnal enuresis is the complaint of involuntary loss of urine occurring during sleep. It is important to differentiate between this complaint and waking with urgency and then leaking before arriving at the toilet, which is urgency urinary incontinence.

Nocturnal enuresis can be primary or secondary. Primary nocturnal enuresis starts in childhood and can persist into adulthood, the woman never having consistently been dry at night. Secondary nocturnal enuresis is when the incontinence restarts in adulthood following a period of nighttime continence, even if it resolved as a child.

The causes of nocturnal enuresis can be abnormal circadian secretion of antidiuretic hormone, detrusor overactivity or abnormal control of the micturition reflex, or abnormal sleep pattern. A family history should be sought and the presence of diurnal symptoms noted.

Nocturnal Urine Volume

This is defined as the total volume of urine passed between the time the individual goes to bed with the intention of sleeping and the time of waking with the intention of rising. Therefore, it excludes the last void before going to bed but includes the first void after rising in the morning.

Nocturnal Polyuria

Nocturnal polyuria is present when an increased proportion of the 24 hour output occurs at night (normally during the 8 hours while the patient is in bed). The normal range of nocturnal urine production differs with age and normal ranges have not been defined. Generally, nocturnal polyuria is present when more than 20% (young adults) to 33% (greater than 65 years) is produced at night.

Stress Urinary Incontinence

Stress urinary incontinence is defined as the involuntary loss of urine with exertion or effort or with coughing and sneezing. It is associated with activities involving a rise in intra-abdominal pressure without associated urgency and must be differentiated from urgency urinary incontinence when obtaining a history. The accuracy of diagnosing urodynamic stress incontinence based on the pure symptom of stress urinary incontinence (even with a normal frequency/volume chart) is poor, with 8% of incontinence in this group being due to detrusor overactivity or other causes [17].

Mixed Urinary Incontinence

Women with mixed urinary incontinence satisfy the definitions for having both stress urinary incontinence and urgency urinary incontinence. The prevalence of mixed urinary incontinence is variable but can account for approximately 40% of Western women who present with symptoms of urinary incontinence [18]. It is important to determine the balance between the two symptoms, ascertaining that one bothers her more as this can guide initial management. Women with mixed urinary incontinence are a challenge to manage and have an associated worse outcome after continence surgery than women with pure stress urinary incontinence [19].

Postural Urinary Incontinence

This is a new definition produced by the joint report of IUGA/ICS [1]. It defines postural incontinence as the complaint of the loss of urine associated with change of body position, for example, rising from a seated or lying position.

Coital Incontinence

The latest definition of coital incontinence produced by the joint report of IUGA/ICS describes coital incontinence as the complaint of involuntary loss of urine associated with coitus that may be further subdivided into incontinence with penetration or with orgasm. Urinary leakage on penetration is more likely to occur in women with urethral sphincter incompetence and with a cystocele. This type of urinary incontinence is not associated with urgency. Urinary incontinence can also occur with orgasm. The leakage may be associated with urgency and is thought to be related to detrusor overactivity [20].

Insensible Incontinence

Insensible incontinence is the occurrence of urinary leakage where the woman is unaware of how it occurred. Women may describe discovering urine in their underwear or on a pad that they wear at the end of the day because of the involuntary leakage of which they were unaware.

VOIDING SYMPTOMS

Voiding difficulties may present with a variety of symptoms. Voiding symptoms are symptoms experienced during the voiding phase [1].

Hesitancy

Hesitancy is defined as the description by an individual of having difficulty in initiating micturition [1] resulting in a delay of the onset of voiding after she is ready to pass urine. It is not common in women but when described the volume voided on these occasions should be noted as attempting to void with only a small volume in the bladder can be difficult even where bladder function is normal. However, hesitancy when voiding with a full bladder may be an indication that (1) the urethral sphincter is not relaxing when the detrusor contracts (voiding dysfunction or there is neurological disease, detrusor sphincter dyssynergia), (2) the detrusor muscle is not contracting effectively during voiding, or (3) psychological inhibition of bladder contraction, which might be considered in women who report only being able to void when alone. This symptom of hesitancy does not discriminate between these potential causes. Women with increased daytime frequency may complain of hesitancy and poor stream but this probably relates to the small volumes of urine passed.

Straining to Void

Straining to void describes the muscular effort used to initiate, maintain, or improve the urinary stream [1]. The intra-abdominal pressure is increased during a Valsalva maneuver, which increases the intravesical pressure and this can improve the instantaneous flow rate. The urinary stream is impaired overall and may be intermittent, each transient increase in flow associated with an increase in intra-abdominal pressure. In the longer term, this method of voiding can lead to the development of urogenital prolapse.

Incomplete Emptying

The feeling of incomplete emptying is a self-explanatory term for a feeling experienced by the individual after passing urine [1]. The sensation can be due to the fluid remaining in the bladder and can be secondary to an abnormality of sensation or due to after contractions in women with detrusor overactivity. Women in the latter group rarely have increased postmicturition urinary residual volumes.

Women with prolapse can develop a functional obstruction of the urethra due to external compression and may have urinary residuals. A cystocele can act as a sump and a rectocele can press anteriorly on the urethra in women who void by straining, preventing complete emptying. Urinary retention is now defined as the inability to pass urine despite persistent effort. This may be also caused by urinary tract infection, the presence of an intra-abdominal mass such as fibroid uterus or gravid uterus, or a consequence of neurological compromise such as women who suffer stroke, spinal cord injury, or multiple sclerosis.

Postmicturition Dribble

Postmicturition dribble is the term used when an individual describes the involuntary loss of urine immediately after she has finished passing urine [1], usually after leaving the toilet in men or after rising from the toilet in women. This symptom may be related to a urethral diverticulum, a cystourethrocele, or detrusor overactivity. Where detrusor contractions occur after the completion of voiding, urgency will often accompany the urinary leakage. Postmicturition dribble should be distinguished from terminal dribble, which is the term used when an individual describes a prolonged final part of micturition when the flow has slowed to a trickle or dribble [1].

Slow Stream

Slow stream is reported by the individual as a perception of reduced urine flow [1], usually compared to previous performance or in comparison to others. Decreased urinary stream is often described as “decreased force.” Urine flow rate is dependent on the volume of urine passed; if it is less than 150 mL, this should be assessed with reference to a frequency/volume chart. A reduced urine flow can be due to voided volumes below 150 mL, bladder outflow obstruction (2% of women), or decreased bladder contractility. Detrusor sphincter dyssynergia can produce intermittent flow that can be due to a neuropathic cause where the urethral sphincter does not relax during voiding or a myopathic cause.

Position-Dependent Micturition

This new definition describes the complaint of having to adopt specific positions to be able to micturate spontaneously or improve bladder emptying. Women may describe squatting, sitting forward on the toilet, or leaning backward in order to void.

Bladder/Urethral Pain

Pain, discomfort, and pressure are part of a spectrum of abnormal sensations felt by the individual. Pain produces the greatest impact on the patient and may be related to bladder filling or voiding, may be felt after micturition, or be continuous. Pain should also be characterized by type, frequency, duration, and precipitating and relieving factors and by location such as bladder, urethral, vulval, vaginal, and perineal pain. Dysuria, strangury, and bladder spasm are not recommended terms as these symptoms are difficult to define.

Urethral Pain

This is felt in the urethra and the individual indicates the urethra as the site [1]. It is often described as “burning on passing urine” and can be aggravated by sexual intercourse. As an isolated symptom, it is associated with urinary tract infections or urethritis.

Bladder Pain

Bladder pain is felt suprapubically or retropubically and usually increases with bladder filling [1]; it may also persist after voiding. Bladder pain may be associated with inflammation of the bladder, bladder stones, or tumor. Some women complain of pain after voiding, which might be associated with detrusor overactivity.

The presence of bladder pain is an indication for cystoscopy and occasionally bladder biopsy.

Suprapubic pain may also be associated with the pathology outside the bladder but within the pelvis and thus would be called pelvic pain. Endometriosis on the bladder may cause urethral pain, which is present at certain times in the menstrual cycle. Pelvic inflammatory disease may cause urethral pain; however, the woman will often have symptoms of vaginal discharge and pyrexia.

Table 28.6 Causes of Loin Pain

Vesicoureteric reflux
Renal trauma
Acute ureteric obstruction Stone Blood clot Papillary necrosis
Chronic ureteric obstruction Tumor (e.g., transitional cell carcinoma, renal cell carcinoma, Wilms' tumor) Ureteric stricture Retroperitoneal fibrosis Stone Congenital anomaly
Renal inflammation Pyelonephritis Perinephric abscess
Renal infarction

Loin Pain

This pain originates in the flank and radiates to the groin of the ipsilateral side. The pain is referred from the sensory nerves innervating the kidney and ureter, for which there are many causes (Table 28.6). Acute or chronic obstruction of the urinary tract can cause pain. This becomes more acute as the pressure generated within the urinary tract is higher. Loin pain during voiding and loin pain associated with urgency in women with detrusor overactivity may indicate vesicoureteric reflux.

Dyspareunia

This is the symptom of pain during sexual intercourse. This can be subdivided into superficial and deep dyspareunia. Superficial dyspareunia may be associated with vaginal dryness or following episiotomy or vaginal wall repair. Dyspareunia associated with compression of the anterior vaginal wall may reflect bladder or urethral pain syndromes. Perineal pain is felt between the posterior fourchette and the anus and may be persistent or recurrent episodic. It may be related to the micturition cycle or associated with symptoms suggestive of urinary tract or sexual dysfunction [1].

Prolapse Symptoms

Pelvic organ prolapse often coexists with and may contribute to LUTS. Women may describe the feeling of a lump, heaviness, a dragging sensation in the vagina, or lower back pain. They may also describe the learned behavior of using their fingers to reduce the bulge in order to successfully micturate or defecate, which is referred to as digitation. As vaginal prolapse alters the range of treatments for urinary incontinence, enquiries about symptoms of vaginal prolapse and prolapse affecting micturition and defecation should be made. The feeling of a lump at or beyond the vaginal introitus, low back ache, heaviness, dragging sensation, or the need to digitally replace or support the prolapse in order to defecate or micturate are among the symptoms that may be described. Over 40% of women with urethral sphincter incompetence will also have significant cystoceles, making this an important symptom affecting management of a woman's urinary incontinence. As vaginal prolapse can mask urethral sphincter incompetence (occult incontinence) it is important to identify any prolapse before a urodynamic test so that a vaginal ring can be inserted during the filling phase of urodynamics to expose any underlying urethral incompetence (21).

Hematuria

Visible blood in the urine (“frank hematuria”) should always be investigated as a priority, according to national guidelines. Microscopic hematuria should also be investigated, but trace amounts of blood on dipstick urinalysis can probably be disregarded.

GYNECOLOGICAL SYMPTOMS

It is important to enquire about changes in urinary symptoms during the menstrual cycle and note the woman’s menopausal state as the lower urinary tract has estrogen receptors [22]. Previous continence operations have an important influence on the future success of continence surgery, as the urethral sphincter may be altered by scarring and damage to sphincter innervation by previous vaginal surgery, as well as distortion and narrowing of the bladder neck. Operations on the uterus may interfere with the innervation of the bladder, particularly after radical hysterectomy for carcinoma and radiotherapy.

PAST MEDICAL HISTORY

It is important to record all past major abdominal and pelvic surgery, and urinary complications as a result of the surgery should be noted. The postoperative course can often be revealing, particularly when women have been unable to void spontaneously and required catheterization. This could indicate prolonged overdistension that can lead to voiding difficulties due to detrusor underactivity. Surgery to the spine and any resulting neurological impairment must be recorded. Operations on the large bowel, especially those involving dissection at the side wall of the pelvis, such as abdominoperineal resection of the rectum may result in denervation.

Conditions increasing abdominal pressure, such as chronic cough or constipation, can produce the symptom of stress urinary incontinence and make the problem more severe. Cardiac and renal failure can increase daytime and nighttime voiding frequency through polyuria. Obstructive sleep apnea leads to the release of atrial natriuretic peptide due to cardiac distension caused by the negative pressure environment in the chest. This cardiac hormone increases sodium and water excretion and also inhibits other hormone systems that regulate fluid volume, vasopressin, and the renin–angiotensin–aldosterone complex leading to nocturnal polyuria. Endocrine disorders such as diabetes mellitus or diabetes insipidus may lead to polyuria and polydipsia. Chronic diabetes mellitus can increase frequency as a result of overflow incontinence secondary to a hypotonic detrusor and impaired bladder sensation.

There does appear to be an association between schizophrenia and detrusor overactivity [23]. Additionally, women suffering from dementia may not empty their bladders frequently and may not be aware of the need to void.

The number of proven urinary tract infections during the past 2 years should be recorded. Childhood enuresis after the age of 6 years is particularly important as often these patients have detrusor overactivity.

The obstetric history should include parity, length of labor, mode of delivery, and weight of the largest infant; however, such information may not be useful as the details of labor are not always recalled accurately. Cesarean section or epidural block during labor and the retention of urine postpartum are possible progenitors of voiding difficulties [24,25].

NEUROLOGICAL HISTORY

Many neurological conditions can cause problems for the bladder, bowel, or sexual function. Women should be questioned regarding symptoms of limb weakness or altered sensation. This may be subtle, such as altered sensation during sexual intercourse or an inability to feel their urinary stream during micturition. Women with neurological symptoms may also report the symptom of intermittency. Any history of multiple sclerosis, parkinsonism, spinal cord injury, stroke, or spina bifida should be recorded. Diabetes mellitus and cerebrovascular accidents can also result in symptoms secondary to peripheral neuropathy. Worsening symptoms of back pain with urinary and neurological symptoms warrants a general neurological examination.

DRUG HISTORY

Many drugs affect the lower urinary tract. Diuretics can produce urgency, increased daytime frequency, and urgency urinary incontinence. Benzodiazepines sedate and may cause confusion and secondary incontinence, particularly in elderly patients [27]. Alcohol impairs mobility, produces a diuresis, and can impair the woman’s perception of bladder filling. Drugs that have anticholinergic side effects impair detrusor contractility and may cause urinary retention with secondary overflow incontinence. These include antipsychotic drugs, antidepressants, opiates, antispasmodics, and antiparkinsonian drugs. This could be compounded by other drugs such as beta-3 adrenoceptor agents. Drugs that improve bladder storage are shown in Table 28.7.

Sympathomimetic drugs, often found in cold remedies, can increase the urethral sphincter resistance and produce voiding difficulty. Alpha-adrenergic blockers, such as doxazosin used to treat hypertension, may have cause bladder smooth muscle or urethral relaxation and resultant stress urinary incontinence [26,27]. Cystitis is a common complication of chemotherapy treatment, and hemorrhagic cystitis can result from certain types of antineoplastic treatment. Chemotherapy-induced cystitis can arise from agents directly instilled into the bladder as part of a treatment program for superficial cancer of the bladder or from toxic metabolites of renally excreted antineoplastic agents, which come in contact with the bladder. Drugs that improve bladder emptying are shown in Table 28.8.

Table 28.7 Drugs That Improve Urine Storage

- Anticholinergic drugs
  - Propantheline bromide
  - Emepronium bromide/carrageenate
  - Tolterodine
  - Darifenacin
  - Solifenacin
- Musculotropic drugs
  - Oxybutynin chloride
  - Dicycloverine chloride
  - Flavoxate hydrochloride
- Calcium antagonists
  - Nifedipine
  - Flunarizine
- Tricyclic antidepressants
  - Imipramine
  - Doxepin
- b-adrenoceptor agonists
  - Mirabegron
  - Terbutaline
  - Salbutamol
  - Isoprenaline
- a-adrenoceptor antagonists
  - Phenoxybenzamine
  - Prazosin
- Prostaglandin synthetase inhibitors
  - Flurbiprofen
  - Indomethacin
- Neurotoxins
  - Capsaicin
  - Resiniferatoxin
- Drugs reducing urine production
  - Desmopressin
- Drugs increasing outlet resistance
  - a-adrenergic agonists
    - Phenylpropanolamine hydrochloride
    - Midodrine
  - Serotonin–noradrenaline reuptake inhibitors
    - Duloxetine
  - b-adrenergic antagonist
    - Propranolol
- Estrogens

Table 28.8 Drugs That Improve Bladder Emptying

Increased detrusor contractility
Cholinergic agents
Carbachol
Bethanechol
Anticholinesterase
Distigmine
Prostaglandins
$E2_{\alpha}$
$F2_{\alpha}$
Decreased outlet resistance
a-sympathetic blocking agents
Phenoxybenzamine
Phentolamine
Prazosin
Striated muscle relaxants
Baclofen
Dantrolene
Lisidonal
Diazepam

More recently, questionnaires assessing goals and expectations have been developed and validated in a number of languages. They appear to show some promise in an open-label study of treating patients suffering from overactive bladder [28–30].

EXAMINATION

Before examining the woman, it is important to reassure her about the possibility of urinary leakage and explain that she should not be embarrassed as a result of this. The woman’s mobility and mental state play a role in her ability to react to her incontinence problem and may influence management. A minimental state examination can be performed, as well an assessment of the woman’s motivation and manual dexterity, as these may influence her compliance with possible treatments and follow-up.

Abdominal examination precedes vaginal assessment. Inspection will reveal evidence of previous abdominal surgery, and palpation may demonstrate the presence of a full or distended bladder as well as other abdominal or pelvic masses or elicit pain. It is important to perform a screening neurological examination testing the tone, strength, and movement of the lower limbs. It is particularly useful to test the abduction and spreading of toes as the innervation for the lateral abductors comes from S3. The anal tone should be assessed. In women with neurological disease, the presence of the bulbocavernosus reflex (reflex contraction of the anal sphincter elicited by gentle tapping of the clitoris) indicates that sensory and motor pathways related to the urogenital tract are intact. Additionally, a voluntary cough should cause a reflex contraction of the anal sphincter. An intact sacral reflex can be tested by stroking the skin lateral to the anus, which should elicit a contraction of the external anal sphincter.

GYNECOLOGICAL EXAMINATION

The condition of the vulval skin is important as there may be signs of excoriation, edema, or erythema due to exposure of the skin to urine on the vulva for prolonged periods of time and concomitant candidiasis. Vaginal atrophy, particularly in women more than 10 years after the menopause, may be seen. The skin has deep rugae where the skin is rubbing on underwear secondary to vaginal prolapse.

Genital prolapse can now be assessed using the methods produced by the ICS and IUGA’s most recent report on the standardization of terminology [1]. It suggests that women should be assessed with an empty bladder and ideally an empty rectum because an increased bladder volume can restrict the degree of descent of the vaginal prolapse. Any cystocele, rectocele, uterine, or vault descent can be best assessed in the Sims’ (left lateral) position on coughing and straining using a Sims’ speculum. Alternatively, examination may also be made in lithotomy using the lower blade of a Graves’ speculum to assist in assessing the opposite vaginal wall [31]. Women may also be examined standing and this may be the only way for a vaginal prolapse to be demonstrated successfully [32]. The best position is one which the woman feels best reproduces her prolapse. After the examination for pelvic organ prolapse, the clinician should report the degree of prolapse in terms of the descent of the anterior and posterior vaginal walls, as well as the cervix, or in the case of a woman who has had a hysterectomy, the vaginal vault. Various staging or grading methods have been described and the level of the hymen is usually used. The pelvic organ prolapse quantification system is a validated method that involves using a measuring device marked in centimeters to measure specific points on the anterior and posterior vaginal wall as well as the descent of the cervix or vaginal cuff allowing quantification of the degree of vaginal prolapse [33]. This method allows prolapse staging from 0 to IV where 0 is no prolapse, stages I to III are increased descent of the prolapse through the vagina, and stage IV is complete eversion of the total length of the genital tract. Women can be reproducibly examined in the left lateral and standing positions [32]. The vagina should also be examined for evidence of atrophy, inflammation, pain, or scarring from previous surgical procedures. Other aspects of pelvic examination include examination of the urethra where urethral mucosal prolapse or a caruncle may be seen. A urethral diverticulum may present with a midline anterior vaginal wall swelling or with tenderness over the length of the urethra as well as postmicturition leakage. Vaginal cysts such as Gartner's duct cyst may present with similar findings. If a woman is complaining of a discharge or has had a recent onset of symptoms of urgency and frequency, it may be useful to obtain swabs to culture for *Chlamydia*, atypical organisms, or gonococcus. A bimanual examination should be performed to exclude abnormal pelvic organs, masses, or uterine impaction and can exclude a large postmicturition urinary residual. Pelvic masses such as ovarian cysts and uterine enlargement greater than 12 weeks size can cause pressure symptoms on the bladder and rectum resulting in urinary frequency or retention; often, the symptoms resolve once the mass has been removed.

Table 28.9 Modified Oxford Scale

Grade 0: No discernable PFM contraction
Grade 1: A flicker or pulsing under the examining finger—a very weak contraction
Grade 2: A weak contraction—an increase in tension in the muscle without any discernable lift or squeeze
Grade 3: A moderate contraction—characterized by a degree of lifting of the posterior vaginal wall and squeezing on the base of the finger with indrawing of the perineum
Grade 4: A good PFM contraction producing elevation of the posterior vaginal wall against resistance and indrawing of the perineum
Grade 5: A strong contraction of the PFM

Pelvic floor muscle (PFM) examination may be appropriate that assesses tone at rest and strength with voluntary and reflex contraction. This may be assessed with digital palpation circumferentially. The ICS has produced a standardized document that details PFM assessment [34], and the Oxford classification has been used as a simple clinical assessment [35] (Table 28.9). If pelvic pain is a problem, it is important that a digital examination is performed to assess where the pain originates and in particular to determine trigger points in the levator ani and also tenderness upon palpation of the pelvic organs adjacent to the vagina. The PFM hyperalgesia scoring system has been proposed as a validated method of pelvic floor assessment in women with chronic pelvic pain [36]. Finally, rectal examination is particularly important in the elderly to exclude fecal impaction, which can aggravate urinary incontinence.

CONCLUSION

History and examination alone cannot diagnose female urinary disorders but are used to guide future investigation and management. The method in which symptoms are ascertained may alter the results and self-completed questionnaires seem to be the best. It is important to use reproducible and validated questionnaires as symptoms alone have become the basis of conservative management and have been suggested as indicators for the surgical treatment of pure stress incontinence. In some cases, an obvious cause can be found and treated, thus potentially avoiding the need for further investigations.

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29 Bladder Diary and Symptom Scores

Alan Uren and Nikki Cotterill

INTRODUCTION

Patients that present with lower urinary tract dysfunction can complain of a variety of symptoms. However, lower urinary tract and voiding disorder symptoms are notoriously unreliable for an accurate diagnosis [1–3]. There are a number of approaches that a clinician may employ in order to lend some objectivity to the formulation of clinical hypotheses, of which patient-reported outcome (PRO) measures are gaining increasing importance. Symptom scores calculated through the completion of PRO questionnaires are also important for initial diagnostic and outcome assessment. Follow-up questionnaires also allow the monitoring of any improvement, placing the patient's lived experience at the center of ongoing evaluation.

URINARY DIARY

One of the most commonly used methods of investigating a patient's symptoms is by the completion of a urinary diary (UD). It is typically completed by the patient over a number of days prior to the visit to the doctor and records information such as the times of micturition, voided volumes, and fluid intake. The use of such tools is stipulated in the guideline algorithms in the assessment of lower urinary tract symptoms (LUTS) and incontinence. The UK National Institute for Health and Care Excellence (NICE) currently recommends their use for the initial assessment of women presenting with urinary incontinence or overactive bladder [4]. However, despite the value of bladder diaries for clinical diagnosis and patient management, an audit by the Royal College of Physicians [5] concluded that bladder diaries are often underused in primary and acute care.

Although the UD in various formats has been used extensively as a clinical tool for many years [6], until recently there has been very little attempt at formal diary development and validation [7]. The format and content of a UD is often left to the discretion of the clinician so as a result, many different diaries are currently in use [8]. The International Continence Society (ICS) recognizes three types of UDs in terms of the parameters that are recorded [9]:

1. Micturition chart records the times of micturition, day and night, for a period of at least 24 hours.
2. Frequency–volume chart (FVC) records the voided volumes as well as the times of micturition, day and night, for at least 24 hours.
3. Bladder diary records the voided volumes and times of micturition as well as other information, day and night, for at least 24 hours.

A large number of additional parameters have been suggested for inclusion in a bladder diary (e.g., pad use or fluid intake). However, there is a balance between collecting enough useful clinical information and minimizing any burden placed on the patient during completion [2]. Bright et al. [8] collated patient and clinician opinions in order to identify the content thought essential. Over 30 different parameters were considered, but time of void, volume of void, fluid intake, time and amount of incontinence were deemed to be the most important parameters for the utility of a generic bladder diary. Pad use and bladder sensation are also considered important information, as these can have a significant effect on the quality of life of the patient.

DURATION

Studies that investigate optimal diary duration have shown that a UD that is too short may not capture the desired information, whereas one that is too long may reduce patient compliance, resulting in poor completion rates [2,10,11]. Several studies explore optimum diary duration [2,10–12] and vary from 24 hours to 7 days in length [7].

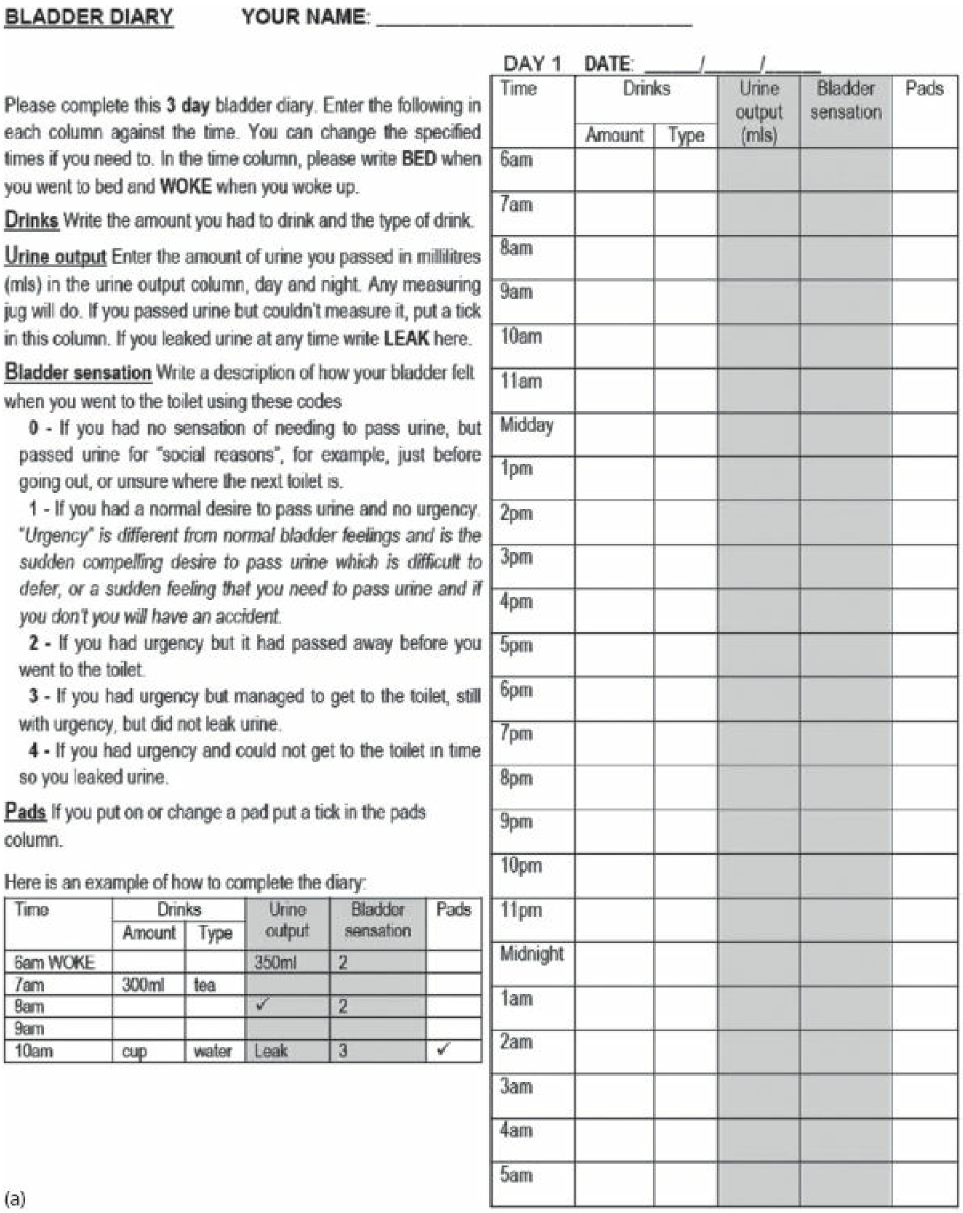
There are no clear guidelines for the optimal duration of record keeping. However, a 3-day or 4-day FVC or diary for day-to-day use in clinical practice is suitable for the assessment of LUTS [8]. It is also recognized that a 1-day FVC can sometimes be sufficient to gain insight into daily voiding habits, but a 7-day diary may be required for "atypical clinical patterns or research." The current NICE guidelines recommend the diary should be of at least 3 days duration and cover both work and leisure days to represent variations in their usual activities [4].

ICIQ BLADDER DIARY

A comprehensive validation process for a standardized patient reported measure is required when introducing new assessment tools for their acceptance in the guidelines and regulatory context. Validation should include the "assessment of content, construct and criterion validity, and analysis of reliability and responsiveness" [7]. Until recently, no fully validated diaries existed. However, following a review of the existing literature [7], a 3-day diary has been developed and subjected to the full psychometric validation protocol used to develop the International Consultation on Incontinence Questionnaire (ICIQ) modules [13]. It is accepted as the "ICIQ bladder diary [14] (Figure 29.1)." The final UD records urinary frequency, voided volume, and fluid intake (including type, time, and amount). The time of each event is recorded next to the time covering the full 24 hours for each of the 3 days. In addition to this, there is a column in which to record the bladder sensation score, included within the diary, which allows the patient to describe their sensation of urgency for each micturition. The versatility of the diary is also improved by the inclusion of a further column to record pad use. Although it is recognized that no diary is likely to be "one size fits all," following the rigorous validation process, the ICIQ bladder diary is accepted as being a good generic diary to assess patients with LUTS for day-to-day clinical practice.

ELECTRONIC DIARIES

The development of an electronic diary is particularly relevant when considering the rapid increase of electronic technology both in clinical practice and within our society. There are several potential advantages for the use of an electronic bladder diary. Primarily, it facilitates data entry and allows automatic calculation, allowing the immediate review of the essential parameters by the clinician. This has the potential to reduce the workload in busy clinics, reduce calculation errors, and ultimately improve clinical outcomes. A recent pilot study using a sample of 22 patients tested the clinical utility of a handheld electronic diary [15]. The accuracy of the report was 58% when calculated manually from the paper version, compared with 100% accuracy when electronically calculated. In addition, the handheld electronic diary was preferred by 81% of patients over the paper diary with reasons given such as "saves time" and "easier to complete." This preference by some patients for an electronic diary is supported by previous studies [16,17]. However, it is recognized that a definitive study in order to test this electronic diary equivalence is required, particularly noting that younger people are more likely to adopt such approaches more readily than the elderly. An electronically based adaptation of a paper-based diary must be shown to produce data that are of at least equivalent or higher reliability. This may be shown through full psychometric testing [18].



BLADDER DIARY **YOUR NAME:** ______________________________

Please complete this **3 day** bladder diary. Enter the following in each column against the time. You can change the specified times if you need to. In the time column, please write **BED** when you went to bed and **WOKE** when you woke up.

Drinks Write the amount you had to drink and the type of drink.

Urine output Enter the amount of urine you passed in millilitres (mls) in the urine output column, day and night. Any measuring jug will do. If you passed urine but couldn't measure it, put a tick in this column. If you leaked urine at any time write **LEAK** here.

Bladder sensation Write a description of how your bladder felt when you went to the toilet using these codes

0 - If you had no sensation of needing to pass urine, but passed urine for "social reasons", for example, just before going out, or unsure where the next toilet is.

1 - If you had a normal desire to pass urine and no urgency. *"Urgency" is different from normal bladder feelings and is the sudden compelling desire to pass urine which is difficult to defer, or a sudden feeling that you need to pass urine and if you don't you will have an accident.*

2 - If you had urgency but it had passed away before you went to the toilet.

3 - If you had urgency but managed to get to the toilet, still with urgency, but did not leak urine.

4 - If you had urgency and could not get to the toilet in time so you leaked urine.

Pads If you put on or change a pad put a tick in the pads column.

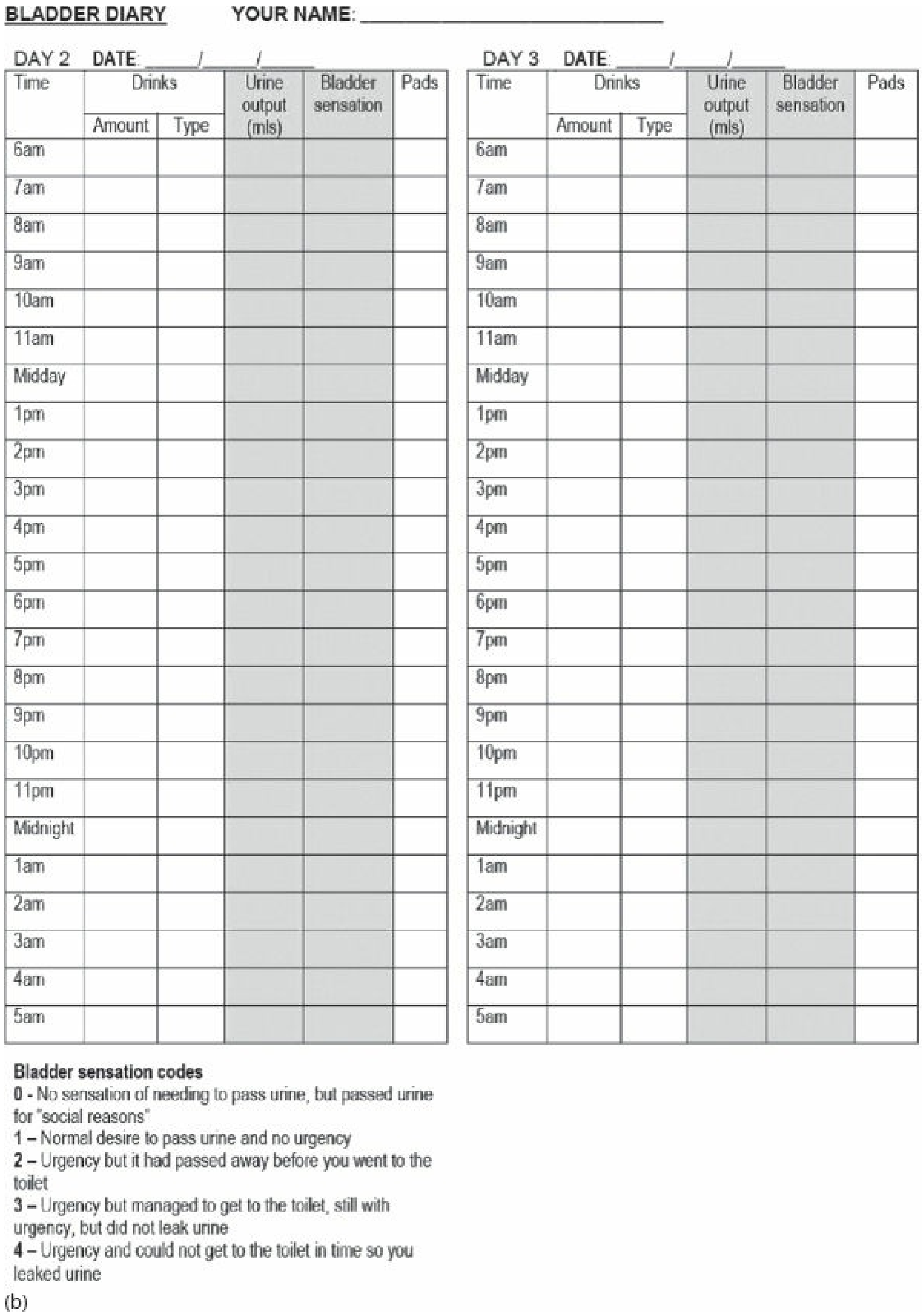
Here is an example of how to complete the diary:

Time	Drinks		Urine output	Bladder sensation	Pads
	Amount	Type			
6am WOKE			350ml	2	
7am	300ml	tea			
8am			✓	2	
9am					
10am	cup	water	Leak	3	✓

(a)

DAY 1 DATE: ____/____/____

Time	Drinks		Urine output (mls)	Bladder sensation	Pads
	Amount	Type			
6am					
7am					
8am					
9am					
10am					
11am					
Midday					
1pm					
2pm					
3pm					
4pm					
5pm					
6pm					
7pm					
8pm					
9pm					
10pm					
11pm					
Midnight					
1am					
2am					
3am					
4am					
5am					



BLADDER DIARY **YOUR NAME:** ____________________

DAY 2 DATE: _____/_____/_____

Time	Drinks		Urine output (mls)	Bladder sensation	Pads
	Amount	Type			
6am					
7am					
8am					
9am					
10am					
11am					
Midday					
1pm					
2pm					
3pm					
4pm					
5pm					
6pm					
7pm					
8pm					
9pm					
10pm					
11pm					
Midnight					
1am					
2am					
3am					
4am					
5am					

DAY 3 DATE: _____/_____/_____

Time	Drinks		Urine output (mls)	Bladder sensation	Pads
	Amount	Type			
6am					
7am					
8am					
9am					
10am					
11am					
Midday					
1pm					
2pm					
3pm					
4pm					
5pm					
6pm					
7pm					
8pm					
9pm					
10pm					
11pm					
Midnight					
1am					
2am					
3am					
4am					
5am					

Bladder sensation codes

0 - No sensation of needing to pass urine, but passed urine for "social reasons"

1 – Normal desire to pass urine and no urgency

2 – Urgency but it had passed away before you went to the toilet

3 – Urgency but managed to get to the toilet, still with urgency, but did not leak urine

4 – Urgency and could not get to the toilet in time so you leaked urine

(b)

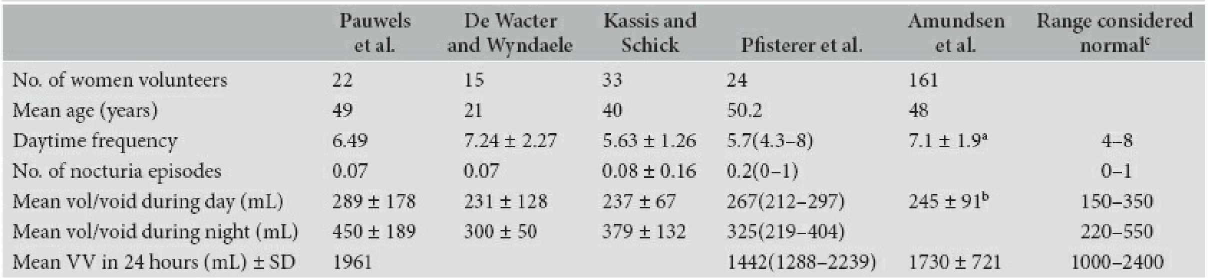
Figure 29.1 International Consultation on Incontinence Questionnaire bladder diary developed by Bright et al. [14].

NORMATIVE VALUES

A number of studies have attempted to provide a reference range for the parameters calculated from voiding diary data [19–24]. However, all parameters are extremely variable so actually defining what is considered "normal" presents challenges [23–25]. There is also considerable overlap in the range of what may be considered "normal limits" between asymptomatic patients and symptomatic patients [24,26,27]. Table 29.1 represents the values obtained from populations of asymptomatic volunteers as reported in the published literature.

Further to this variability, independent studies by Amundsen et al. [24] and van Haarst et al. [23] show that in asymptomatic females, as the age of the patient increases, the volume/void decreases and the frequency increases. For example, an older woman of 70 years old is likely to have a higher frequency and smaller volume/void than a 20-year-old woman. In addition to this, independent of age, there is a positive relationship between maximum volume voided during the day (functional bladder capacity) and the total 24 hour volume. Here, a woman who voids a large amount over 24 hours is likely to have a higher frequency and larger volume per void than a woman of similar age who only voids a smaller amount over 24 hours. One hypothesis is that this may be an adaptation to keep the voiding frequency relatively constant by adjusting the bladder capacity to compensate for changes in fluid intake. Nevertheless, these relationships have implications for the clinical interpretation of bladder diaries.

Table 29.1 "Normal Limit" Range Obtained from Populations of Asymptomatic Patients as Reported in Published Literature



	Pauwels et al.	De Wacter and Wyndaele	Kassis and Schick	Pfisterer et al.	Amundsen et al.	Range considered normal[c]
No. of women volunteers	22	15	33	24	161	
Mean age (years)	49	21	40	50.2	48	
Daytime frequency	6.49	7.24 ± 2.27	5.63 ± 1.26	5.7(4.3–8)	7.1 ± 1.9[a]	4–8
No. of nocturia episodes	0.07	0.07	0.08 ± 0.16	0.2(0–1)		0–1
Mean vol/void during day (mL)	289 ± 178	231 ± 128	237 ± 67	267(212–297)	245 ± 91[b]	150–350
Mean vol/void during night (mL)	450 ± 189	300 ± 50	379 ± 132	325(219–404)		220–550
Mean VV in 24 hours (mL) ± SD	1961			1442(1288–2239)	1730 ± 721	1000–2400

Source: Adapted from Al Afraa T et al., *Int Urogynecol J*, 23, 681, 2012.

Note: Values are presented as mean ± standard deviation and for Pfisterer et al., the median and interquartile range.

[a] Value represents frequency over 24 hours.

[b] Value represents average voided volume over 24 hours.

[c] Approximate range taken from values obtained from the literature shown.

Amundsen et al. argue that as age and the total 24 hour voided volume influence the functional bladder capacity, it is necessary to adjust for these parameters. Table 29.2 shows the voiding frequency, mean 24 hour voided volume, and maximum 24 hour voided volume after adjusting for age and 24 hour volume by subjecting the data to multiple regression analysis. As might be expected, even after adjustment, the voiding frequency still increases with both age and voided volume over 24 hours. However, it is reported to reduce the variability of the frequency and functional bladder capacity by about 25% and 50%, respectively. Here, correcting for age and fluid intake increases the sensitivity of the diary to detect increased frequency and reduced FBC.

SYMPTOM SCORES

Further information about symptoms may be collected by the completion of a PRO questionnaire [28]. This usually includes some assessment of the impact on the quality of life, as well as the perceived severity of symptoms as reported by the patient. A scoring scheme for each question provides some quantification of the severity of symptoms and may also be used to evaluate the effectiveness of any management strategy at a later stage [14,29]. Information gathered from symptom scores combined with the UD forms the basis for the consultation by which the clinician attempts to reach a provisional diagnosis before proceeding with any necessary further diagnostic testing. Despite this, an audit by the Royal College of Physicians [5] found that over a quarter of acute care patients did not have their urinary symptoms recorded. An assessment of the impact of incontinence on the quality of life was recorded in only 69% of primary care and 25% of acute care patients.

Although PRO measures are widely used in order to assess patient perspectives [30], several clinician-completed scores are also available [31,32]. However, it is acknowledged that there is likely to be the potential for bias introduced by the interviewer [33] and the agreement between patients and clinicians regarding satisfaction with treatment outcomes is known to be poor [34]. There is also a direct relationship between patient satisfaction and the fulfillment of treatment expectations [35]. For this reason, the emphasis in current clinical practice is capturing the patients' lived experience rather than from the clinicians' perspective.

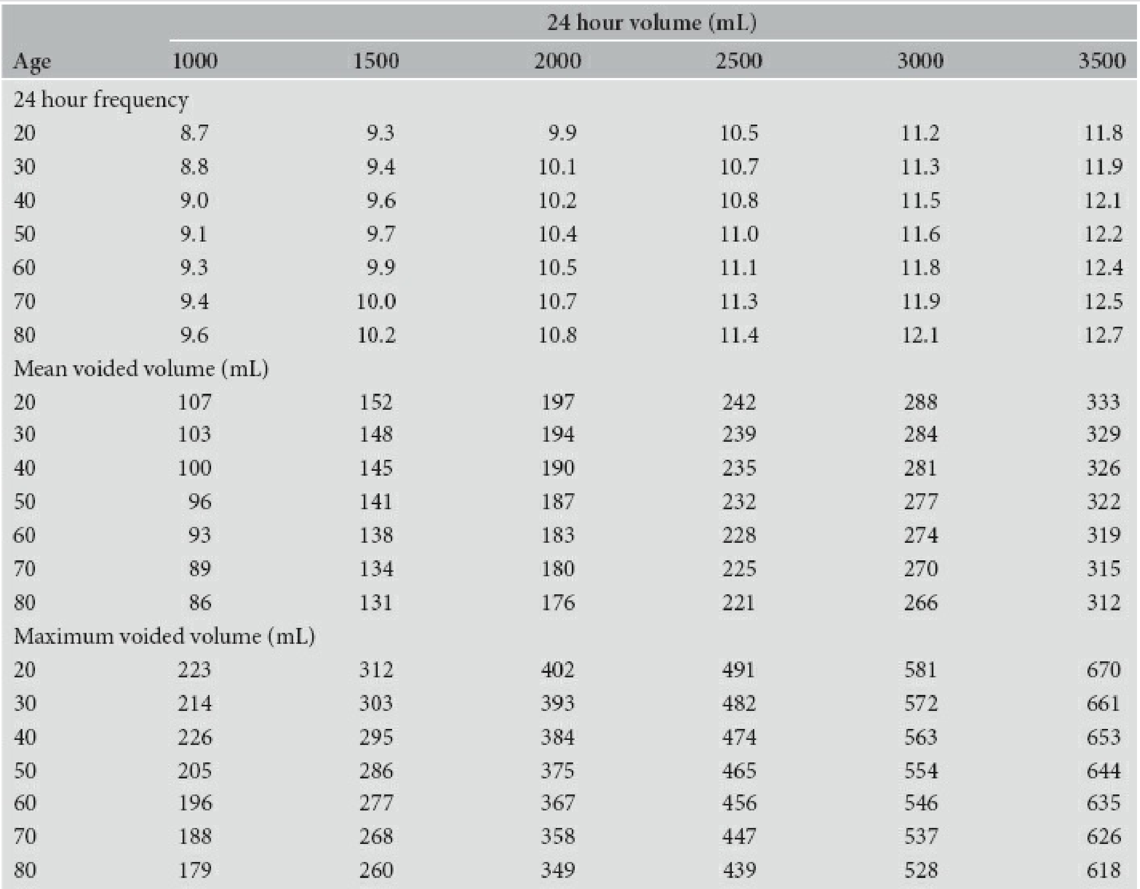
VALIDITY AND RELIABILITY

Consideration of the development and validation studies employed to develop symptom scores is essential given their importance for clinical assessment [36–38]. Section 2 provides a detailed discussion of how PRO questionnaires are developed, but it is important to ensure that clinical symptom scores have published evidence of their

- Validity (appropriateness and acceptability to the population of interest)
- Reliability (homogeneity and stability over time)
- Responsiveness (ability to detect change) where outcome following intervention is to be evaluated

Individual symptom score selection will depend on a number of factors including the intended population and symptoms to be evaluated. It is important that the choice of questionnaire is appropriate to the intended use. Section 2 covers the variety of questionnaires that are available and provides some guidance as to the content covered by the available questionnaires in clinical use.

Table 29.2 “Normal” Values for 24 Hour Frequency, Mean Voided Volume and Maximum Voided Volume in Asymptomatic Women as Published in Amundsen et al. [24], When Adjusted for Age and 24 Hours Volume by Subjecting the Data to Multiple Regression Analysis



	24 hour volume (mL)					
Age	1000	1500	2000	2500	3000	3500
24 hour frequency						
20	8.7	9.3	9.9	10.5	11.2	11.8
30	8.8	9.4	10.1	10.7	11.3	11.9
40	9.0	9.6	10.2	10.8	11.5	12.1
50	9.1	9.7	10.4	11.0	11.6	12.2
60	9.3	9.9	10.5	11.1	11.8	12.4
70	9.4	10.0	10.7	11.3	11.9	12.5
80	9.6	10.2	10.8	11.4	12.1	12.7
Mean voided volume (mL)						
20	107	152	197	242	288	333
30	103	148	194	239	284	329
40	100	145	190	235	281	326
50	96	141	187	232	277	322
60	93	138	183	228	274	319
70	89	134	180	225	270	315
80	86	131	176	221	266	312
Maximum voided volume (mL)						
20	223	312	402	491	581	670
30	214	303	393	482	572	661
40	226	295	384	474	563	653
50	205	286	375	465	554	644
60	196	277	367	456	546	635
70	188	268	358	447	537	626
80	179	260	349	439	528	618

CONCLUSION

The UD, or more specifically the bladder diary, is accepted as being an integral tool in the initial assessment of women with LUTS. A number of diaries are available for clinical use but the ICIQ bladder diary is currently the only fully validated UD. The most recent research suggests optimum diary duration of 3 or 4 days in order to strike balance between capturing the necessary information and not placing any unnecessary burden upon the patient. Electronic diaries are showing promise but still require full psychometric evaluation. Normative values calculated from bladder diaries are extremely variable, but recent research has reduced this uncertainty by providing parameter-adjusted reference tables.

Symptom scores from validated PRO questionnaires are now widely used in preference to clinician-completed scores in order to capture the patients' lived experience. When used in combination with information from a bladder diary, these are essential tools for initial investigation of LUTS.

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30

Pad Tests

Marie-Andrée Harvey

HISTORICAL ASPECTS

James et al. first described in 1971 the quantification of urine loss to determine response before and after treatment [1]. This was achieved using a pair of elongated electrodes embedded within the absorbent layer of a diaper, which contained dry electrolytes. Following urine loss, the moisture between electrodes resulted in a change in electrical conductivity that could be detected and recorded. It was marketed under the name of Urilos (N. H. Eastwood & Son, Ltd, London, England) [2]. However, the equipment was rather cumbersome and never caught on.

The pad test as we know it today was originally simultaneously described by Sutherst et al. and by Walsh and Mills [3,4]. It consists of the use of a perineal pad to document urinary incontinence and quantify its severity quantitatively, under natural conditions. The amount of loss is calculated by subtracting the weight of the pad before the test from its weight after the end of the test. A standardized 1-hour pad test (see Table 30.1) was then proposed in 1983 [5] and endorsed by the International Continence Society (ICS) in 1988 [6].

Other innovative methods were developed, going from the distal urethral electrical conductance test (DUEC) [7,8] to temperature-sensitive device [9]. The DUEC involves a 7 Fr catheter placed in the distal urethra, on which two rings, mounted 1 mm apart, register the electric potential change occurring when fluid gets into contact with the electrodes. The temperature-sensitive device uses a diode temperature sensor imbedded in the outermost layer of a pad, which records a change in voltage across the diode when urine (warmer than the perineum) is lost. These two methods are devised to detect urine leakage during ambulatory urodynamic studies without the bulk of the Urilos but are unable to quantify loss.

The clinical use of these devices has never been evaluated and their accuracy was disputed. The Urilos was said to be able to detect volumes from less than 1 mL to approximately 100 mL, with a variation of up to 20% when repeated. In subsequent reliability studies, the difference in volume recorded between different nappies varied between 13% [2] and 25% [10]. When comparing nappies from different boxes, the variation between them was as much as 68% [10]. Furthermore, the Urilos was noted to be more uncomfortable and not to absorb large volumes of fluid [11]. Consequently, the Urilos nappy never gained widespread popularity. The DUEC test has experienced a similar fate. In a small study comparing the ICS pad test to the DUEC, the DUEC showed no benefit over the 1-hour ICS pad test, with a greater complexity involved [12]. A recent study [13] evaluated its role in the diagnosis of women with symptoms of stress urinary incontinence (SUI) but without demonstrable leak on urodynamic or cough stress test (in which a leak is observed when coughing with a comfortably full bladder). While it detected SUI in 28% of symptomatic women with negative urodynamic studies, the DUEC test failed to detect stress incontinence in 33% of symptomatic women with demonstrable stress incontinence during standard urodynamic study.

INDICATIONS

A pad test can be used in two manners: as an objective means of detection of urine leakage when clinical testing is otherwise negative or to quantify urine loss prospectively in the clinical or investigational settings. It will not, however, diagnose the type of urinary incontinence [14,15]. The objective demonstration of urinary incontinence is of importance in its diagnosis and should be part of the clinical assessment of all patients with incontinence [16], and adding a pad test likely improves the identification of a woman with SUI [17]. It may be of particular value during research studies for the objective evaluation of treatment response [18]. Neither the patient’s perception of incontinence [2] nor her perception of its severity [19] is well correlated with urodynamic measures.

Pad tests are generally divided into short (<1, 1, 2 hours) or long (24, 48 hours). Standardization only exists for the ICS 1-hour pad test [6]. Short pad tests are easily performed in an outpatient clinical setting [20]. Long pad test protocols have, as yet, not been subject to standardization. A pad test should not be done during menstruation.

RELIABILITY AND VALIDITY

> Before one can obtain evidence that an instrument is measuring what is it intended, it is first necessary to gather evidence that [it] is measuring something in reproducible fashion; it says nothing about what is being measured. To determine that the test is measuring what was intended requires some evidence of "validity" [21].

> Validity expresses the relation between observed measurements and the true state of the entity being studied [22].

Reliability can be defined broadly by two characteristics: internal consistency and stability [21]. As internal consistency represents the average of the correlations (e.g., Cronbach's alpha) among all items in the instrument (e.g., questionnaire with multiple questions), this would not apply to assess reliability for the pad test. In this case, reliability is best demonstrated through its stability, i.e., the degree of agreement between different observers (interobserver reliability), between observations made by the same observer on two different occasions (intraobserver reliability), or between observations on the same patient on two distinct occasions, separated by a time interval (test–retest reliability).

Table 30.1 Standardized 1-Hour Pad Test

0 minute
- Apply preweighed pad
- Drink 500 cc sodium-free liquid
- Sit and rest

30 minutes
- Walk and stairs climbing

45 minutes
- Activities: Sit/stand × 10
- Cough × 10
- Run in place × 1 minute
- Pick up objects from floor
- Wash hands under running water × 1 minute

60 minutes
- Collect and weigh pad
- Patient voids, volume measured

Source: Adapted from Abrams P et al., *Scand J Urol Nephrol Suppl*, 114, 5, 1988.

The second dimension that is important in an instrument is its validity. Validity seeks to determine that the tool is measuring what it is intended to measure (urine loss) and does so by comparing the performance of a new tool against that of a known tool, a "gold standard." When such standard is nonexistent, validity can be obtained by comparison with other tools or "constructed." In the former situation, the current tool is compared to other tools testing the same or similar condition. This is usually referred to as *criterion, convergent*, or *concurrent validity* and, in the case of pad test, can be achieved by comparing pad tests to symptom questionnaires, urodynamic studies, or other validated pad tests. *Construct validity* is achieved by studying two or more different (e.g., continent versus incontinent) or similar populations in which it is expected to find a difference or similarity, respectively, between test results. Validity of the pad test can further be reflected by the accuracy of the measured volume lost and its sensitivity in detecting such a loss. If the sensitivity is poor, the test will at times not detect the true state of the entity, namely the presence of incontinence. However, as there is currently no means of detecting the true amount of urine leak with each incontinence episode, the validity of the pad test will be reflected in its ability to demonstrate incontinence in a patient who complains of urinary incontinence and a lack of urine loss in patients who report continence.

SHORT PAD TESTS

This category includes the following tests: standardized ICS 1-hour pad test; modified version of the ICS 1-hour test, usually incorporating different exercise intensity; or pad tests <1 hour, using a fixed bladder volume, with retrograde filling (through a temporary urethral catheter).

The type of activity leading to urine loss and the impact of voiding during the test period have been evaluated [23a]. Irrespective of urodynamic diagnosis, activities leading to leakage in all women included (in increasing order of urine loss) walking around/bed-making (3–4 g); climbing stairs up and down, with or without heavy pack (5–6 g); picking objects on the floor (6 g); and spending several minutes hand washing (10 g). Voiding (with the pad removed for the voiding) during the test had no effect on the result, with a similar proportion being dry on the pad test whether they voided or not.

The validity of the pad test in women with postmicturition dribble is unknown as no studies have evaluated the pad test results in affected women, This potentially relevant condition is present between 3.1% [23b] and 4.6% [23c] of women, mostly if they have other LUTS (more often with symptoms compatible with overactive bladder): only 1.5% of women without other LUTS had isolated post micturition dribble [23c]. Perhaps, one should screen for the presence of postmicturition dribble and, if present, recommend a pelvic floor contraction before drying the vulva, as an equivalent to manual urethral compression (“milking”) shown to help men [26d].

Some studies have evaluated the feasibility of a short pad test undertaken at home, where a subject would be given preweighted pads and return the pads in a watertight sealed plastic envelope [24,25]. Mailing delays were not shown to significantly alter the measurement of pad weight.

Detection Limit

Increased weight of the pad test may be due to urine but also to vaginal discharge, sweating, or menstruation. Comparing 50 continent women to 100 incontinent women, a maximum pad weight gain of 1 g was measured in all continent patients versus a mean of 12.2 g in incontinent women [3]. Walsh [4] tested six healthy continent volunteers for three consecutive days from 9 a.m. to 9 p.m., during which pads were changed every 2 hours and reported a 1.2 g/2 hours weight gain due to perspiration. Versi and Cardozo [26] compared the 1-hour pad test to video-urodynamic studies (v-UDS) in 90 continent and 99 UDS-confirmed stress incontinent women. In continent women with normal v-UDS, the mean pad weight gain was 0.4 g, with a 99% upper confidence limit of 1.4 g. These results confirm the validity of the short pad test in its ability to detect incontinence between self-proclaimed continent and incontinent populations.

ICS 1-Hour Pad Test

The ICS 1-hour pad test was set out to define a standardized objective measure, which would facilitate comparison between studies. The ICS fixed the threshold for a negative pad test at <2 g. However, despite earlier favorable reports, the ICS 1-hour test has been subsequently shown to have insufficient reliability [27–29], except in one study [30]. However, a better reproducibility was noted [27] when bladder volume at the start of the test was taken into account. Interobserver [31] and test–retest [29] reliability studies were found to be poor, as shown by wide limits of agreement.

It is important to note that a correlation coefficient merely quantifies *association* between two test results. If the two tests compared measure the same variable, evidently they will be associated, but high association does not necessarily translate to high agreement. The limit of agreement using the Bland and Altman method [32] is a better statistical analysis in describing *agreement* between two tests measuring the same outcome.

Convergent validity of the ICS 1-hour pad test compared to symptoms and quality of life questionnaire has been tested and was generally found to be poor: the International Consultation on Incontinence Short Form Questionnaire (ICIQ-SF) [33,34], Urogenital Distress Inventory (UDI-6) [33], Incontinence Impact Questionnaire (IIQ-6) [33], the Stamey grading scale [33], the King’s Health Questionnaire [35], the Symptom Impact Index and Symptom Severity Index [36], the Urogenital Distress Inventory and the Incontinence Impact Questionnaire [37,38], I-QOL [39], the “patient’s perception of incontinence severity” [35,40], and the frequency of incontinence episodes on diary [15] with at times significant but mostly weak correlations.

Similarly, construct validity testing of the ICS 1-hour pad test when compared to UDS [26,28,37] correctly identifies continent subjects but has a substantial false-negative rate in incontinent women (6%–32%), except in one study [41], where all 42 women were correctly identified. Versi et al. studied a further 311 additional women presenting with urinary complaints and failed to show that the test could screen for the pathology found on v-UDS, as the sensitivity was poor (68%) [42]. The measure of agreement (kappa's coefficient) between the pad test and the presence of pathology on UDS denoted a moderate agreement [43]. Studies evaluating the relationship between the ICS 1-hour pad test and specific urodynamic measures of urethral integrity reported a weak but significant negative correlation between the urine loss on pad test and the Valsalva leak point pressure (VLPP) in some studies [44,45] but not in others [46] and a correlation with maximal urethral closure pressure (MUCP) [37]. That is, with increasing urine loss on pad testing, the VLPP decreased and MUCP decreased. The correlation with MUCP was weak and not found in other studies. The urodynamic diagnosis has a variable effect on pad weight. In one study, women with urodynamic stress incontinence have greater leakage on 1-hour pad testing than those with detrusor overactivity; however, the amount of loss was not discriminatory of urodynamic diagnosis [15]. The opposite was noted elsewhere [14].

Assuming that UDS would represent the gold standard, the pad test seems to be able to most of the time discriminate between continent and incontinent women (construct validity); a positive test correctly identifies an incontinent patient, but a negative test may be found in women demonstrated to be incontinent on UDS. It is unable to discriminate among the different incontinence pathologies found on UDS or to consistently determine incontinence severity when compared to v-UDS studies [26,42]. However, a strong correlation was noted between the Stamey incontinence grading and the 1-hour pad test in a study including 320 women with stress or mixed urinary incontinence symptoms [47]. The pad test was slightly modified, whereby serial ultrasound was obtained to confirm a minimal bladder volume of 300 mL, at which time the prescribed exercises were completed within a 10 minutes window. Accuracy of the 1-hour pad test was measured using an ROC curve. The threshold between mild and moderate was found to be 3.4 g (sensitivity 79.7%, specificity 91.6%) and between moderate to severe, 10.2 g (sensitivity 82.7%, specificity 89.6%), with excellent area under the curve (0.908 and 0.900, respectively) (0.5 represents a worthless test and 0.9–1, an excellent one). The authors concluded that based on the 1-hour pad test, women with less than 3 g were considered to have mild incontinence, 3–10 g moderate, and >10 g severe incontinence.

Pad tests may also help predict surgical outcome: women with more severe SUI as judged by weight gain on 1-hour pad test were shown to respond more poorly to surgical repair (87.1 g ± 8.2 vs. 29.8 g ± 2.8, $p < 0.05$) [45,48]. This may be more significant for women with pure stress incontinence, compared to those with mixed symptomatology [45,49].

The 1-hour pad test that is sensitive to change was used as an outcome measure in therapeutic trials [50,51].

The importance of a negative pad test as an outcome measure following therapy varies considerably between patients, nurses, and physicians. Patients scored the importance of an objective success (as determined by a dry pad test) as 67 on a visual 100 mm analogue scale, whereas physicians rated the importance of a dry pad test 53 on the VAS and nurses were the least convinced that a dry pad test was important (score of 28 on 100 mm VAS) [52]. The role of pad testing in outcome research remains to be determined [53].

In light of its limited reliability, it may not come as a surprise that, although endorsed by the ICS, the ICS 1-hour pad test is only rarely (33%) used in outcome research [54]. Surprisingly, despite reports of its poor reproducibility, high urine loss detected on the pad test nevertheless influences clinicians in selecting a surgical treatment option rather than a conservative management [55]. Furthermore, when used in the research setting, women tend to be less compliant with the study protocol when follow-up involves a pad test and a diary [56].

Modified 1-Hour Pad Tests

Consequently, some have sought to improve the reliability of 1-hour pad test, through increasing exercise intensity or controlling the bladder volume.

Validity studies on modified 1-hour pad tests are limited. A study of short-duration pad testing with standard volume reported only a weak correlation with symptoms (recall of number of clothing changes) [57].

There is insufficient data to stipulate that an aggressive protocol adds any reliability or sensitivity to the current 1-hour test. Subjects were asked to drink 1 L of water in 15 minutes. One hour after starting drinking, they were asked to drink an additional 500 mL [58]. Pad testing was started as soon as the subject felt they had a full bladder. A total of 14 different vigorous exercises were performed. At the end of the test, voided volume was measured. Exercises included, but were not limited to, star jumps, sprinting, vacuuming, lifting, carrying and putting down a 10 kg box, and pulling on an elastic band, in addition to standard exercises as included in the ICS 1-hour pad test. None of the 18 controls reported or demonstrated any leakage. Among the 25 women with symptoms of urinary incontinence tested, eight (32%) still had a negative test. Test–retest was obtained in 16 of the 25 women, with a correlation of 0.73.

Reproducibility studies have demonstrated an improved correlation when fixed bladder volume was used. Subjects have significantly more urine loss with increased bladder volume [27,59]. Using a fixed 250 cc bladder volume, a 20 minute pad test is more sensitive than the ICS 1-hour pad test [60]. Performing the pad test once a strong desire (mean 292 mL) is reached further improves sensitivity of the short pad test [61]. At 200 cc, a modified 1-hour pad test did not correlate with leak point pressure [38].

Test–retest reliability of a fixed-bladder volume short pad test shows a substantial difference in the test and retest pad weight, limiting reliability. Although correlations between tests were generally good [14], such measure of agreement is generally a poor choice when the two tests compared are the same (see earlier discussion). When looking at the limit of agreement [32] a considerable variability (± 24–30 g) was noted, with authors admitting that sensitivity was "hardly much better" than the ICS 1-hour [62]. The difference in mean pad weight was significantly different between the test and the retest (9 g), thus limiting the test reliability. A similar result was reported when the bladder is filled at 75% capacity [63], at 50% capacity [62,64], and at 300 cc [65].

Impact of Pelvic Organ Prolapse on the Short Pad Test

Thus far, most studies evaluating the value of the 1-hour pad test have excluded women with pelvic organ prolapse. In a recent pilot study, Chang et al. [66] studied 27 women with stage II or more anterior wall prolapse who had a negative 20 minutes pad test when unreduced and inserted a 10 cm rolled vaginal gauze (20 × 40 cm) before repeating the pad test. Those with a pad test ≥8 g were deemed eligible for a midurethral sling. The number of women who had no evidence of occult incontinence (i.e., incontinence only discerned when any prolapse is reduced) and did not receive a midurethral sling is 23, except for 2, who did at the surgeon's discretion. Only one requested a sling after prolapse surgery. Four women had occult incontinence and received a sling; of those, none required a second sling. Unfortunately, the continence status of the 27 women after their prolapse surgery was not reported. Additionally, the pad test result appears to be affected by the presence of advanced prolapse [37]. Costantini et al. found that women with voiding difficulties were more likely to have a negative pad test compared to those without these difficulties. Furthermore, the majority of women with voiding difficulties had an anterior wall prolapse grade 3 or greater, which contrasted with women without voiding difficulties whose majority had no such advanced prolapse. They postulated that women with advanced anterior wall prolapse seemed to experience a "physical obstacle against urine leakage."

The committee on Imaging and Other Investigations from the fifth International Consultation on Incontinence [67] concluded that the 1-hour pad test was not very accurate, unless done at fixed bladder volume and with set exercises. Consequently, it was deemed an optional investigational tool in the routine evaluation of incontinence, while being considered useful in outcome research. Standards suggested included a 20–60 minutes, fixed volume bladder pad test, with a positive test being a pad weight gain ≥1 g.

Pyridium Test

Phenazopyridine hydrochloride (Pyridium^{TM}, Parke–Davis) ingestion results in renal excretion of the dye with orange coloring of the urine. It has been used by clinicians to detect incontinence using the compound's property of coloring urine orange. Wall et al. [41] reported the sensitivity and specificity of Pyridium as a qualitative test in incontinent patients. While very sensitive, the addition of pyridium was not specific. The poor specificity was due to a high false-positive rate in asymptomatic patients. This may be explained by staining of the perineum at the time of a prior void, resulting in tinting of a subsequent pad on vulvar contact, or by a minimal, nonclinically significant, loss of urine in normal women. These results were subsequently confirmed in a study testing continent (self-reported) women, during exercise [68], in which Pyridium staining was noted in nearly 100% of subjects after physical activity was conducted, with a mean pad weight of 4.59 ± 3.55 g (outdoor exercise) or 1.33 ± 0.97 g (indoor exercise). Pyridium staining was minimal, with a mean stained area of 2.66 mm (range 0–11 mm). No cutoff limit in the pad weight has been previously established to define a normal pad test during exercise, given that there would be a greater weight gain due to perspiration alone.

In the light of these reports, the use of pyridium in detecting transurethral incontinence can be perceived as unreliable and nonspecific.

LONG-DURATION PAD TESTS

The 1-hour pad test has been criticized because of its artificial setting and short duration. A longer pad test was first described by Sutherst's group, in an abstract form [69]. However, the aim of the study then was to determine if the 1-hour pad test was representative of urine loss experienced during regular activity, not to assess if it was better in detecting and quantifying incontinence than its shorter counterpart. It was suggested by Lose et al. that performing a test during regular daily activities would be more sensitive than during a single 1-hour test [70]. However, the pad test result is influenced by the intensity of the activity, even between "minimal" (5.2 g) and "normal" (9.9 g) activities [71].

Generally, a long-duration pad test is performed at home, during a typical day's activities. The subject is given a number of preweighted pads, placed in individually sealed envelopes. She is instructed to wear pads consecutively for a given period (12, 24, 48 or 72 hours) and to return the pads in their sealed envelope for weighing. The use of sealed plastic bags for storage of used pads did not alter significantly the results [72,73]. The 24-hour pad test showed only limited diagnostic value for self-reporting of incontinence in pregnancy or postpartum [74].

Detection Limit

Lose et al. first established a detection limit by studying 23 asymptomatic female subjects [70]. They noted that the median weight obtained for the 24-hour pad test was 4.0 g, with a 99% upper limit of 8 g for the 24-hour period. Ryhammer et al. [75] studied 78 self-reported continent women. Their mean loss was 3.1 g (range 0–9 g) during a 24-hour pad test. Versi et al. [72] studied 24 young continent women during a 48-hour pad test and reported a mean loss of 7.1 g, with a 95% upper confidence limit of 14.5 g. Mouritsen et al. [76] reported a mean leakage of 2.6 gm in continent women during a 24-hour pad test, with a 95% upper confidence limit of 5.5 g. In a more recent study, an upper limit of 1.3 g/24 hours was noted [77]. Although only supported by the latter study, the committee on Imaging and Other Investigations from the second International Consultation on Incontinence [67] recommend that a pad gain of ≥ 1.3 g during a 24-hour pad test be considered as positive.

Validity and Reliability

The construct and convergent validity of home pad test, i.e., its ability to not record weight gain in continent women and its ability to detect urine loss in patients with established urinary incontinence on UDS, has been reported. Using continent volunteers, Molloy et al. [73] noted the weight gain of up to ±1.3 cc for each 12-hour periods, likely representing vaginal discharge. One study failed to confirm construct validity, with continent and incontinent women showing no difference in pad weight gain [75]. More recently, it was noted that there was little [78] or no [79] correlation between a 24-hour pad test and a cough stress test.

Convergent validity showed moderate or weak correlation between a 24-hour pad test and the severity index [80], the quality of life questionnaire (Incontinence Impact Questionnaire) [78], and the symptom questionnaire (Urogenital Distress Inventory) [78] but high correlation with a complaint of stress incontinence [70] and the number of incontinence frequency as recorded on diary [81,82] and on ICIQ-SF questionnaire [82]. No correlation with Stamey grade was noted [82]. The 48-hour pad test correlated moderately with the Urinary Incontinence Severity Score and strongly with a visual analogue scale quantifying bothersomeness of current incontinence [83].

Convergent validity with UDS was assessed in numerous studies. Some concluded that the 24-hour pad test is perhaps more sensitive than v-UDS [72,84]. The false negativity of the 24-hour pad test has been estimated to be around 8% [72]. These earlier studies suggest a reasonably low false-negative 24-hour pad test compared to UDS and an improved detection of urinary incontinence in symptomatic subjects with negative UDS. This is in contrast with later study in which 33% of women with urodynamic stress incontinence, 43% of those with detrusor overactivity, and 37% of women with missed UDS diagnoses were dry on the 24-hour pad test [15]. The amount lost on 24-hour pad test is not discriminatory of urodynamic diagnosis [15]. Furthermore, the 24-hour pad correlates negatively only very weakly with the vesical leak point pressure [81].

The long pad tests have a good test–retest reliability as shown by the correlation obtained, keeping in mind the limitations of the ability of this measure of association in determining agreement. Victor et al. were the first to compare test–retest of the 24-hour pad test [85]. A 48-hour pad test was performed by 15 women and repeated it 1 week later. When comparing the first 24 hours of the two 48-hour pad tests, correlation was significant ($r = 0.66$). Lose et al. [70] performed test–retest evaluation of the 24-hour home pad test in 31 women referred for incontinence. A significant correlation ($r = 0.82$) was noted between the two tests. The limit of agreement was approximately ±100 g, which means that the second test done could yield greater or lesser results the second time by as much as 100 g. This represents a large variability of results. Rasmussen et al. [86] evaluated 14 women for test–retest reliability of the 24-hour pad test. They failed to find a linear correlation between the two tests. The second test could be anywhere between a third less to three times more than the first 24-hour period tested. Versi et al. [72] looked at the reproducibility of the first 24 hours from a 48-hour pad test compared to the first 24 hours of a second 48-hour pad test in 140 symptomatic patients. They noted a strong correlation (0.9) and a difference between the two tests of 7%. When looking at the test–retest done during the first 24 hours of a 72-hour pad test done twice in 106 women, Groutz et al. [87] used another statistical marker of reliability (Lin's concordance correlation coefficient [88], in which reliability was defined as a coefficient > 0.7). The coefficient obtained was 0.72. More recently, Karantanis et al. [89] assessed the repeatability of 7 consecutive 24-hour pad tests on 108 women using repeated measures ANOVA. No difference in mean pad test among the 7 days was detected, suggesting repeatability.

Similarly, the test–retest reliability of the 48- and 72-hour pad test has been reported to be very good, although the statistic used (correlation) are of limited strength to measure association. Victor et al. [85] reported a correlation coefficient of 0.9 between two tests at least 1 week apart. Versi et al. [72] reported similar correlation, with a difference in weight between the two tests of only 1.6%. Groutz et al. [87], when comparing the first 2 days of a 72-hour pad test done on two different occasion, found a concordance correlation coefficient (Lin's CCC) of 0.88. The test–retest correlation (using Lin's concordance correlation coefficient) was at the greatest for the 72-hour pad test (CCC = 0.94). The first 24 hours of a 48-hour pad test has been compared to the full 48-hour test and the two tests have been shown to highly correlate ($r = 0.92$), suggesting that the 48 hour did not add much to a 24-hour test [90]. More recently, Karantanis et al. [89] reported high correlation ($r = 0.88$) between the first 24-hour pad test and the 7-day average of 7 consecutive 24-hour pad tests.

Attempts at categorizing severity of incontinence according to weight gain on long pad test were done by applying the percentage of the data that were classified as mild, moderate, or severe on the 1-hour tests. Leak < 20 g on a 24-hour pad test was classified as mild, 20–74 g as moderate, and ≥75 g as severe [91]. Here also, no validity study has been done to assess agreement of this categorization with other measures of incontinence severity.

Attention must be given to local climate, as a test performed in a warmer, more humid climate leads to a higher pad humidity (1.9 g) than normative data supported by the ICS [67], as shown by testing 257 continent women [92].

A balance between the desired response rate and accuracy of the method must be struck, as the need to perform a 24-hour pad test had been shown to deter patient's participation in trial [56]. The committee on Imaging and Other Investigations from the fifth International Consultation on Incontinence [67] concluded that the 24-hour pad test was reproducible and recommended that a test lasting more than 24-hour had little advantage. It has been suggested that the 24-hour pad testing should be used as a composite outcome measure in research along with a 24-hour diary and a satisfaction questionnaire, as it was noted to reflect surgical results more accurately [93].

SHORT- VERSUS LONG-DURATION PAD TESTING

Overall, the home pad tests (24- or 48-hour) correlate poorly with 1-hour pad tests and are more sensitive than the shorter 1-hour pad test.

Ali et al. [69] first compared in an abstract the 1-hour to a 12-hour pad test, and they noted a "close correlation." In another study [70,95], 31 women with urinary incontinence who had a 1-hour pad test (standard volume of 200–300 mL) and a 24-hour pad test were studied. Of these, 13 had a negative 1-hour pad test, of which, however, 10 had a positive 24-hour pad test, giving a false-negative rate of 39% for the 1-hour pad test, compared to the 24-hour. No correlation was found between the 1-hour and the 24-hour. This report was echoed by others [84,85,90]. More recent studies have found a moderate-to-strong correlation between the 24-hour and the 1-hour tests, in addition to reporting that the 1-hour detected more incontinent women than the 24-hour [15,38].

Both tests lack the ability to discriminate between possible UDS diagnoses as there is considerable overlap between pad losses across the UDS diagnoses [15].

PAPER TOWEL TEST

Most of the methods objectively quantifying urine loss preclude detection of small volumes, as these may overlap with perspiration and vaginal secretions. A simple noninvasive test was developed to detect such losses associated with stress incontinence [96]. While a trifold brown paper towel is held under the perineum, the patient is asked to cough three times consecutively. The surface of the wetted area is calculated using the ellipse formula (πxy), x and y being the orthogonal axes of the area, and then converted to volume of urine lost (using a standard curve). The relationship between the measured area and a known fluid volume was found to have a very strong correlation ($r = 0.998$). In a test–retest evaluation within the same visit and between visits the authors also showed a high correlation coefficient and concluded that the quantitative paper towel test was accurate and reliable in detecting small losses of urine due to stress incontinence. The paper towel test has not been found to correlate with self-reported severity of incontinence [97]. Test–retest reproducibility was within 1 cc [98]. This test has not been validated against a gold standard diagnostic method such as multichannel v-UDS.

SUMMARY

To date, the objective urine loss test most useful in clinical practice remains to be the perineal pad test. A short version has been standardized to a certain degree by the ICS, rendering its use more uniform for research data collection. However, the bladder volume at the beginning of the 1 hr test should be standardized. The 1-hour pad test has not been found to have good reproducibility, though it is improved with standardized bladder volume. The short-term pad test was found to be valid in differentiating normal from abnormal continence mechanisms; however, its validity is somewhat limited as it has a significant false-negative rate. Finally, the ability of the short-term pad test (≤1-hour) to categorize severity of incontinence was noted to be poor.

The long-term pad test (≥24 hours), on the other hand, is valid in detecting incontinence, with a good sensitivity and a lower false-negative rate. The reproducibility was similarly noted to be good for both a 48-hour and a 24-hour test period. Hence, a 24-hour home pad test represents a good tool in detecting and quantifying incontinence. Neither test can distinguish between different types of urodynamic diagnosis.

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31 Basic Urodynamic Tests: Uroflowmetry

Matthias Oelke

INTRODUCTION

Urodynamic observations (e.g., measurement of urinary flow) have been defined by the joint committee of the International Urogynecological Association (IUGA)/International Continence Society (ICS) to be observations made during urodynamic studies [1]. A particular urodynamic observation (e.g., decreased urinary flow rate) can have a variety of underlying causes and, therefore, is unsuitable to make a definitive diagnosis concerning a disease or condition. Hence, free uroflowmetry (spontaneous or no-catheter uroflowmetry) should never be used as a single test but always combined with clinical information (e.g., history, physical examination, frequency-voiding chart, or pad test) and other tests (e.g., measurement of postvoid residual urine, ultrasound assessment of the lower or upper urinary tract) to draw useful conclusions with regard to diagnosis or treatment benefit. Urodynamic observations may occur in the absence or presence of symptoms and signs.

Abrams regarded uroflowmetry as a screening test that should be performed as an essential examination prior to all other urodynamic testing and as a routine examination for the pre- and postoperative assessment of lower urinary tract dysfunction (LUTD) [2]. The report of the ICS Standardization Committee on Good Urodynamic Practices (2002) confirms this postulate [3]. The French Committee of Female Urology and Urogynecology (2007) recommends evaluation of bladder emptying by uroflowmetry and measurement of postvoid residual urine in all patients prior to surgery [4]. In women with urinary incontinence, the current version of the European Association of Urology (EAU) Guidelines on Urinary Incontinence (2012) does not mention uroflowmetry anymore [5]. However, the previous version of the EAU Guidelines (2009) considered uroflowmetry useful in incontinent patients who have “complicated” incontinence that includes—besides others—recurrent urinary tract infections, reported voiding dysfunction, significant pelvic organ prolapse, failed previous incontinence surgery, and after radiotherapy or pelvic surgery.

This chapter deals with the urodynamic observation of urinary flow. Such measurement objectively determines the volume of urine expelled from the bladder per time sequence and quantifies micturition. Moreover, if this volume–time equation is drawn as a curve, the measurement of urinary flow also gives information on how urine evacuation exactly proceeds. Objective and quantitative data, which primarily help in the understanding of voiding symptoms, are provided by measurement of urinary flow. As with all investigations, the diagnostic value of uroflowmetry depends on the way the test is performed, the quality of the measuring equipment, and the knowledge of the individual who interprets the measurement. This chapter provides information accordingly.

SYMPTOMS RELATED TO URINARY FLOW

Uroflowmetry aims to reproduce, qualify, and quantify urinary symptoms that have brought women to consultation or patients reported about during systematic assessment. However, uroflowmetry can only objectively investigate symptoms related to voiding but cannot explain symptoms related to urinary storage. Additionally, uroflowmetry cannot qualify or quantify voiding in women with urinary retention. In daily life, the individual is usually the only observer of her urinary flow, and the interpretation of subjective observations may need to be objectively confirmed and quantified by flow measurements. There may appear a discrepancy between subjective reporting and objective findings of urinary flow. Long or everlasting uroflow abnormalities might not be realized as abnormal because a comparison with normal voiding is lacking in those individuals. Furthermore, most women void in privacy and have little opportunity to compare voiding patterns [6].

The following urinary symptoms are related to voiding and have been defined by the joint IUGA/ICS Standardization Committee on Terminology of pelvic floor dysfunction in the year 2010 [1]:

- *Hesitancy* is the complaint of a delay in initiating micturition (i.e., difficulty in initiating micturition resulting in a delay in the onset of voiding after the individual is ready to pass urine).
- *Slow stream* is the complaint of a urinary stream perceived as slower compared to previous voids or in comparison to others.
- *Intermittency* is the complaint of urine flow that stops and starts on one or more occasions during voiding. In contrast, continuous flow is when the individual reports emptying the bladder without pauses during a single voiding attempt.
- *Straining to void* describes the complaint of the need to make an intensive effort (by abdominal straining, Valsalva or suprapubic pressure) to either initiate, maintain, or improve the urinary stream.
- *Spraying (splitting) of the urine stream* is the complaint that the urine passage is a spray of split rather than a single discrete stream (i.e., when urine flows to different directions).
- *Position-dependent micturition* is the complaint of having to take specific positions to be able to micturate spontaneously or to improve bladder emptying, for example, leaning forward or backward on the toilet seat or voiding in the semistanding position.
- *The need to immediately revoid* is the complaint that further micturition is necessary soon after passing urine.
- *Retention (urinary)* is the complaint of the inability to pass urine despite persistent effort (i.e., inability to void despite having a full bladder).

UROFLOWMETRY EQUIPMENT

The first documented urine flow measurement was performed by Eugen Rehfisch in Berlin, Germany, in 1897 using a flowmeter based on air displacement [7]. Historically, many different types of uroflowmeters were proposed. Some were based on the principle of voiding distance [8,9], audio [10], weight [11], variations of a constant magnetic field [12], rotating disk, measurement of size and velocity of drops [13], and air displacement [14]. Susset et al. [15] compared weight, rotating disk, and air displacement techniques and found that all of them have certain values and limitations. Gammie et al. [16] described the most commonly used uroflowmeters employing one of the following methods:

- *The gravimetric method*: This technique operates by measuring the weight of the collected fluid or hydrostatic pressure at the base of the collecting cylinder. In both cases, the output signal is proportional to the collected fluid mass. Gravimetric meters therefore measure accumulated mass, and mass flow rate is obtained by differentiation. Nowadays, most of the uroflowmeters use this principle of uroflow measurement that is considered as the most precise measurement technique.
- *The electronic dipstick method*: The electrical capacitance of a dipstick mounted in the collecting chamber changes as urine accumulates. The output signal is proportional to the accumulated volume and the volumetric flow rate is obtained by differentiation.
- *The rotating disk method*: The voided fluid is directed onto a rotating disk, thereby increasing the inertia of the disk. The power required to keep the disk rotating at a constant speed is proportional to the mass flow rate of the fluid. The accumulated mass is obtained by integration.

The accuracy of uroflowmeters was discussed in the ICS Good Urodynamic Practices Report [3]. There are differences in accuracy and precision of the flow rate signals that are dependent on the type of the uroflowmeter, internal signal processing, the proper use, and calibration of the flowmeter. The desired and actual accuracy of uroflowmetry should be assessed in relation to the potential information that could be obtained from the measurement of urinary stream compared to the information actually abstracted for clinical and research purposes. Some relevant aspects of the physiological and physical information contained in the urinary stream are outlined in the report.

The desired clinical accuracy may differ from the technical accuracy. The ICS report on Good Urodynamic Practices [3] recommends as standards a range of 0–50 mL/s for maximum urinary flow rate (Q_{max}), 0–1000mL for voided volume, maximum ±5% relative to full scale. As most uroflowmeters are mass flowmeters using the gravimetric method, variations in the specific gravity of the fluid have a direct influence on the measured flow rate. For example, urine of high concentration increases apparent flow rate by up to 3%. With x-ray medium, the flow rate may be overestimated by as much as 10%. Correction by calibration software is possible but seldom performed.

Since the overall accuracy of flow rate signals is not better than ±5%, it is not important to report Q_{max} to a resolution better than a full milliliter per second. A better resolution is possible under carefully controlled research conditions but such advanced measurement accuracy is usually not required in daily clinical practice, especially when screening for LUTD.

UROFLOW MEASUREMENT

Normal voiding occurs when the bladder outlet (urethra and internal and external urethral sphincters) completely relaxes and the detrusor actively contracts. The mechanical properties of a relaxed bladder outlet are usually constant, and the properties can be defined by the relationship between the cross-sectional area of the urethral lumen and the intraurethral pressure at the flow controlling zone. Below the minimum urethral opening pressure, the urethral lumen is closed and urine remains in the bladder; the lumen then widely opens with little additional pressure increase and urinary flow starts to emerge. The interpretation of uroflow curves can be performed by measuring several parameters and by gross interpretation of the flow curve itself.

PARAMETERS OF UROFLOWMETRY [1] (FIGURE 31.1A AND B)

- *Flow time* is the time over which measurable flow actually occurs. Flow time is expressed in seconds (s).
- *Voiding time* is the total duration of micturition, including interruptions. When voiding is completed without interruption, voiding time is equal to flow time. Voiding time is expressed in seconds.
- *Voided volume* is the total expelled volume via the urethra and expressed in milliliters (mL).
- *Flow rate* is defined as the volume of expelled fluid via the urethra per time unit and expressed in milliliters per second (mL/s).
- *Maximum flow rate* (Q_{max}) is the maximum measured value of the flow rate after correction for artifacts and expressed in mL/s.
- *Time to maximum flow* is the elapsed time from onset of flow to Q_{max} and expressed in seconds.
- *Average flow rate* (Q_{ave}) is voided volume divided by flow time, expressed in mL/s. The average flow should be interpreted with caution if the flow is interrupted or there is terminal dribbling.

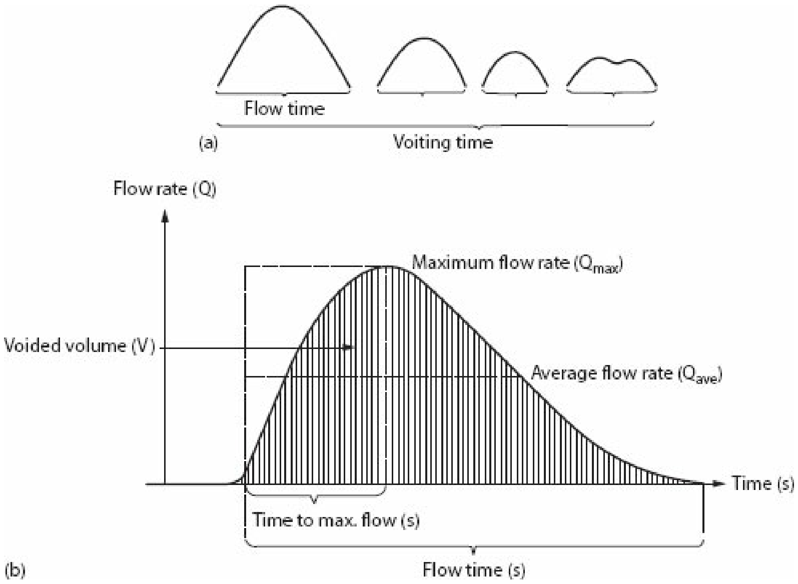

Figure 31.1 (a)Difference between flow time and voiding time. (b) Schematic explanation of uroflow recording, with nomenclature and units recommended by the International Urogynecological Association and International Continence Society. (From Haylen BT et al., *Neurourol Urodyn*, 29, 4, 2010.)

SHAPE OF THE FLOW CURVE

The shape of the flow curve is determined by the contractile properties of the detrusor, the ability to relax the bladder outlet, and the absence/presence of abdominal straining during voiding [1]. The ICS Good Urodynamic Practices Guidelines [3] state that an easily distensible, relaxed bladder outlet together with a normal detrusor contraction will result in a smooth, arc-shaped curve with high amplitude (Figures 31.1 and 31.2). When the bladder outlet is completely relaxed and the woman voids without straining, the shape of the curve is only determined by the kinetics of the detrusor contraction that reflects the properties of slow contracting detrusor smooth muscle cells; therefore, flow rate should not have rapid variations. The continuous uroflow curve is defined either as a smooth arc-shaped curve or as fluctuating when there are multiple peaks during a period of continuous urine flow (Figure 31.3). It is a widespread assumption that micturition of a healthy, asymptomatic woman is always associated with a normal flow pattern. However, this would also mean that a normal flow curve would correspond with normal voiding and would even permit the exclusion of LUTD. Pauwels et al. [17] demonstrated that a "normal" bell-shaped flow curve does not exclude female voiding dysfunction by investigating the value of a normal flow pattern in women with stress urinary incontinence (SUI), detrusor overactivity, healthy middle-aged volunteers, and healthy young students. These women voided with a bell-shaped flow curve in 50%, 65%, 57%, and 50%, respectively. Women who strained during voiding (a major component of dysfunctional voiding) managed to void a bell-shaped flow curve in 46%, 60%, 70%, and 100%, respectively.

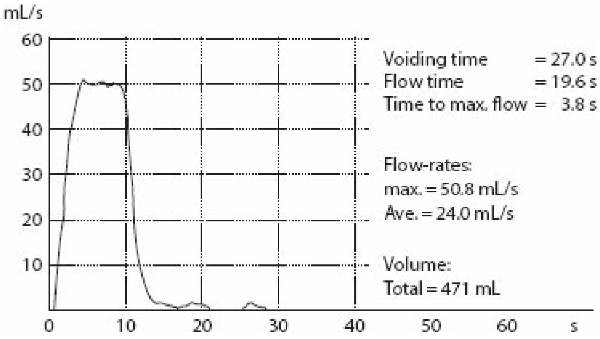

Figure 31.2 Bell-shaped uroflow with normal flow values.

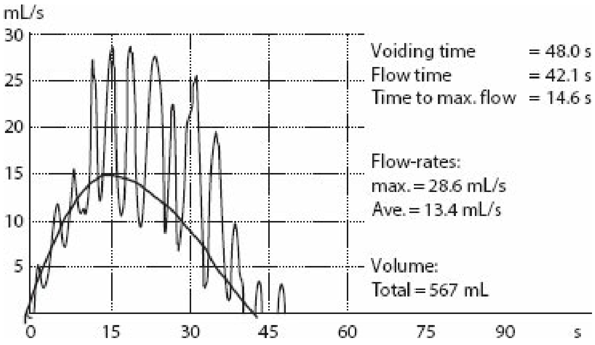

Figure 31.3 Fluctuating flow curve with multiple peaks, prolonged flow time, and normal maximum urinary flow rate (Q_{max}) during automatic evaluation but decreased Q_{max} after correction (straight arc drawn in flow recording). Flow curve possibly due to straining.

Other shapes of flow curves, such as flat (Figure 31.4), asymmetric, or multiple interrupted curves (Figure 31.5), are indicative of abnormal voiding but not specific for a certain underlying disease or condition. Decrease of detrusor contraction power (detrusor underactivity) and/or increased urethral pressure will both result in decreased Q_{max} and Q_{ave} as well as a smooth, flat curve. Constrictive obstruction, e.g., due to urethral strictures, meatal stenosis, or perforated vaginal tapes, is caused by a reduced size of the urethral lumen and results in a plateau-like curve (Figure 31.4). The magnitude of Q_{max} is determined by the residual urethral diameter at the level of obstruction. However, the same pattern may also originate from detrusor underactivity.

Fluctuations in detrusor contractility, straining, or intermittent sphincter activity during voiding may result in complex flow patterns (Figures 31.3 and 31.5). Rapid changes in urinary flow rate may be due to sphincter/pelvic floor contractions, mechanical compression of the urethral lumen or interference at the meatus, or changes in the driving energy—as with straining. Rapid changes may also be due to artifacts caused by interference between the stream and the collecting device, movement of the stream across the surface of the funnel, or patient movements. If fast variations of urinary flow have been observed, patients should be asked whether this voiding pattern reflects normal voiding at home or they have strained or emptied their bladder next to the collecting device. A visual control with regard to urine remnants next to the flowmeter is useful in cases of suspected voiding next to the uroflowmeter.

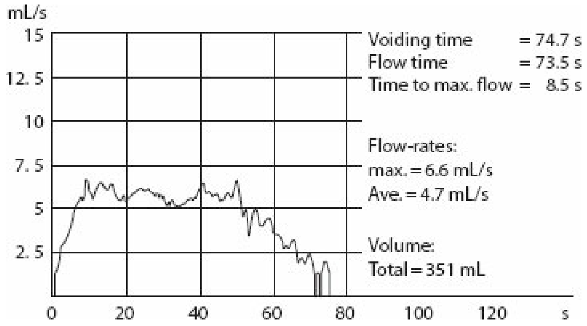

Figure 31.4 Flat flow curve with decreased maximum urinary flow rate (Q_{max}) and increased flow/voiding time, suspicious of bladder outlet obstruction, detrusor underactivity, or dysfunctional voiding

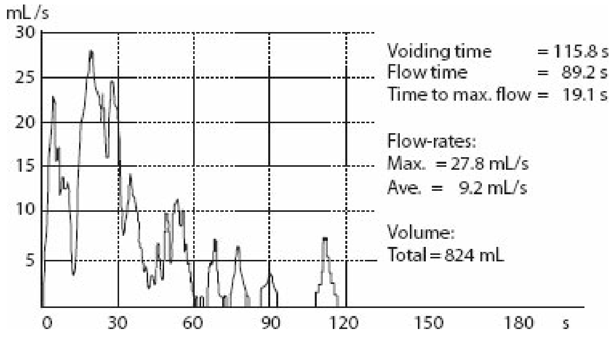

Figure 31.5 Multiple interrupted flow curve (staccatos) with normal maximum urinary flow rate (Q_{max}) but prolonged flow/voiding time, possibly due to straining, detrusor-sphincter dysfunction, or voiding next to the collecting device of the uroflowmeter.

INTERPRETATION OF UROFLOW VALUES AND CURVES [3]

As already mentioned, uroflow values and the shape of the flow curve may suggest LUTD but reliable, specific, and detailed information about the exact cause for abnormal voiding cannot be derived from uroflow (curve) alone [18]. Only measurement of the pressure–flow relationship by computer-urodynamic investigation can clarify the exact pathophysiology. Urine flow measurements are influenced by several factors that have to be taken into consideration during flow evaluation and interpretation. Not all relationships between voiding and specific conditions have been equally investigated in both men and women but are assumed to be similar in the context of this chapter:

- *Detrusor contraction power* (*contractility*): For steady outflow conditions and voiding without straining, all variations in urinary flow rate are only related to changes of detrusor activity and power. Detrusor contraction power can decrease with aging and in patients with neurogenic, myogenic, and combined diseases.
- *Bladder outflow resistance*: With changes of outflow resistance, for example, due to voluntary or involuntary urethral sphincter contractions during voiding or due to bladder outlet obstruction,

flow rate will change if detrusor contractility is constant. Q_{max} < 15 mL/s and/or postvoid residual urine volume >50 mL with a minimum total bladder volume of 150 mL before voiding (volume voided + postvoid residual) as well as the 10th centile curve of the Liverpool Nomogram for Q_{max} both correlate well with bladder outlet obstruction in women (Figure 31.6) [19].

- All *intra-abdominal pressure modulations* will result in physiological artifacts of the urinary flow rate and should be minimized, e.g., by asking the patient to relax and not to strain.
- *Patient age*: Healthy female volunteers aged between 16 and 64 years showed no statistically significant variation in urinary flow rate with regard to age, parity, or first vs. repeated voiding [20]. In female patients aged 40 years or older, Madersbacher et al. [21] described decreasing urinary flow rates (Q_{max},Q_{ave}) and increasing postvoid residuals with aging, indicating that older individuals have reduced bladder contraction power (detrusor underactivity) and/or a less compliant urethra. Additionally, bladder capacity, voided volume, functional urethral length, and maximum urethral closure pressure significantly decrease with increasing age. Deterioration of Q_{max} with aging was also described by Barapatre et al. in 308 healthy women aged 13–47 years [22]. A nomogram was developed to correct Q_{max} for age (Postgraduate Institute of Medical Education and Research, Chandigarh, India (PGIMER)—nomogram) [22].

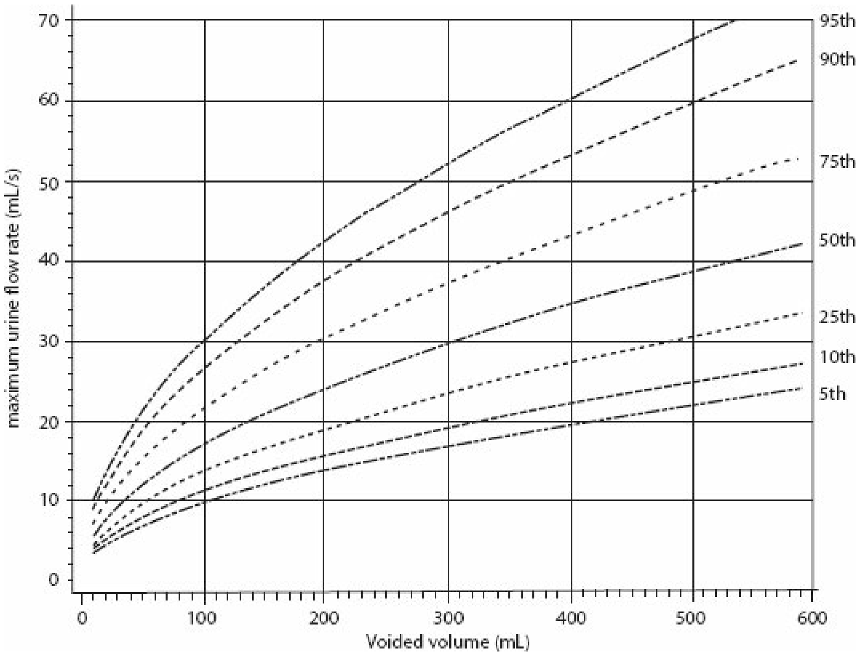

Figure 31.6 Liverpool Nomogram for the judgment of maximum urinary flow rate (Q_{max}) relative to voided volume in women. The patient has an abnormally low Q_{max} when the flow value relative to voided volume is under the 10th centile; these women should be further evaluated. (From Haylen BT et al., *Br J Urol*, 64, 30, 1989.)

- *Weight/body mass index*: A significant positive correlation between Q_{max} and body weight, body mass index, and body surface area has only been described recently [22]. Higher vesical resting pressures in the supine, sitting, and standing positions may be responsible for this positive association between Q_{max} and weight/body mass index [23]. This relationship could explain why Indian women have lower uroflow rates (Q_{max}) compared to women of western societies (Table 31.1).
- The *influence of urethral manipulation* on uroflowmetry results remains controversial. One study in women showed no difference between pre- and postcatheterization flow rates [24]. However, catheterization to rapidly fill the bladder in order to perform quick uroflowmetry can alter the following flow parameters: Q_{max} and Q_{ave} can decrease and time to Q_{max} as well as

duration of flow can increase [25–27]. Especially, catheters with a diameter of ≥7 French are likely to alter urine flow [28]. Although the effect of cystoscopy on urine flow parameters has only been evaluated in men, Issa et al. [29] demonstrated that Q_{max} significantly decrease by 27% after instrumentation. Therefore, urethral manipulation should be avoided prior to uroflowmetry whenever possible.

- Oral or intravenous *diuretics* as well as increased fluid intake can significantly reduce waiting time for urine flow measurement but do not significantly alter uroflow parameters such as Q_{max} or voided volume [30–32]. Although uroflowmetry is a noninvasive test suggesting no morbidity, excessive fluid intake has been associated with water intoxication resulting in hyponatremia and seizure [33].
- *Patient behavior and nervousness* during flow testing in the office may lead to incomplete sphincter relaxation and decreased urinary flow rates or even intermittent flow. Therefore, repeated uroflowmetry measurements should be carried out in women with altered flow parameters.
- *Circadian rhythm*: It was shown in men that urine flow varies during the 24 hour period with higher Q_{max} values, smaller voided volumes, and reduced flow time in the early afternoon when compared with the late evening, early morning, and midnight to morning periods [34]. Equivalent studies have not as yet been reported in women.

Table 31.1 Normal Uroflowmetry Values in Healthy, Symptom- and Disease-Free, Young to Middle-Aged Women Who Voided with a Comfortably Full Bladder

	Wyndaele [50]	**Pauwels et al. [37]**	**Oelke et al. [51]**	**Barapatre et al. [22]**
Population	10 healthy women	32 healthy women	30 healthy women	308 healthy women
Country	Belgium	Belgium	Germany	India
Voiding position	Sitting	Sitting	Sitting	Squatting
Age (years)	24	49 ±6	26.2 ±7.3	33.7 ±8.9
Range	19–28	38–60	16–40	13–47
Voided volume (mL)	338 ±234	340 ±165	492 ±175	291 ±167
Q_{max} (mL/s)	31 ±11	29 ±12	33 ±12	23 ±9
Q_{ave} (mL/s)	22 ±14	18 ±8	19 ±9	13 ±6
Time to Q_{max} (s)	8.3 ±8.1	7 ±3	10 ±5	8 ±6
Voiding time (s)	7.6 ±22	23 ±12	32 ±15	22 ±12
Flow time (s)	26 ±20	20 ±9	30 ±17	Not mentioned

*Note:*The values are given as mean ±standard deviation, unless otherwise indicated.

Q_{max}, maximum urinary flow rate; Q_{ave}, average urinary flow rate.

- *Influence of posture*: Devreese et al. [35] investigated the influence of three different postures on urine flow parameters in 21 healthy volunteers. Sitting in anteversion, retroversion, or forward bending, all without straining, showed no significant differences for Q_{max}, Q_{ave}, and total flow time. However, intermittent flow (staccatos) was less frequently seen in the forward-bending position, suggesting that this position permits optimal relaxation of the pelvic floor muscles and, therefore, is the most preferable voiding position. Nonadapted height of the toilet seat preventing the feet from resting on the floor or crouching over the toilet is associated with postvoid residual urine. In many Asian countries, women void in the squatting rather than in the sitting position; it was shown for Indian women that urinary flow rates were significantly lower (and postvoid residuals higher) in the sitting than in the squatting position [36].
- *Influence of straining*: A considerable proportion of healthy women strain to initiate or maintain voiding; in a prospective study of healthy, asymptomatic women, 42% strained during voiding [37]. Independent of the posture on the toilet, straining has been shown to increase Q_{max} and Q_{ave} and decrease total voiding time [35]. This reinforcement of flow occurs only when the urethra is completely relaxed and the flow controlling zone of the urethra is not under the influence of the abdominal pressure. Needle or surface electrodes did not show relevant

sphincter activity in healthy women who strained during voiding [37,38]. As discussed previously, straining can also produce a bell-shaped flow curve [17].

- *Bladder volume*: Q_{max} and Q_{ave} are physiologically dependent on bladder volume. A positive correlation has been found between bladder volume and Q_{max}/Q_{ave} (Figures 31.6 and 31.7) [20,39–41]. During bladder volume increase and progressive stretching of the detrusor, the potential bladder contraction power also increases. This is most pronounced in the range from an empty bladder up to approximately 200 mL of bladder filling. At bladder filling volumes higher than 400–500 mL, the detrusor becomes overstretched and contractility may decrease again; however, there are large interindividual differences [22]. The flow–bladder volume relationship also varies with the type and degree of pathology as, for example, in constrictive obstruction, where Q_{max} is almost independent of bladder volume.
- *Nomograms* were developed to correctly judge the relationship between voided volume and Q_{max} or Q_{ave} [40,41]. The Liverpool Nomogram gives the investigator quick advice about the volume-adjusted Q_{max} (Figure 31.6) or Q_{ave} (Figure 31.7) of the individual woman.
- *Free uroflowmetry vs. flow recording during pressure–flow studies*: It is necessary to insert a catheter into the bladder for vesical pressure recording; however, a transurethral catheter may interfere with voiding. Flow time is significantly increased and flow rates are significantly decreased in women with inserted urethral catheters compared to those without catheters, indicating that invasive uroflowmetry does not reflect physiological urination [27,28,42]. In women with invasive flow measurement, there were no differences between 4.5 and 6 F catheters, but significant differences between 4.5 and 7 F catheters. Furthermore, intermittent flow is more common with inserted catheters [27].

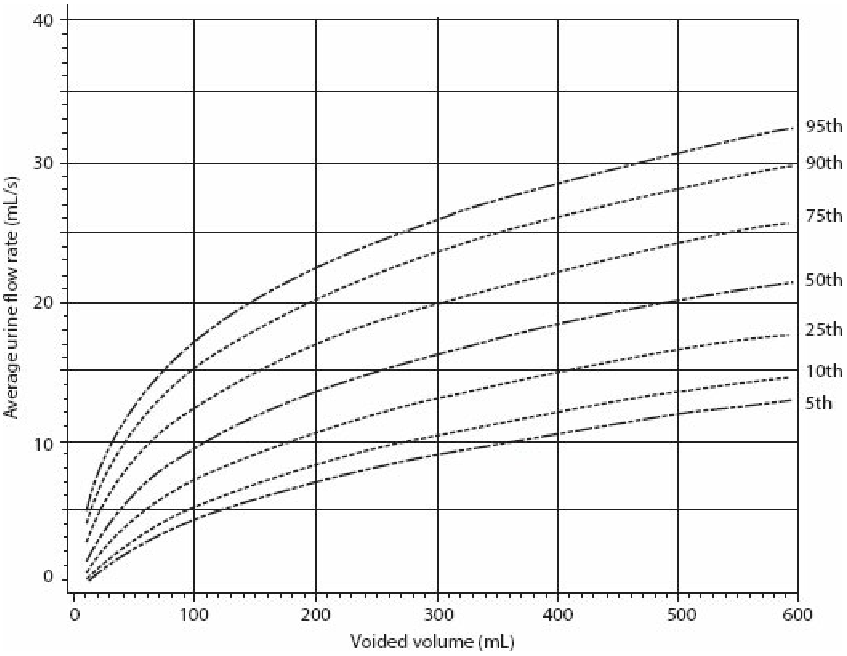

Figure 31.7 Liverpool Nomogram for the judgment of average urinary flow rate (Q_{ave}) relative to voided volume in women. (From Haylen BT et al., *Br J Urol*, 64, 30, 1989.) The patient has an abnormally low Q_{ave} when the flow value relative to voided volume is under the 10th centile; these women should be further evaluated.

- *Intraobserver variability* of measurements: Variability in interpretation proved relevant when done by 4 physicians with a minimum of 6 months of experience in urogynecology and with 8-week intervals between evaluations [18]. The difference was not large in the study by Jørgensen et al. [43] when the evaluation showed that visually read values were significantly lower than the mechanically determined ones, especially for Q_{max} in abnormal curves. The authors concluded that automatic computerized evaluation of uroflow curves may be misleading and cannot replace visual evaluation.

- *Interobserver variability* of measurements*:* Visual assessment of uroflow curves by urodynamicists demonstrated a substantial agreement of Q_{max}, Q_{ave}, flow time, voiding time, and the judgment of the curve as being "normal" or "abnormal" [44]. These results were independent of physicians' age or experience with uroflowmetry (<5, 5–10, or >10 years). Interestingly, there was a higher agreement between physicians who dedicated a relevant amount of their time to uroflowmetry compared to those who spent less than 5% of their working time on urodynamic practices. Computerized artifact detection and correction eliminates a relevant fraction of the variability of uroflow (Q_{max}) and decreases intra- and interobserver variability [45,46].
- *Home uroflowmetry* by means of a portable device proved to be a more accurate because it facilitates multiple measurements in a familiar environment [47,48]. A close relationship between Q_{max} at home and in the office was found, but voided volume was significantly larger and voiding time significantly longer in the office [47]. However, these variations between home and office flows appear to be irrelevant for screening of LUTD.

RECOMMENDATIONS FOR UROFLOW MEASUREMENT [3,4,49]

1. The flowmeter should be regularly calibrated and the calibration documented.
2. Patients should void with a "comfortably full bladder." Since this may be difficult to arrange in an office, patients should have the opportunity to drink fluids and void several times during one consultation.
3. Provide a separate room with clean material but without stimuli that might interfere with voiding (e.g., noise, music, disturbance, smell, dark atmosphere, or insufficient light). The flow curve should be recorded outside the flow room using electronic data transfer in order to avoid distraction during uroflow measurement.
4. Offer a toilet seat that allows the feet to rest on the floor.
5. After voiding in the office toilet, patients should be asked whether the void was representative compared to their usual voiding pattern at home. Additionally, patients should be asked whether they strained during uroflow measurement.
6. Compare the results of uroflowmetry with data obtained by the patient's own recordings on a frequency–volume chart (is voided volume in the office during uroflowmetry similar to voided volumes documented in the frequency-voiding chart?).
7. For graphical scaling of the flow curve, the x-axis represents time and 1 mm should equal 1 second. The y-axis represents the flow rate and 1 mm should equal 1 mL/s and 10 mL voided volume.
8. A sliding average over 2 seconds should be used to remove positive and negative spike artifacts in order to make electronically read Q_{max} values more reliable, comparable, and clinically useful.
9. Flow traces and the computer output derived form should be carefully scrutinized for artifacts and corrected, if necessary.
10. Only flow rate values smoothed either electronically or manually should be reported [40]. When reading Q_{max} graphically, the line should be smoothed by eye into a continuous curve so that, in each period of 2 seconds, there are no rapid changes (Figure 31.3).
11. Q_{max} should be rounded to the nearest whole number (e.g., a recorded value of 10.25 mL/s should be reported as 10 mL/s).
12. Voided volume and postvoid residuals should be rounded to the nearest 10 mL (e.g., a recorded value of 322 mL should be reported as 320 mL).
13. Q_{max} should always be documented together with voided volume and postvoid residual urine volume.
14. If a flow–volume nomogram is used, the name should be stated and referenced (e.g., Liverpool Nomogram, Figures 31.6 and 31.7).
15. Do more than one test, especially when the first flow does not permit a clear interpretation, has shown pathological values or an abnormal flow curve, or was reported not to be representative

compared to home flows.

16. Measurement of postvoid residual urine improves interpretation of the test.

UROFLOWMETRY IN HEALTHY VOLUNTEERS

For correct judgment of measurement values and curves and for adequate interpretation of uroflowmetry results, it is important to have data of age-matched healthy individuals. These normative data should derive from groups of healthy, symptom-free, and disease-free volunteers. Table 31.1 lists free uroflowmetry data of healthy asymptomatic volunteers who voided with a full bladder [22,37,50,51]. Normal Q_{max} depends on the voided volume and ranges between 12 and 40 mL/s [52]. When women void with a full bladder, mean Q_{max} is between 23 and 33 mL/s and mean Q_{ave} between 13 and 22 mL/s. Voiding time varies from 10–20 seconds at a volume of 100 mL to 25–35 seconds for a volume of 400 mL [53].

Arbitrary criteria have been proposed by a number of authors to diagnose LUTD. For bladder outlet obstruction, the equation of Q_{max} <15 mL/s and/or postvoid residual urine volume >50 mL in a bladder filled with a minimum of 150 mL before voiding (volume voided + postvoid residual) was suggested [19,54]. Costantini et al. [19] showed that these criteria correlated well with the results of the Liverpool Nomogram when voided volumes less than 15 mL and more than 600 mL were excluded. It was concluded that values below the 10th centile are abnormal (Figure 31.6).

Wyndaele [50] compared the uroflow curve in 10 young female volunteers and found 7 to have a bell-shaped curve on free flow, 1 voiding in two separate curves, and 2 presenting a continuous but undulating curve during the entire flow. When compared to the curve obtained during a subsequent pressure–flow study, 7 had the same pattern but 3, with bell-shaped curve during free uroflowmetry, had an irregular or interrupted flow pattern. Pauwels et al. [17] found that during free uroflowmetry only 83% of middle-aged healthy women and only 75% of young and healthy individuals voided with a normal voiding pattern. In uroflowmetry recorded during pressure–flow analysis, only half of the healthy women voided with a normal flow pattern. The flow patterns during free uroflow (without catheter) and pressure–flow recording (with catheter) corresponded in 47%–75%, respectively, depending on patients' symptoms. Free uroflow and pressure–flow patterns matched better in healthy women than in patients.

Miyata et al. [55] analyzed voiding parameters in 36 healthy adult females and found voiding time to be a useful parameter that was independent of the voided volume between 100 and 400 mL and never exceeded 21 s in all voiding attempts. Voiding time was shorter in healthy volunteers than in 84% of neurogenic patients and 67% of patients with chronic cystitis.

UROFLOWMETRY IN FEMALE PATIENTS

Several conditions may influence uroflow values and shapes and, therefore, should be taken into consideration before flow measurement and during interpretation of the flow curve. Voiding difficulties, defined as abnormally slow and incomplete voiding, have frequently not been reported by the affected women and are often only detected during systematic evaluation of voiding function. Therefore, a detailed voiding history and screening uroflowmetry are recommended in women at risk:

- *Pregnancy and puerperium*: A significant increase in uroflow rate was only seen in the second trimester of pregnancy [56]. A significant decrease of uroflow rate was documented during intravenous tocolysis with α-adrenoceptor agonists. Urinary flow rates were worse after forceps delivery but better after spontaneous delivery compared to controls; however, all flow rates remained within the normal range.
- *Delivery*: Comparison of urinary flow curves between primiparas and nulliparas showed no differences with regard to Q_{max}, Q_{ave}, voided volume, voiding time, and time to Q_{max} [35]. However, cesarean section seems to be more frequently associated with postvoid dribbling.
- *Menstrual cycle*: No differences were seen in any measured uroflowmetry parameter when comparing similar voids between different phases of the menstrual cycle. Therefore, when evaluating premenopausal patients, uroflowmetry may be scheduled and performed during any phase of the menstrual cycle [26].
- *SUI*: Conflicting data have been published with regard to Q_{max} in women with SUI. Bottaccini

and Gleason [57] contended that stress incontinent women void with a lower uroflow rate than healthy women because the distal urethral cross-sectional area appears to be incapable of opening as widely as the distal urethra of normal women. However, other studies have demonstrated the opposite: SUI women void with higher flow rates because of lower bladder outlet resistance [58]. Free uroflow appears to have a low positive predictive value for indicating abnormal pressure–flow studies in SUI women with or without previous surgery [59,60].

- *Genital prolapse*: Q_{max}, Q_{ave}, and voided volume have been described to be significantly lower than in healthy controls [48]. Cystocele appears significantly more frequent in patients with voiding difficulties and, vice versa, the frequency of cystocele and voiding dysfunctions was shown to be significantly higher in women with abnormal uroflowmetry [19]. Valentini et al. [61] demonstrated a constrictive effect on the bladder outflow in women with various degrees of cystocele. Poor uroflow rates and elevated postvoid residuals appear to be associated with higher grades of cystoceles [62].
- *Large uterine fibroids*: One study reported that Q_{max}, Q_{ave}, and voided volume are significantly lower in disease than in healthy controls [48].
- *Uroflowmetry in women before and after SUI surgery*: Normal or abnormal uroflow parameters before surgery, including Q_{max}, do not predict urinary retention after SUI surgery [63,64]. There is, however, some evidence that poor bladder emptying before surgery, defined as low flow rates and/or evidence of postvoid residuals, may predict voiding difficulties after SUI surgery [65,66]. Free uroflow at a follow-up of 1 year after tension-free vaginal tape (TVT) implantation showed —compared to preoperative values—a statistically significant decrease of Q_{max} and increase of postvoid residual urine [67]. By applying modeling of free uroflow, Fritel et al. [68] showed development of compressive obstruction in 34/50 patients (68%) after the TVT procedure. The counterpressure of the tape on the urethra results in continence. During voiding, this effect can be unmasked if women strain, resulting in lower flow rate. The hypothesis of constrictive obstruction with reduction of the cross section of the urethra of about 60% was proposed for 27 patients.
- *Radical hysterectomy for cervical cancer*: Compared to the preoperative situation, increased postvoid residuals and decreased uroflow rates were detected in women after radical hysterectomy [69]. Bladder dysfunction was attributed to a significant reduction of detrusor contraction power (contractility) with concomitant abdominal straining due to impaired parasympathetic motor innervation [70]. However, the values improved from baseline to 6 months after surgery.

CONCLUSIONS

Uroflowmetry is a valuable, cheap, noninvasive, and fairly reliable screening test for women with suspected LUTD. Practical application and interpretation of free uroflowmetry results have to follow strict rules. Uroflowmetry should always be combined with other clinical tests for the assessment of bladder function/dysfunction or screening of treatment. In patients with a pathological uroflow, additional pressure–flow studies are recommended to evaluate the exact cause of LUTD.

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32

Basic Urodynamic Tests: Filling and Voiding Cystometry

Hashim Hashim and Paul Abrams

DEFINITION

Cystometry, a part of urodynamic studies, is the measurement of relevant physiological parameters taken during the filling and voiding phases of micturition, allowing direct assessment of lower urinary tract function [1]. It can be divided into two parts:

1. *Filling cystometry*: The method by which the relationship of pressure and volume in the bladder is measured during bladder filling.
2. *Pressure–flow studies of voiding*: The method by which the relationship of pressure in the bladder and urine flow rate is measured during bladder emptying.

AIMS

Cystometry is performed clinically as part of urodynamic investigations in patients complaining of lower urinary tract symptoms (LUTS) to help make a diagnosis and hence plan a suitable treatment or further appropriate investigations.

Cystometry aims to evaluate detrusor and urethral function during the storage (filling) and voiding phases of micturition. It is essential that diagnoses made at the time of cystometry are related to the patient's signs and symptoms and the physical findings at the time of examination. The aim is to reproduce the patient's symptoms and to quantify the pathophysiological processes, thus providing an explanation of the patient's problems and an understanding of their implications. Cystometry can also be used for research purposes or to provide objective measurements following particular treatments.

INDICATIONS

Ideally, all patients with LUTS suggesting a bladder or urethral disorder should undergo urodynamic studies. The bladder is known to be an "unreliable witness": urinary symptoms alone do not always allow the correct diagnosis to be made and inappropriate treatment may be given [2–6]. However, with limited health-care resources and access to such a service, patients with "clear-cut" symptoms can initially be managed empirically, for example, by pelvic floor exercises or with duloxetine (serotonin norepinephrine reuptake inhibitor), available in some parts of the world, for suspected stress urinary incontinence, and bladder training, antimuscarinics, and/or mirabegron for overactive bladder syndrome and suspected detrusor overactivity (DO).

Urodynamics should not be performed without clear indications and a proposed *urodynamics question(s)* that will be answered by the investigation [7]. Cystometry should be preceded by the completion of a 3-day frequency/volume chart or bladder diary, e.g., ICIQ-BD (Figure 32.1) [8], and free uroflowmetry. Ideally, two successive free flows are performed [9,10].

Urodynamic tests should be considered in women:

- With mixed LUTS in whom surgery is contemplated (e.g., urgency/urgency incontinence and stress urinary incontinence)
- With a suspected voiding disorder
- Being considered for bladder neck surgery
- With previous unsuccessful incontinence surgery
- With neurogenic bladder disorders
- Complex cases, e.g., prior to kidney transplant
- In whom conservative and pharmacologic measures have failed; for example, physiotherapy for symptoms of stress urinary incontinence and antimuscarinic drug treatment, mirabegron, and

bladder training for symptoms of overactive bladder syndrome

PREPARING FOR CYSTOMETRY

Quality Control during Cystometry

Quality control is vital to allow accurate, reproducible, and interpretable pressure readings and to allow identification of artifacts. The International Continence Society (ICS) has defined these steps in the 2002 Good Urodynamic Practices report [7]:

Flushing: The manometer tubing connecting the transducers must be flushed before setting zero to remove any air bubbles that could give low false pressure readings.

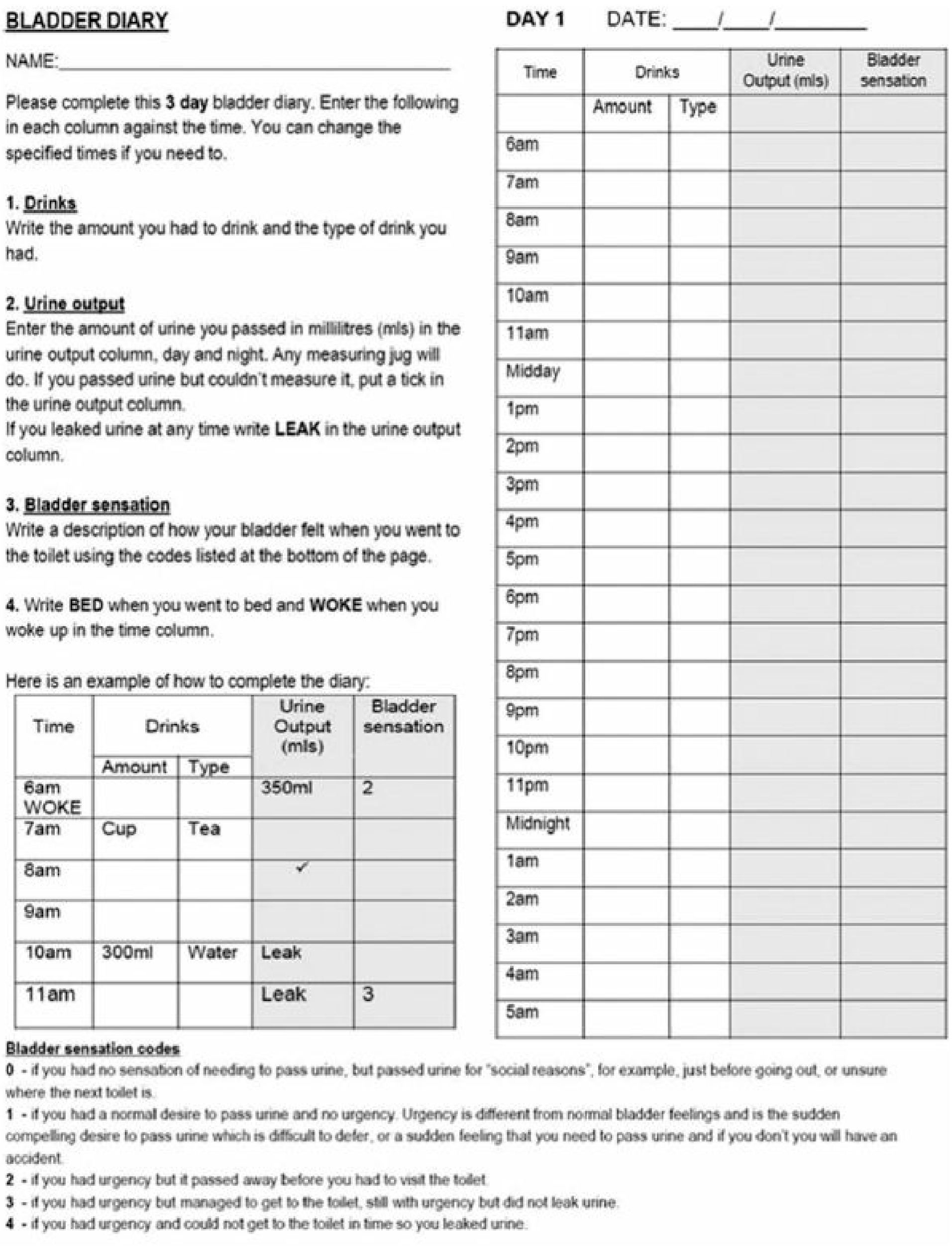
Setting zero at atmospheric pressure: This can be done either prior to inserting the catheters into the patient or after insertion as long as the transducers are open *only* to the atmosphere. Zero pressure is set when an external transducer is open only to the environment (the other two sides of a 3-way tap are closed) or when the open end of a connected, fluid-filled tube is at the same vertical level as the transducer before insertion into the patient (Figure 32.2).

Calibrating the transducers: They should be calibrated at 0 and +100 cmH_2O; the bladder (vesical) pressure (p_{ves}) and rectal or vaginal intra-abdominal pressure (p_{abd}) lines should be in the positive range +5 to +50 cmH_2O (depending on body position, lying or standing, and body habitus); the detrusor pressure (p_{det}) should be between –5 and +5 cmH_2O [11]. Neither the abdominal nor vesical pressure lines can be zero or negative as it is not possible to have these pressures physiologically. Detrusor pressure can be slightly negative as it is an artificial number from the subtraction of abdominal pressure from vesical pressure.

Establishing a reference level for pressure: The superior border of the symphysis pubis is the fixed reference level for external and fluid-filled catheter systems; the transducers should be levelled to this horizontal plane so that all measurements have the same hydrostatic component.

It is easier to add two 3-way taps to the pressure transducers, so that all procedures can be done by turning the valves alone without disconnecting any tubing and using syringes in a vertical position, maintaining connections, eliminating all air bubbles, and avoiding any new air bubbles (Figure 32.2).

During the investigation, quality control is ensured by asking the patient to cough at regular (e.g., 1 minute) intervals (Figure 32.3). Before recording is started, the patient is asked to cough and the p_{ves} and p_{abd} traces are observed. The two cough spikes should show an equal rise in the two pressure lines (p_{ves} and p_{abd}) and a complete subtraction of these two pressures should result in no change of the p_{det} line. Sometimes, a small artifactual biphasic blip (Figure 32.3) is seen on p_{det}, but this also indicates acceptable subtraction. The biphasic blip occurs due to different speeds of transmission of the pressure waves from the bladder and rectum/vagina to the two transducers and is seen mainly in older urodynamic systems. The two blips of the biphasic wave should be equal in size; if they are not equal in height, this can indicate poor quality. The patient should cough before and after voiding to reconfirm quality control and that no displacement of catheters has occurred. During filling, the p_{ves} and p_{abd} lines should not decline.



BLADDER DIARY

DAY 1 DATE: ____/____/________

NAME:____

Please complete this **3 day** bladder diary. Enter the following in each column against the time. You can change the specified times if you need to.

1. Drinks
Write the amount you had to drink and the type of drink you had.

2. Urine output
Enter the amount of urine you passed in millilitres (mls) in the urine output column, day and night. Any measuring jug will do. If you passed urine but couldn't measure it, put a tick in the urine output column.
If you leaked urine at any time write **LEAK** in the urine output column.

3. Bladder sensation
Write a description of how your bladder felt when you went to the toilet using the codes listed at the bottom of the page.

4. Write **BED** when you went to bed and **WOKE** when you woke up in the time column.

Here is an example of how to complete the diary:

Time	Drinks		Urine Output (mls)	Bladder sensation
	Amount	Type		
6am WOKE			350ml	2
7am	Cup	Tea		
8am			✓	
9am				
10am	300ml	Water	Leak	
11am			Leak	3

Time	Drinks		Urine Output (mls)	Bladder sensation
	Amount	Type		
6am				
7am				
8am				
9am				
10am				
11am				
Midday				
1pm				
2pm				
3pm				
4pm				
5pm				
6pm				
7pm				
8pm				
9pm				
10pm				
11pm				
Midnight				
1am				
2am				
3am				
4am				
5am				

Bladder sensation codes

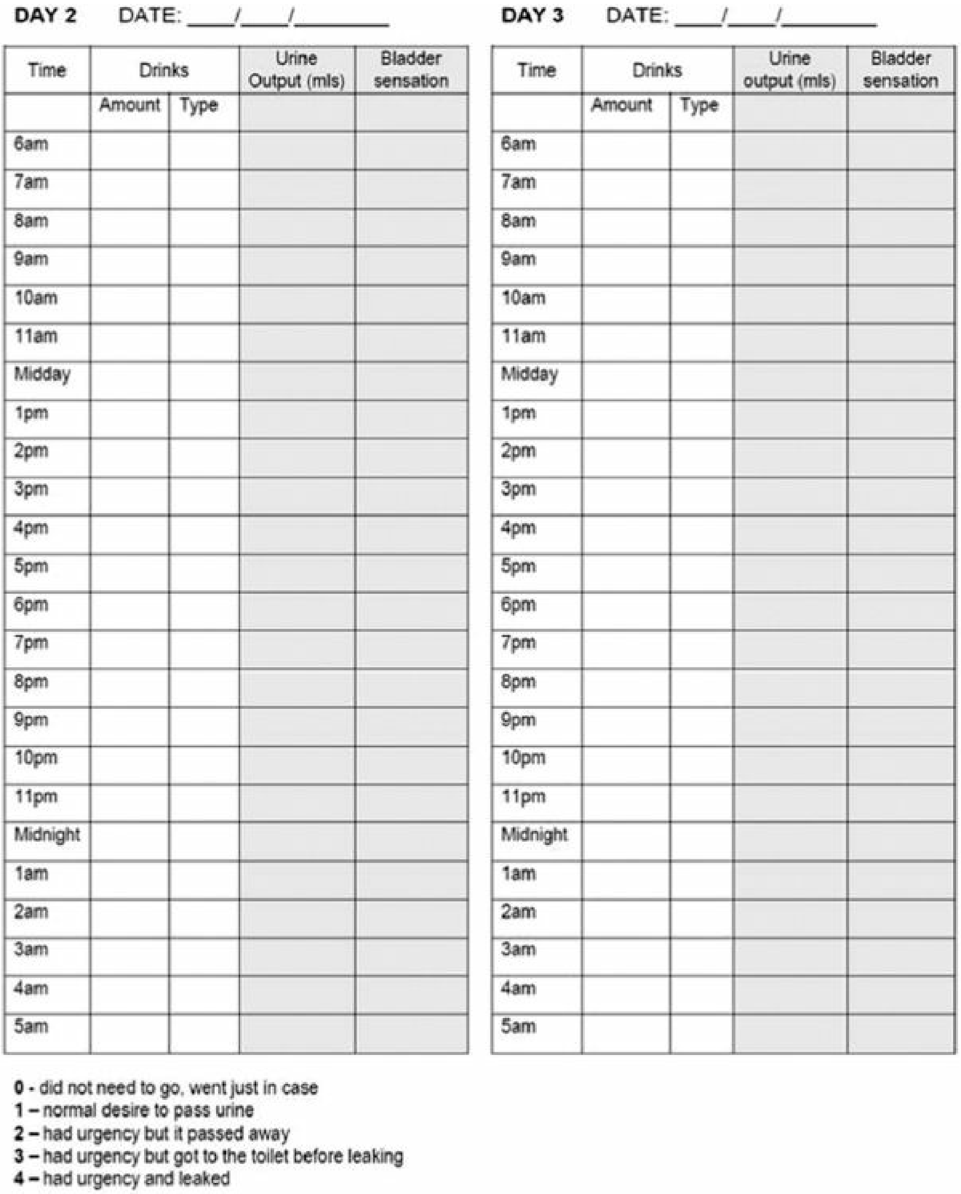
0 - if you had no sensation of needing to pass urine, but passed urine for "social reasons", for example, just before going out, or unsure where the next toilet is.

1 - if you had a normal desire to pass urine and no urgency. Urgency is different from normal bladder feelings and is the sudden compelling desire to pass urine which is difficult to defer, or a sudden feeling that you need to pass urine and if you don't you will have an accident.

2 - if you had urgency but it passed away before you had to visit the toilet.

3 - if you had urgency but managed to get to the toilet, still with urgency but did not leak urine.

4 - if you had urgency and could not get to the toilet in time so you leaked urine.



DAY 2 DATE: ____/____/________

Time	Drinks		Urine Output (mls)	Bladder sensation
	Amount	Type		
6am				
7am				
8am				
9am				
10am				
11am				
Midday				
1pm				
2pm				
3pm				
4pm				
5pm				
6pm				
7pm				
8pm				
9pm				
10pm				
11pm				
Midnight				
1am				
2am				
3am				
4am				
5am				

DAY 3 DATE: ____/____/________

Time	Drinks		Urine output (mls)	Bladder sensation
	Amount	Type		
6am				
7am				
8am				
9am				
10am				
11am				
Midday				
1pm				
2pm				
3pm				
4pm				
5pm				
6pm				
7pm				
8pm				
9pm				
10pm				
11pm				
Midnight				
1am				
2am				
3am				
4am				
5am				

0 - did not need to go, went just in case
1 – normal desire to pass urine
2 – had urgency but it passed away
3 – had urgency but got to the toilet before leaking
4 – had urgency and leaked

Figure 32.1 International Consultation on Incontinence Questionnaire Bladder Diary.

Patient Position

For convenience, the catheters are put in position with the patient supine after the physical examination (Figure 32.4). Cystometry should then be done in the upright (sitting) position because (1) this is the physiological position in which women spend a substantial proportion of their time when awake, (2) the majority of women complain of symptoms when upright and active, and (3) at least 30% of DO will be missed if the patient is filled supine, resulting in suboptimal treatment decisions [12]. It is expedient to ask the patient to sit on a commode with a flowmeter situated below it to measure any leakage of urine during the test and also because most women void when sitting down. Some women complain of leakage when changing position (e.g., on bending over or getting up from the sitting position); these changes in posture can be mimicked during the test to try to reflect everyday stresses on the bladder and to reproduce leakage. Whenever the patient's position is altered, the position of the transducer must be readjusted to the pressure reference level of the upper border of the symphysis pubis.

With the catheters in position, the filling catheter is connected to a bag of suitable filling medium (see Figure 32.4). The rest of the equipment should be close to the patient for convenience, and if a computer screen is available, this should be in a position viewable by the patient so that explanations can be given during the test.

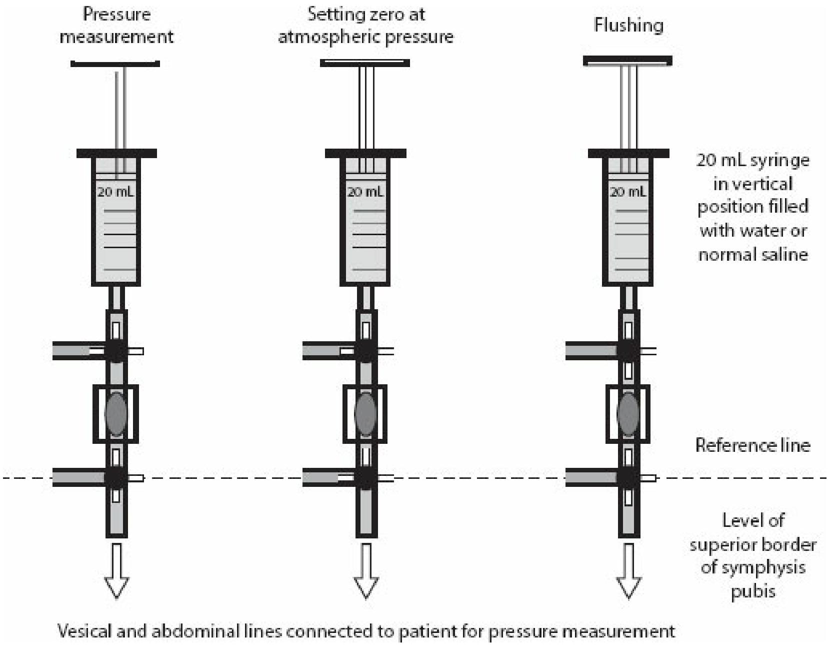

Pressure measurement
Setting zero at atmospheric pressure
Flushing
20 mL
20 mL
20 mL
20 mL syringe in vertical position filled with water or normal saline
Reference line
Level of superior border of symphysis pubis
Vesical and abdominal lines connected to patient for pressure measurement

Figure 32.2 Pressure transducer and 3-way tap configurations.

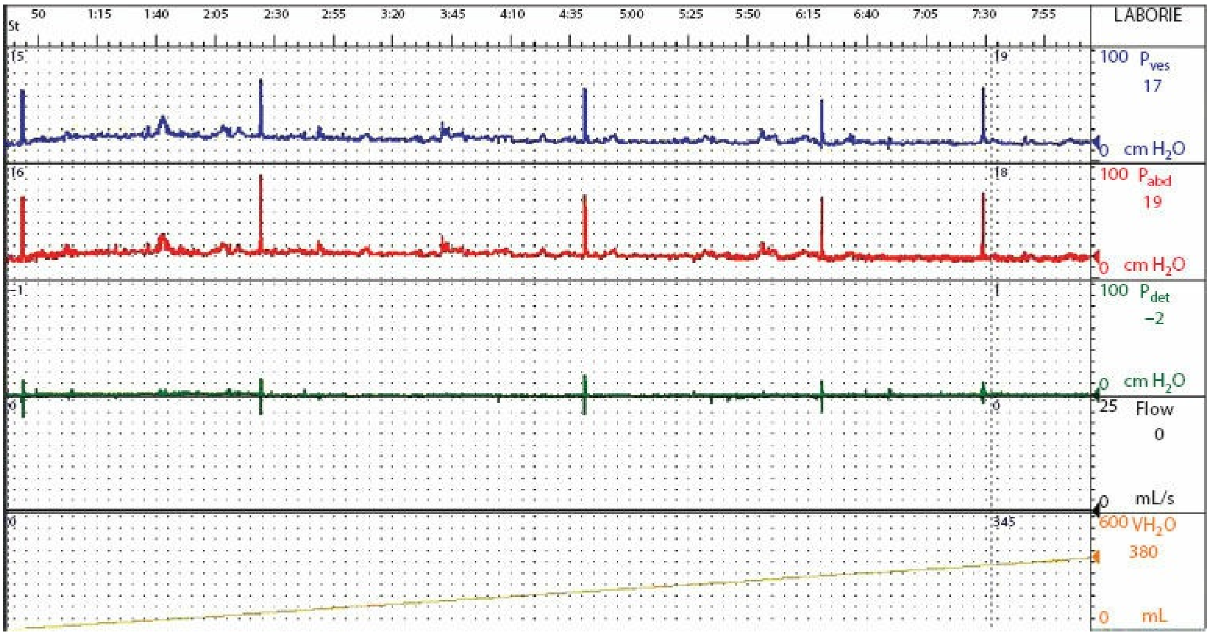


Figure 32.3 Normal cystometrogram with coughs showing equal rises on intravesical pressure (p_{ves}) and intra-abdominal pressure (p_{abd}).

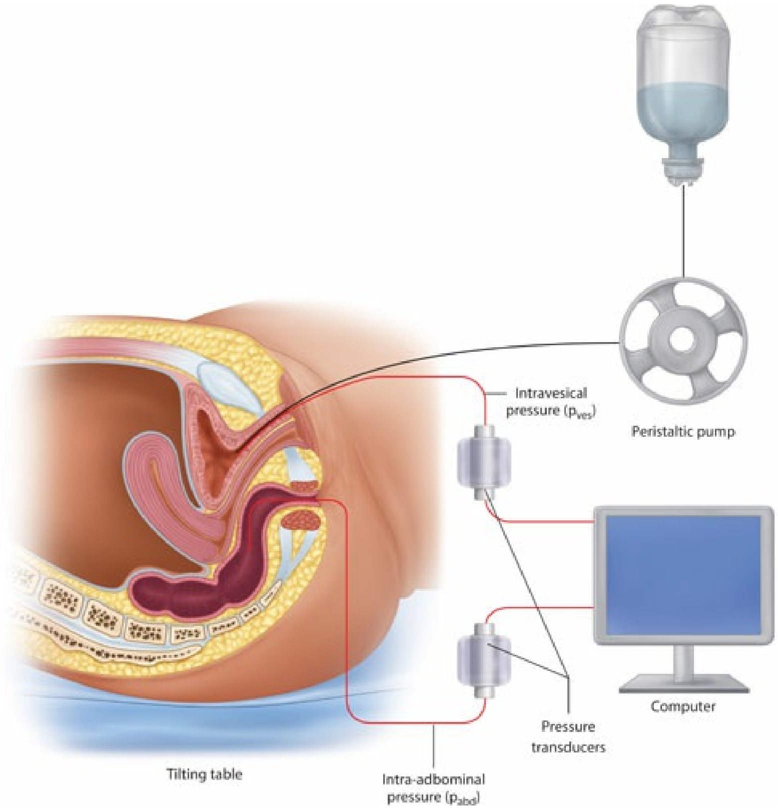

Intravesical pressure (p_{ves})
Peristaltic pump
Computer
Pressure transducers
Tilting table
Intra-adbominal pressure (p_{abd})

Figure 32.4 Catheter positions. The patient is in supine position only for catheter insertion.

If there is severe DO that prevents adequate filling, even at a reduced rate (10–20 mL/min), then filling in the supine position may be required in order for any useful information to be gathered from cystometry.

Reduced mobility or severely disabled patients (e.g., by neurological disease) may necessitate cystometry in the supine position.

Filling Medium

Water and 0.9% (normal) saline are the fluids most frequently used for bladder filling, as they are cheap, convenient, and mimic urine. The fluid is commonly used at room temperature (22°C); however, body temperature (37°C) may be more physiological. Cystometry has been performed with the filling medium warmed to body temperature with no observable difference in results [13]; however, this has not yet been scientifically investigated and standardization is required. It is known that ice-cold infusion fluid can stimulate bladder contraction at low bladder volumes [14] and therefore should not be used in routine cystometry.

In the past, carbon dioxide has been used in gas cystometry [15] but is no longer recommended as it is not a physiological medium for the bladder, it dissolves in urine to form irritant carbonic acid, and it can cause pain in “hypersensitive” bladders; furthermore, capacity measurement is inaccurate as the gas is both compressible and soluble in urine [16]. In addition, it is not possible to obtain a pressure–flow analysis of the voiding phase of micturition after gas cystometry.

Filling Rates

Previously, three filling rates were defined by the ICS [1]:

1. Slow-fill cystometry up to 10 mL/min
2. Medium-fill cystometry between 10 and 100 mL/min
3. Fast-fill cystometry when the rate is greater than 100 mL/min

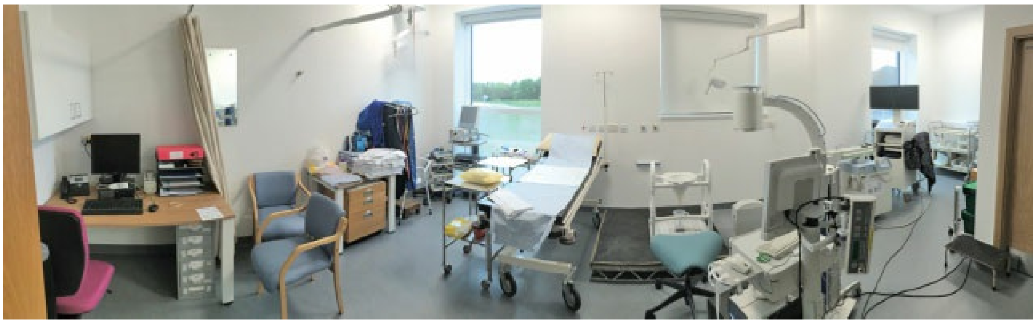


Figure 32.5 The equipment used are the couch, cystometry unit, patient unit, flowmeter—the image intensifier is used in videourodynamics.

In the latest standardization report, the ICS no longer divides filling rates into slow, medium, or fast. Currently, the term “nonphysiological filling rate” is used, and the precise filling rate should be stated. We recommend a filling rate of 50 mL/min, which, although convenient in the setting of a busy urodynamic unit, is not so fast as to be grossly nonphysiological; it also allows time to discuss symptoms with the patient and to assess whether those symptoms have been successfully reproduced. In a patient with very marked DO, the rate should be reduced to 30 mL/min or lower.

Slower filling rates (10 mL/min) are indicated in patients with neurogenic bladder dysfunction. There is little point in more rapid filling, and there is risk of artifactually affecting bladder compliance, although some believe it to be a further provocative test for DO.

Equipment

Multichannel cystometry requires a urine flowmeter, two (or three) transducers, an electronic subtraction unit to derive p_{det} ($p_{ves} - p_{abd}$), a recorder with a printout, and an amplifying unit (Figure 32.5). All pressure measurements are made in centimeters of water (cmH_2O).

The bladder pressure is measured using either

- A fluid-filled line (a double-lumen or single-lumen epidural-type catheter is inserted into the bladder and connected to an external pressure transducer; Figure 32.6).
- A solid microtip pressure transducer (a transducer is mounted on the tip of a solid 7 Fr catheter and hence is an internal pressure transducer system; Figure 32.7). This catheter-mounted transducer eliminates artifacts arising from the fluid-filled system, which needs to be connected to an external transducer.

Abdominal pressure is measured with a rectal (or occasionally vaginal) [17] catheter (6 Fr single-lumen manometer tubing covered with a small perforated balloon to prevent blockage by feces; the perforation ensures that flushing the balloon does not build up elastic pressure) that is inserted into the rectum to a distance approximately 10 cm above the anal margin (or into the vaginal fornix, if the vagina is used). If the patient has no rectum or vagina but a colostomy, then that can be used for the abdominal pressure measurement. This line is taped to the patient’s buttock close to the anal verge to prevent any slippage during the test. The tubing must be flushed from the transducer end before recording is commenced. Some commercial rectal catheters do not have a hole and thus the balloon continues to expand with repeat flushing, resulting in false rectal pressures. It is therefore advisable to make a small cut in the rectal balloon even if you are using a commercial rectal catheter (Figure 32.6). Making a hole in the rectal balloon is not in the ICS Good Urodynamic Practices report [7] and the report suggests filling the balloon to 10%–20% of its capacity. However, this is often difficult to gauge and the balloon could easily be filled more than that, causing error in measurement. Some companies produce double-lumen catheters for measuring rectal pressure to allow insertion of fluid and aspiration to remove all air bubbles. The use of these commercial catheters may not be economical in some centers, and therefore a cheaper way of measuring abdominal pressure, which offers very good results for measuring abdominal pressure through the rectum, is to use a 6 Fr filling catheter or feeding tube and cover the end of it with a fingerstall obtained from a nonsterile surgical rubber glove and taped securely, but ensuring that a small hole is made in fingerstall to allow expulsion of fluid during flushing.

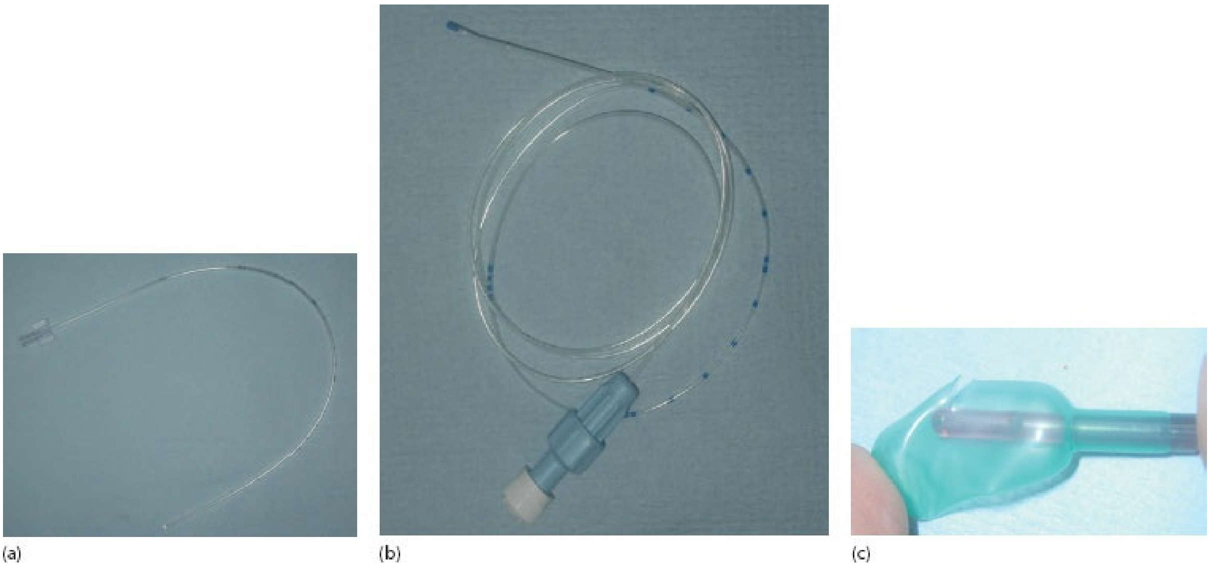


Figure 32.6 (a) Filling catheter (8 Fr), (b) epidural-type catheter (16G), and (c) rectal line with a hole made in balloon.

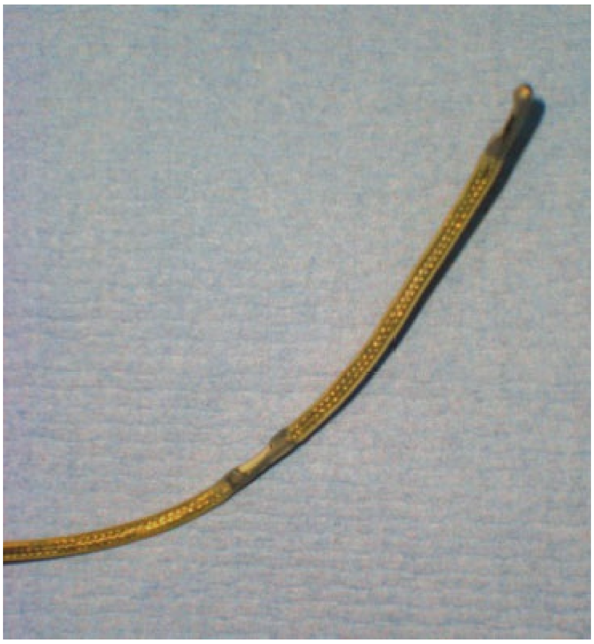


Figure 32.7 Solid catheter-tip transducer (Gaeltec).

The reference height for all measurements is taken as being level with the upper edge of the symphysis pubis and the transducers are zeroed to atmospheric pressure. A double-lumen filling catheter (6 Fr) is inserted into the bladder via the urethra (or, occasionally, by the suprapubic route). Sometimes a single-lumen (7 Fr) filling catheter with a 16G catheter for pressure measurement inserted alongside it can be used instead of the double-lumen [18]. 16G catheters are generally readily available in hospitals as they are commonly used for administration of epidural anesthesia. Double-lumen catheters are expensive and thus the two-catheter combination is a cheaper alternative that gives similar results. The single-lumen filling catheter is pulled out just before voiding and the 16G catheter is left in the bladder and used to measure pressure. The advantage of the double-lumen catheter is that the patient’s bladder can be filled and refilled multiple times should the test require it, and the postvoid residual (if any) can easily be drained and measured through it; however, it is more expensive to use.

The double-lumen catheters are also sometimes subject to more pump artifacts during filling (i.e., the small surges in pressure from the filling pump may transmit through the catheter to be detected by the pressure transducer). The catheters are fixed in place by tape close to the external urethral meatus on the medial aspect of the thigh.

Recently, air-filled catheters have been introduced to the market. However, it is important that those thinking of using air-filled catheters know that there has not been any standardization of technique or reference values produced, and it is not known whether the measurements made are equivalent to the fluid-filled catheters or not.

MEASUREMENTS

The following measurements are made (Figure 32.3):

- p_{ves} is measured via a urethral or suprapubic catheter connected to the bladder transducer.
- p_{abd} is the pressure within the abdomen, outside and around the bladder, and is measured in the rectum or vagina.
- p_{det} is obtained by subtracting the abdominal from the intravesical pressure ($p_{det} = p_{ves} - p_{abd}$) and represents the pressure generated by the bladder wall, usually as detrusor contractions.
- The volume infused into the bladder is recorded.
- The urine flow rate, as leakage during filling and flow during voiding, is recorded.

Measuring bladder and intra-abdominal pressure simultaneously ensures that any pressure changes observed can be interpreted correctly. A rise in the vesical pressure could be due to either DO or abdominal straining being transmitted to the bladder. The electronic subtraction allows detrusor pressure to be measured and any change in pressure seen on the traces to be attributed appropriately.

Detrusor function is assessed directly from observation of the pressure changes. Urethral function must be inferred from the pressure changes within the bladder and by measuring any leakage during filling and urine flow during voiding.

METHOD

The basic details of the test and the most frequent side effects (e.g., risk of urinary tract infection) should be fully explained to the patient, and, in particular, the importance of indicating any bladder sensations during the test, as they happen, should be emphasized. The symptoms can then be used to annotate the cystometry trace and help with interpretation.

Urinalysis and free uroflowmetry should be performed before embarking on cystometry to exclude any abnormality that may preclude proceeding with the test or may need extra precautions to be taken during the test, such as a urinary tract infection. Any residual urine on subsequent catheterization is then measured. We normally empty the bladder of any residual urine in nonneurogenic bladders, as this allows us to assess bladder function when the bladder is empty, which may be important if treatment involves emptying the bladder, such as when using intermittent self-catheterization.

Filling Cystometry

The filling phase starts when filling commences and ends when the patient is given permission to void by the urodynamicist. Bladder sensation, detrusor activity, bladder compliance, bladder capacity, and urethral function should all be assessed during this procedure. The degree of bladder filling should be guided by the voided volumes recorded on the bladder diary.

Bladder Sensation

During the filling phase, the patient is asked to indicate when and if the following occur:

- First sensation of bladder filling [1]: This is the feeling of first becoming aware of bladder filling. This sensation may not be truly representative, owing to the interfering presence of the catheter.
- First desire to void (FDV) [1]: This is the feeling that would lead to passing urine at the next convenient moment, but voiding can be delayed if necessary. Essentially this is the normal

desire to void in the old ICS terminology [19].

- Strong desire to void (SDV) [1]: This is the persistent desire to void, without the fear of leakage.
- Urgency [1]: This is the complaint of a sudden compelling desire to void, which is difficult to defer. It is an abnormal sensation, distinct from SDV.

The volumes should be noted. The aforementioned terminology has been defined by the ICS [1]. Other terms that are also used during filling cystometry and related to bladder sensation include first sensation of bladder filling, bladder pain, and bladder sensation—which can be categorized as increased, normal, reduced, absent, or nonspecific (seen mainly in neurological patients).

Bladder hypersensitivity is a term that has been used in the past and found to be helpful [13]. It is defined as a condition where there is an early FDV at less than 100 mL and this persists and worsens, limiting the bladder cystometric capacity to a maximum of 250 mL. This term has now been replaced with the term "increased bladder sensation," which is an early first sensation of bladder filling (or an early desire to void) and/or an early SDV, which occurs at low bladder volume and which persists. The new term is subjective and thus it is not possible to quantify volumes.

Detrusor Activity

Detrusor activity, during filling, is described as either "normal" or "overactive." A normal detrusor allows bladder filling with little or no change in pressure and with no involuntary phasic contractions occurring during cystometry, despite provocation [1].

The presence of involuntary phasic detrusor contractions, occurring throughout filling, is diagnosed by a rise in the detrusor pressure line (there is no lower limit for the amplitude of an involuntary detrusor contraction) with a similar pressure rise in the vesical line, but no fall in pressure in the abdominal line, during filling cystometry (Figure 32.8). The patient should be asked whether there is any associated sensation (urgency) and if the sensation mimics the one that is normally experienced and causes problems. Provocative factors such as coughing or running water maybe used to provoke symptoms, such as stress incontinence or urgency due to DO, and should be noted.

If the bladder is shown during cystometry to contract spontaneously or with provocation, then it is said to have phasic DO. Some women will not experience any symptoms at the time of these contractions, in which case the significance of DO is unknown. If a single involuntary detrusor contraction occurs at the end of filling, resulting in incontinence, with no overactivity during filling, then this is known as terminal DO.

When there is a known neurological condition (e.g., multiple sclerosis), any DO observed is termed neurogenic DO (this replaces the older term of detrusor hyperreflexia). DO is idiopathic if there is no identified cause.

Bladder Compliance

The term bladder compliance describes the relationship between change in bladder volume and detrusor pressure ($\Delta V/\Delta p_{det}$) and is measured in mL/cmH_2O. Normal compliance is at least 40 mL/cmH_2O. As a normal bladder fills, there is very little or no change in the pressure (i.e., the bladder is a high-compliance system). As filling rates can alter bladder compliance, the filling rate of cystometry must always be documented. In neurologically normal women, reduced compliance is usually artifactual owing to the bladder being filled excessively fast. Should compliance start to rise during filling, the filling should be stopped for approximately 1 minute to see if the compliance returns to normal: if compliance returns to normal, the increase is artifactual and secondary to fast filling; if compliance does not return to normal, then it is secondary to a pathological condition. Continued filling should be at a slower rate of not more than 20 mL/min.

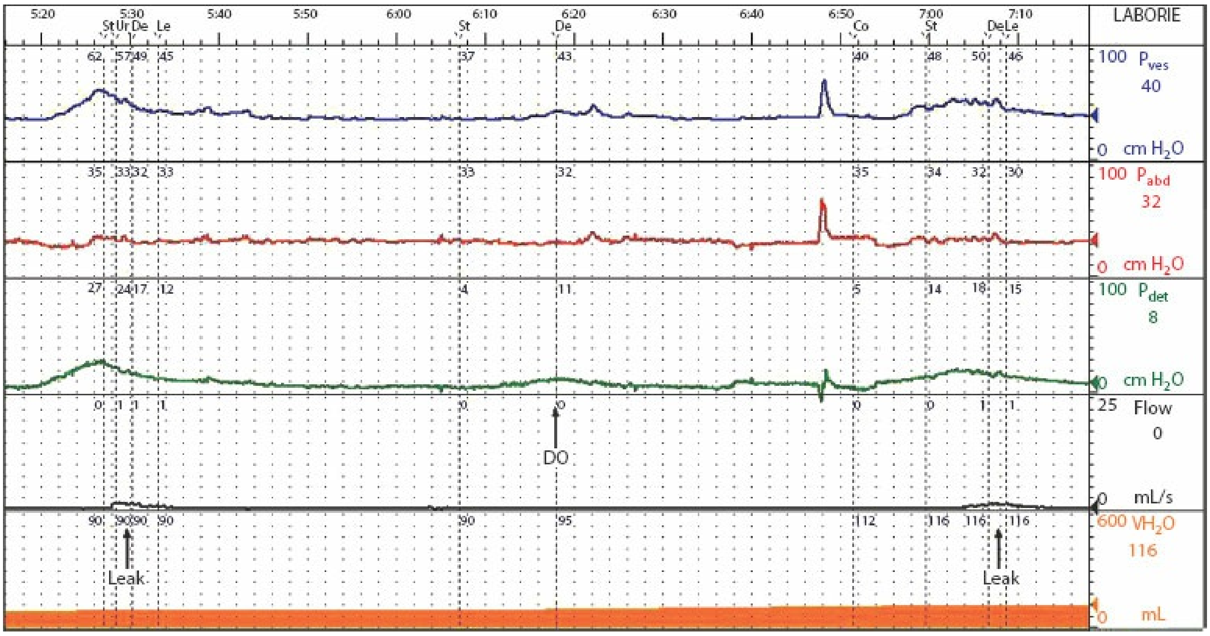


Figure 32.8 Cystometrogram showing detrusor overactivity (DO) and DO incontinence (leak). (p_{det}, detrusor pressure; p_{abd}, intra-abdominal pressure; p_{ves}, vesical pressure; flow rate in mL/s; V_{H2O}, volume of filling medium infused.)

Urethral Function

During the filling phase, in normal women, the urethral closure pressure ($p_{ura} - p_{ves}$) remains positive (i.e., urethral pressure is greater than the vesical pressure), even at times of increased abdominal pressure; hence, continence is maintained. To allow voiding, closure pressure falls to zero as the urethra relaxes. If involuntary loss of urine is observed without detrusor activity, then the urethral closure mechanism is said to be incompetent.

A diagnosis of urodynamic stress incontinence (USI) can be made if leakage is associated with an increase in intra-abdominal pressure that causes the vesical pressure to exceed the urethral pressure in the absence of a detrusor contraction (Figure 32.9). When filling volume reaches 200 mL, filling is stopped and the patient is asked to strain and then to cough to observe any leakage during these two maneuvers that tend to increase abdominal pressure above urethral pressure in women with the symptom of stress urinary incontinence. The intravesical pressure at which urine leakage occurs due to increased abdominal pressure in the absence of a detrusor contraction is known as the abdominal leak point pressure (ALPP) [1]. ALPP can be divided into cough leak point pressure and Valsalva leak point pressure (VLPP). If the patient leaks with a VLPP of less than 60 cmH_2O, then this is more indicative of USI secondary to intrinsic sphincter deficiency. If the VLPP is more than 90 cmH_2O, then the USI is more indicative of urethral hypermobility. These values are not “black and white” but can be used as a rough guide as to the cause of the stress incontinence, thus directing treatment options.

Filling is continued until the patient feels their bladder is full, at which point a cough is performed and permission to void is given.

Voiding Cystometry

At the end of filling, the bladder-filling catheter is removed (only if separate single-lumen filling and pressure catheters are used rather than a double-lumen catheter) to avoid any artifacts during voiding as a result of urethral obstruction. If leakage has not been noted during the filling phase, the patient is asked to cough a few times. If leakage is still not noted at this time, the patient is asked to stand and is given instructions on physical exertions to try to provoke leakage. Provocative maneuvers for DO incontinence include standing with the legs apart and running water from the taps and/or hand washing, whereas coughing, jumping (star jumps), and squatting are tests for USI.

The patient, now back on the commode with the vesical and rectal pressure catheters still in situ, is instructed to void, and the detrusor pressure and urine flow rate are recorded simultaneously. Detrusor pressure at maximum flow ($p_{det}Q_{max}$) and flow rate are recorded. The urodynamicist and any other staff in the room usually leave the room during the voiding phase to allow for privacy, unless video urodynamics are performed.

Voluntary initiation of a detrusor contraction is usually required for normal micturition and this is normally sustained until the bladder is empty, although some women can void by just relaxing their pelvic floor. The pressure rise is dependent on the outlet resistance and on the contraction of the detrusor itself (Table 32.1): if the detrusor pressure is low with low flow rates, the detrusor is defined as underactive; if the pressure is high with low or normal flow rates, this may be indicative of bladder outlet obstruction. If the detrusor muscle is functioning normally, then abdominal straining should not be required for bladder emptying. Many nomograms have been suggested as being able to diagnose bladder outlet obstruction and detrusor underactivity in women; however, neither the ICS nor the International Consultation on Incontinence has yet adopted a nomogram for women and none has been widely used or universally accepted. In general, however, a sustained detrusor pressure of more than 20 cmH_2O and a flow rate of less than 12 mL/s with or without a residual urine are indicative of bladder outlet obstruction in women [20].

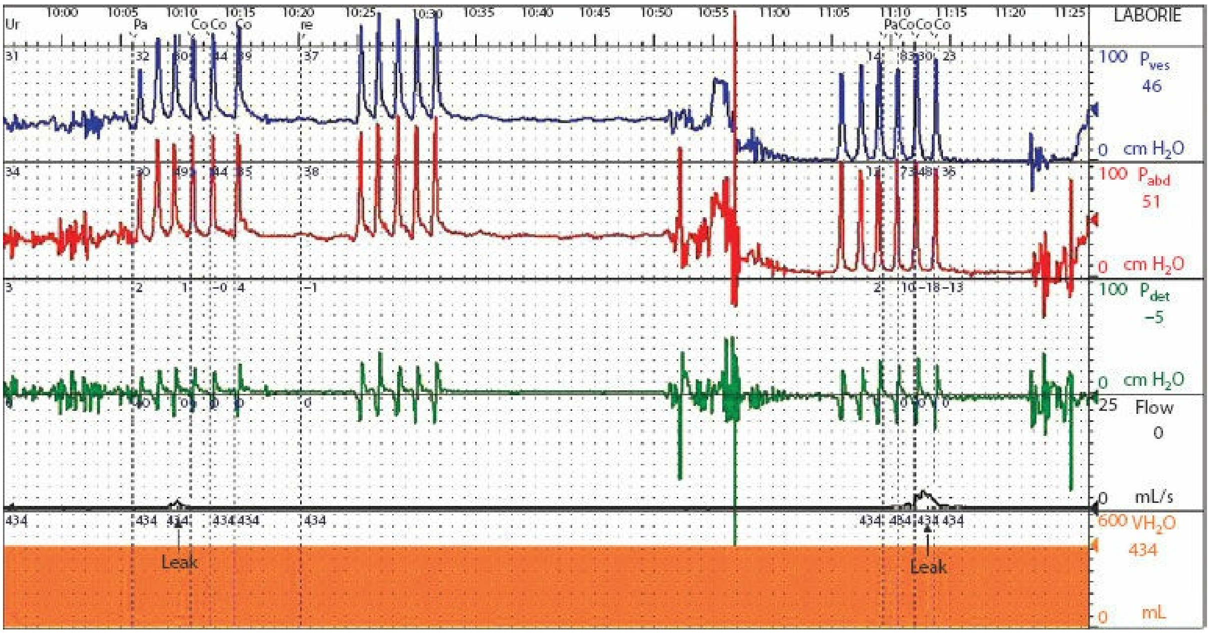
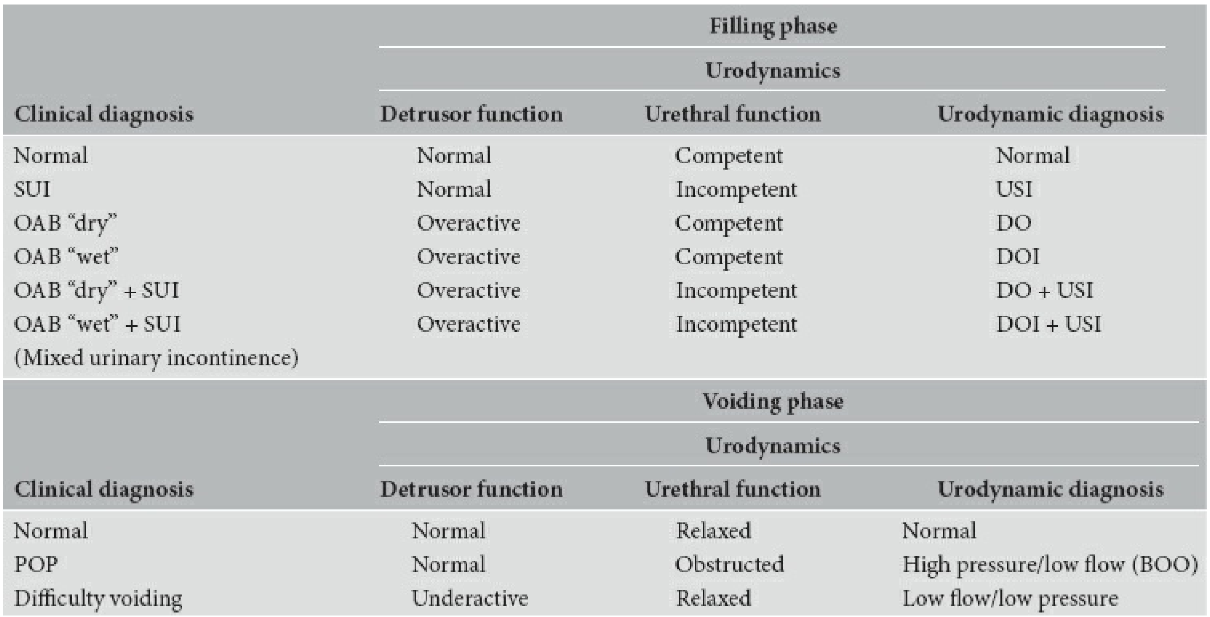


Figure 32.9 Cystometrogram showing urodynamic stress incontinence (leak) with coughing. (p_{det}, detrusor pressure; p_{abd}, intra-abdominal pressure; p_{ves}, vesical pressure; flow rate in mL/s; V_{H2O}, volume of filling medium infused.

Table 32.1 Lower Urinary Tract Function according to Clinical Diagnosis and Detrusor and Urethral Function during the Filling and Voiding Cycles of Micturition with Possible Urodynamic Diagnosis



	Filling phase		
	Urodynamics		
Clinical diagnosis	Detrusor function	Urethral function	Urodynamic diagnosis
Normal	Normal	Competent	Normal
SUI	Normal	Incompetent	USI
OAB "dry"	Overactive	Competent	DO
OAB "wet"	Overactive	Competent	DOI
OAB "dry" + SUI	Overactive	Incompetent	DO + USI
OAB "wet" + SUI	Overactive	Incompetent	DOI + USI
(Mixed urinary incontinence)			

	Voiding phase		
	Urodynamics		
Clinical diagnosis	Detrusor function	Urethral function	Urodynamic diagnosis
Normal	Normal	Relaxed	Normal
POP	Normal	Obstructed	High pressure/low flow (BOO)
Difficulty voiding	Underactive	Relaxed	Low flow/low pressure

Abbreviations:SUI, stress urinary incontinence; OAB, overactive bladder; USI, urodynamic stress incontinence; DO, detrusor overactivity; DOI, detrusor overactivity incontinence; POP, pelvic organ prolapse; BOO, bladder outlet obstruction.

A further rise in detrusor pressure after the completion of voiding, known as an "after contraction," is sometimes seen at the end of a completed void, in patients with DO; however, the significance of this finding is unknown. The patient is asked to cough at the end of voiding to check for quality control and to ensure that the p_{ves} measuring catheter has not moved out of the bladder during voiding. If it has, then the p_{ves} data for voiding should be regarded as unreliable and consideration given to repeating the voiding phase if the required information cannot be extracted.

PITFALLS OF CYSTOMETRY

To ensure accurate measurements, in a fluid-filled system, the bladder line, rectal line, and all tubing should be flushed to ensure that all air bubbles have been removed before recording begins. In addition, all connections should be tight, as any leak will cause errors in the pressure measurements recorded. Pressure values will tend to be lower, and recorded with a delay, if there are bubbles or leaks in the pressure system.

Rectal contractions can sometimes be seen on the recording trace (Figure 32.10) and may be misinterpreted as DO; it is, therefore, important to be aware of rectal activity. If possible, the patient should have an empty rectum for the test. If the rectal line slips slowly during the recording, the p_{abd} line will be seen to drift downward, which could be incorrectly interpreted as a rise in the detrusor pressure and reduced compliance: careful examination of the vesical line shows the bladder pressure to be constant and should allow this artifact to be noticed and corrected.

Quality control at the start of each cystometrogram is vital and should be repeated at regular intervals during the test and again at the end of the test to ensure that good pressure transmission is continuing. This is done by asking the patient to cough and seeing an equal rise in the cough spikes in both the abdominal and vesical lines with no rise (other than a small biphasic deflection in a fluid-filled system) on the detrusor line.

NORMAL CYSTOMETRY

Cystometry of a normal bladder shows the following:

- Residual urine of less than 50 mL
- First desire to void between 150 and 250 mL
- Capacity (taken as SDV) between 300 and 600 mL
- Little or no detrusor pressure rise on filling (Figure 32.11)

- Absence of detrusor contractions during the filling phase
- No leakage on coughing
- No detrusor contraction provoked by coughing or running water (precipitating factors)
- Maximum voiding detrusor pressure of less than 50 cmH_2O, with a maximum flow rate greater than 15 mL/s for a volume greater than 150 mL

If cystometry has been performed for storage symptoms, then at the end of the test, the question that has to be answered is: "Did the cystometry succeed, partially succeed, or fail to reproduce the patient's symptoms?"

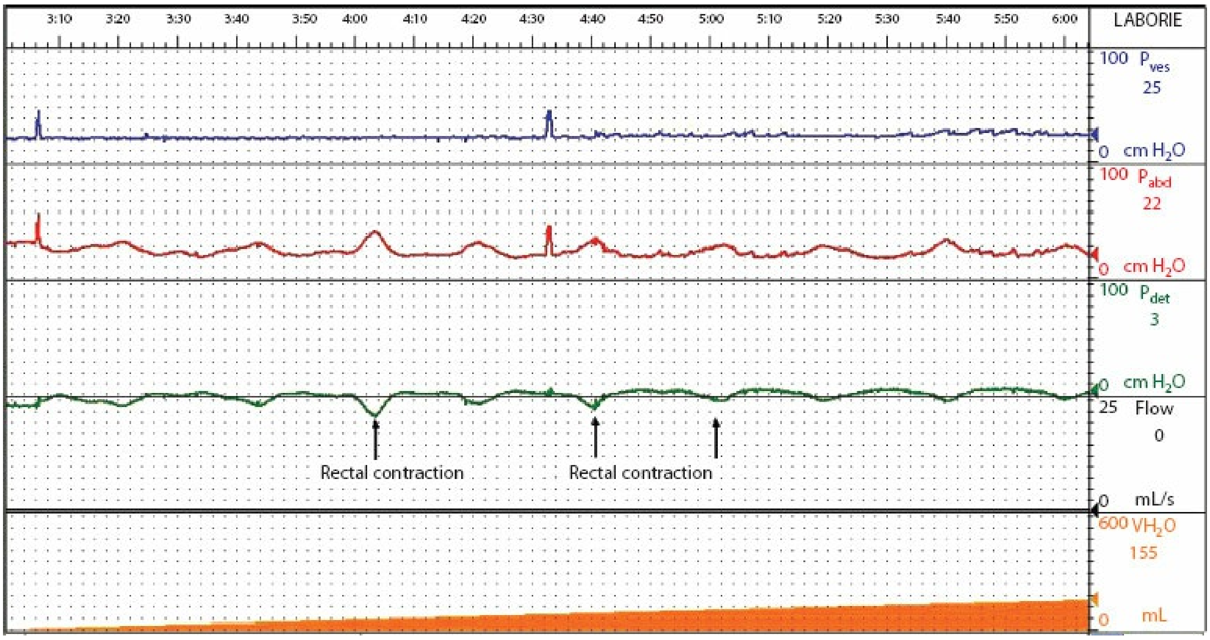


Figure 32.10 Cystometrogram showing rectal contractions. (p_{det}, detrusor pressure; p_{abd}, intra-abdominal pressure; p_{ves}, vesical pressure.)

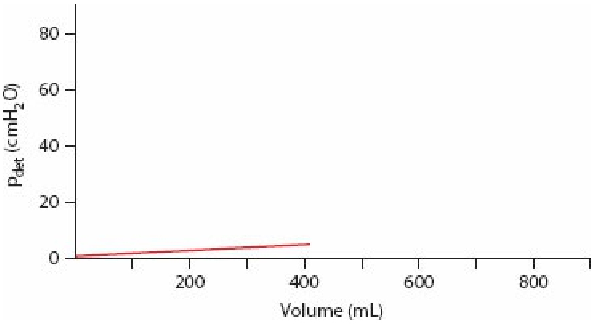


Figure 32.11 Normal filling cystometrogram annotation showing minimal increase in detrusor pressure (p_{det}). The filling speed is 50 mL/min, the patient is seated, the bladder capacity is 400 mL, and the first desire to void is at 160 mL.

CONCLUSION

Cystometry is a component of invasive urodynamic studies used to investigate lower urinary tract dysfunction. It is vital that women are assessed with a proper history and examination, and the results of the cystometric findings are evaluated in light of the signs and symptoms with the aid of voiding diaries. The majority of women will have their symptoms explained during urodynamics, and/or further management decisions can be made from conventional cystometry. Further cystometry can be performed using ambulatory monitoring over a longer period of time and in more natural circumstances or together with video cystourethrography when a simultaneous assessment of the anatomy is desirable.

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33 Tests of Urethral Function

Kristi L. Hebert, Barry G. Hallner, Ryan M. Krlin, and J. Christian Winters

URETHRAL ANATOMY AND MECHANISMS OF URETHRAL CONTINENCE

Adequate bladder outlet resistance is essential in order to maintain urinary continence in women, particularly during periods of increased intra-abdominal pressure. The anatomy and function of the urethra is an important determinant of continence. The female urethra throughout its length has a complex luminal architecture, which serves a dual function as a conduit as well as a barrier protecting the underlying stroma from urinary irritants. The distance between the bladder neck and external urethral meatus determines the anatomic length of the urethra. The urethral mucosa contains many infoldings and is supported by loose elastic connective tissue, containing bundles of collagen fibers. This promotes distention during voiding as well as coaptation (or urethral seal effect) during storage. The mucosa, submucosal tissues, and the periurethral fascia connective tissues promote urethral closure and the urethral seal effect. The urethra contains a complex of smooth and striated muscles, which contribute to the sphincteric mechanism. A relatively thick layer of inner longitudinal smooth muscle continues from the bladder to the external meatus to insert into periurethral fatty and fibrous tissue. A rather thin layer of circular smooth muscle envelops the longitudinal fibers throughout the length of the urethra. It is thought that the longitudinal smooth muscle of the urethra contracts in coordination with the detrusor during micturition to shorten and widen the urethra [1]. The urethral smooth muscle composed of circular and longitudinal fibers joins the detrusor muscle in the base of the bladder to form the intrinsic sphincter mechanism, with its predominant function in the proximal urethra and bladder neck [2]. The striated urethral sphincter invests the distal two thirds of the female urethra [3]. It is composed exclusively of delicate type I (slow-twitch) fibers surrounded by abundant collagen. Proximally, near the midurethra, it forms a complete ring around the urethra that corresponds to the zone of highest urethral closure pressure. This striated muscular complex adds resting tone to the urethra, further enhancing urethral closure. DeLancey et al. [2,4,5], as well as Petros and Ulmsten [6], have contributed greatly to the current understanding of the anatomy of urethral support and function of the urethral continence mechanism. The pubocervical and periurethral fascia support the bladder base and proximal urethra respectively in a sling-like fashion, which is attached bilaterally to the arcus tendineus fascia pelvis (ATFP). In addition, the pubourethral ligament complex provides stability to the midurethra. During periods of increased intra-abdominal pressure, the urethra is closed by the hammock of support created by the periurethral fascia, which increases urethral resistance, thereby promoting continence. This has been proposed as the “hammock hypothesis” [2,4]. In addition, this hammock of support stabilizes the urethra and prevents excessive urethral descent. This facilitates closure of the urethra against the pubourethral ligaments during contraction of the pubococcygeus muscles (levator ani) during periods of increased intra-abdominal pressure. The combination of anatomic support and midurethral closure during periods of increased intra-abdominal pressure is known as the “integral theory” [6] (Figure 33.1). Discrete defects in the pubocervical or periurethral fascia, or detachment of these structures from the ATFP, results in loss of bladder neck and proximal urethral support, creating “urethral hypermobility.” This loss of urethral support prevents the hammock effect of urethral closure or compression of the urethra against the pubourethral ligaments [6]. Thus, defects in the anatomic support of the female urethra can disrupt urethral and pelvic floor function, which should maintain continence during periods of increased intra-abdominal pressure.

Assessment of Urethral Anatomy

Physical examination: An examination of the external genitalia and anterior vaginal wall will provide substantial information regarding urethral anatomy. Urethral caruncles, urethral prolapse, Skene’s gland obstruction, and inflammation are easily detected. The presence of urethral scarring or induration may also suggest postoperative or alternative conditions, which could adversely affect urethral function. Vaginal wall thinning or a pale appearance to the urethra implies vaginal atrophy, which can predispose to certain urological conditions. Lastly, a bulging or purulent expressate is suspicious for urethral diverticulum, which could predispose to leakage, infection, and rarely obstruction. A loss of urethral support can be assessed using a half-speculum to examine the anterior vaginal wall in the resting and straining state. Urethral hypermobility is usually easily discernable on examination by the classic rotational appearance of the urethra when the patient is asked to strain down. In most instances, a visual assessment is enough to confirm the presence of urethral hypermobility. In select instances, a cotton swab test may be used, which is performed by inserting a sterile lubricated cotton swab into the urethra and advancing it into the bladder. It is gently withdrawn until resistance is felt, insuring proper positioning at the urethrovesical junction. The angle of deflection with straining should be measured with a goniometer. Urethral hypermobility is defined as the maximal straining angle of more than 30° from the horizontal [7] or from the resting angle. This test has demonstrated good interobserver reliability [8,9]. In most cases, this test is unnecessary and may be uncomfortable, so its use should be limited to those cases where it will change the course of treatment.

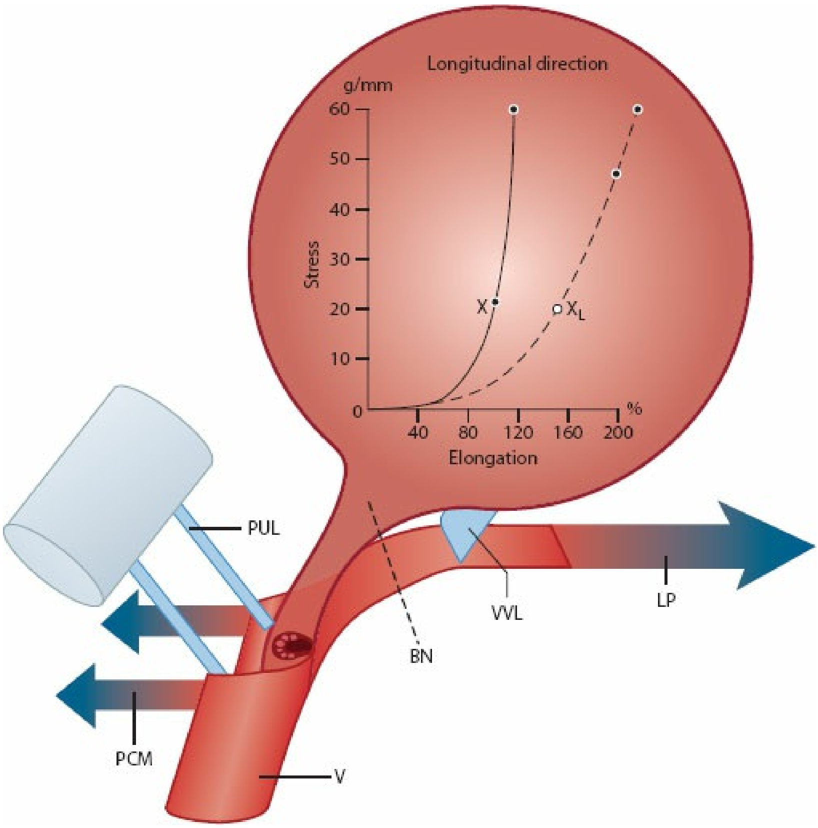


Figure 33.1 Urethral anatomy: Influence of vaginal laxity on muscle force transmission and urinary continence. Inset, Stress extension curve of vagina. BN, bladder neck; LP, levator plate; PCM, pubococcygeus muscle; PUL, pubourethral ligament; V, vaginal hammock; VVL, vaginal attachment to the bladder base; X, normal elasticity; XL, vaginal laxity. The authors propose that an increase in urethral pressure before cough transmission proves that an active continence mechanism is involved in preventing stress urinary incontinence. (Reproduced from Petros PE and Ulmsten UI, *Scand J Urol Nephrol Suppl*, 153, 1, 1993. With permission.)

Ultrasound

Different ultrasound techniques have been used to quantify bladder neck mobility, including transrectal, transvaginal [10], perineal [11], and introital. The transperineal approach is the most commonly used. The bladder neck is identified, and by performing systematic measurements of descent with relation to the symphysis pubis, normal values of descent have been reported with good interobserver reliability [12]. This modality of ultrasound assessment is expensive and requires specific training in order to develop proficiency. In addition, the precise role of ultrasound imaging has not been determined.

FLUOROSCOPY (VIDEOURODYNAMICS)

Urodynamics is a test of vesicourethral function in which specific provocation tests are undertaken to evaluate urethral competence. Videourodynamics (VUDS) is the synchronous measurement and display of urodynamic parameters with radiographic visualization of the lower urinary tract. During VUDS, the clinician can better appreciate the interrelationships between the various urodynamic parameters, with the periodic sampling of fluoroscopic images during filling, voiding, and provocative maneuvers such as leak point pressure (LPP) measurement. The addition of concomitant cystourethrography to urodynamics does allow the clinician to better evaluate the state of the bladder neck and the site of urethral obstruction. VUDS is a useful test in the diagnosis of detrusor sphincter dyssnergia, acquired voiding dysfunction (AVD), and anatomic urethral obstruction. According to the 2012 AUA Guidelines on Adult Urodynamics, VUDS studies are useful in providing additional anatomic detail, particularly in patients with neurogenic bladder, as well as assisting in identifying the site(s) of bladder outlet obstruction [13].

Detrusor External Sphincter Dyssynergia

Detrusor external sphincter dyssynergia (DESD) is defined by the International Continence Society as a detrusor contraction concurrent with an involuntary contraction of the urethral and/or periurethral striated muscle [19]. Detrusor contractions occur with synchronous contractions of the urethral and periurethral striated muscles. It represents inappropriate sphincter activity during voiding, creating functional obstruction of the urethra. This condition is a consequence of underlying neurological disease and can be seen in suprasacral spinal cord injury (SCI), multiple sclerosis (MS), and transverse myelitis [13]. True DESD may only exist in the presence of a neurological lesion that lies within the brain stem or suprasacral spinal cord. In DESD, the contraction of the external sphincter (and increase in EMG activity) occurs prior to the onset of the detrusor contraction. The classic appearance of DESD with VUDS shows a dilated proximal urethra and a narrowed distal urethra associated with increased EMG activity and an involuntary detrusor contraction (Figure 33.2).

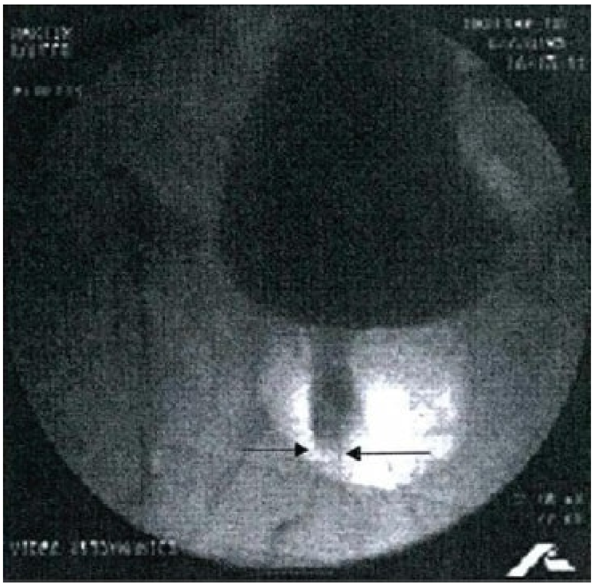


Figure 33.2 X-ray obtained at P_{det} at Qmax in a patient with DESD shows the classic picture of complete obstruction at the membranous urethra (arrows) and a “Christmas tree”–shaped bladder. *Abbreviation:* DESD, detrusor external sphincter dyssynergia. (Reproduced from Jerry B et al., eds., *Atlas of Urodynamics*, 2nd ed., Blackwell Publishing, Oxford, U.K., 2007. With permission.)

Acquired Voiding Dysfunction: Hinman’s Syndrome

With AVD in the absence of a neurological abnormality, the patient involuntarily (and subconsciously) contracts the external urethral sphincter during voiding [14]. The fluoroscopic images of these contractions are identical to those seen in DESD since both cause functional urethral obstruction (Figure 33.3). In contrast, in AVD the detrusor contraction occurs prior to the subconscious contraction of the external sphincter. Concentric needle electrode provides a superior signal source compared with the surface electrode in the evaluation of AVD.

Anatomic Urethral Obstruction

The ICS defines anatomic obstruction in women as reduced urine flow rate and/or the presence of a raised postvoid residual urine and an increased detrusor pressure [19]. Nitti et al. proposed that urethral obstruction be defined as radiographic evidence of obstruction between the bladder neck and the distal urethra in the presence of a sustained detrusor contraction [16]. Urethral obstruction in women causes voiding and postvoiding symptoms (weak stream, hesitancy, and postvoid dribbling). As a consequence of incomplete bladder emptying, storage symptoms may also occur. The two most common causes of anatomic urethral obstruction in women are pelvic organ prolapse (POP) and complications after anti-incontinence surgery. According to the 2012 AUA Guidelines on Adult Urodynamics, clinicians may perform pressure-flow studies in patients with refractory urgency after bladder outlet procedures to evaluate for bladder outlet obstruction [13]. With the use of VUDS, the site of obstruction is defined as the narrowest point in the urethra during voiding cystourethrography.

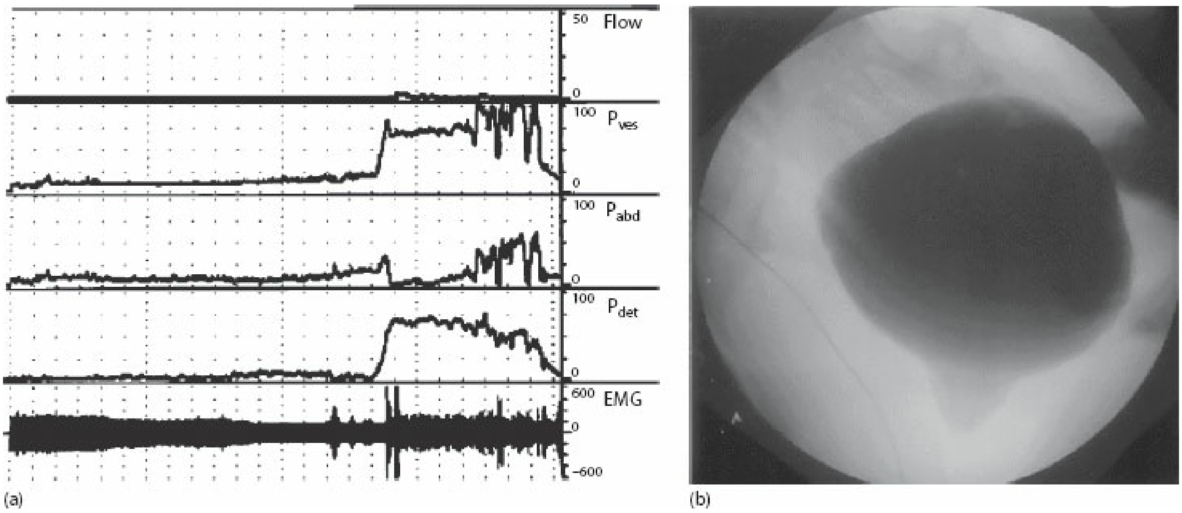


Figure 33.3 VUDS in a 33-year-old woman with AVD. (a) High pressure, low flow is associated with increased EMG activity. (b) Fluoroscopic visualization of urethra during voiding shows dilated proximal urethra with point of obstruction at the external sphincter. *Abbreviations:* AVD, acquired voiding dysfunction; EMG, electromyography; P_{ves}, intravesical pressure; P_{abd}, abdominal pressure; P_{det}, detrusor pressure; VUDS, videourodynamics. (Reproduced from Carlson KV et al., *J Urol*, 165(1), 143, January 2001. With permission.)

In patients with high-grade POP, descent of the anterior vaginal wall may create urethral kinking and compression [17]. Documenting the presence of stress urinary incontinence (SUI) in patients with the prolapse reduced is helpful in the preoperative assessment of women with high-grade POP. SUI occurring after prolapse correction is known as occult SUI. To diagnose occult SUI, the prolapse may be reduced with vaginal packing, rectal swabs, a speculum blade, or pessary. VUDS is helpful in demonstrating both urethral obstruction and occult SUI [18] (Figures 33.4 and 33.5). Prolapse should be reduced during urodynamic testing to assess for occult SUI, particularly in the setting of detrusor dysfunction or lower urinary tract symptoms.

In women with high-stage anterior compartment prolapse, the 2012 AUA Guidelines on Adult Urodynamics recommends that all patients undergoing surgical repair should undergo stress testing with reduction of the prolapse. In women with high-stage anterior compartment prolapse and associated lower urinary tract symptoms, urodynamics with LPP measurement should be performed with the prolapse reduced [13].

While urethral function can be inferred from physical examination, anatomic and radiographic tests, and cystometry (Figure 33.6), more accurate assessments of urethral function are commonly needed. Urethral function may be more accurately characterized in a number of ways: LPP measurement, urethral pressure profilometry (UPP), and electromyography (EMG). A description of these techniques is included.

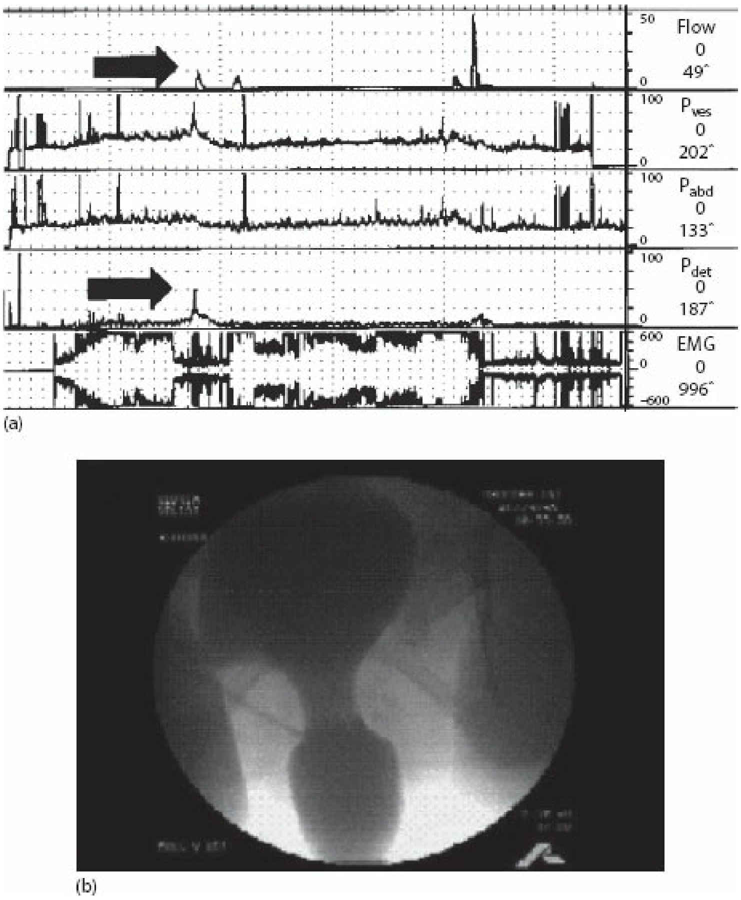


Figure 33.4 VUDS in a 65-year-old woman with grade 4 anterior compartment prolapse. (a) At the arrows, she voids with detrusor pressure (P_{det}) of 50 cmH_2O and a flow of 6 mL/s, indicating urethral obstruction. (b) Voiding cystogram taken at the arrow shows a large cystocele obscuring the urethra and causing urethral obstruction. *Abbreviations:* EMG, electromyography; P_{ves}, intravesical pressure; P_{abd}, abdominal pressure; VUDS, videourodynamics. (Reproduced from Flisser AJ and Blaivas JG, *Urol Clin North Am*, 29(3), 515, August 2002. With permission.)

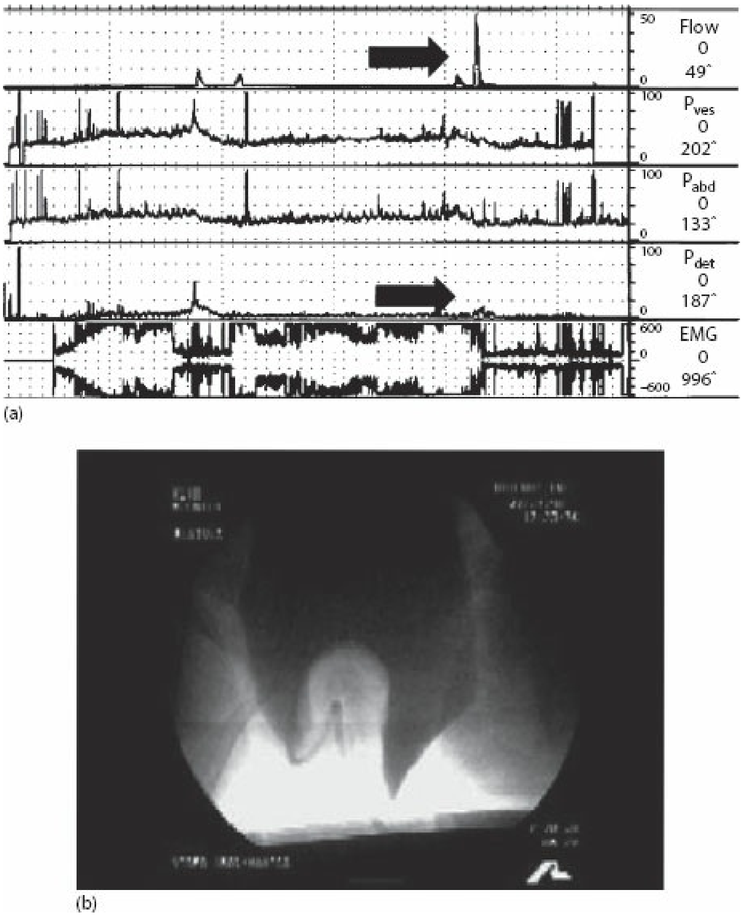


Figure 33.5 The same 65-year-old woman as in Figure 33.4 with her POP reduced. (a) At the arrows, she voids with a detrusor pressure (P_{det}) of <10 cmH_2O and a flow of 49 mL/s. VLPP was about 90 cmH_2O. (b) Voiding cystogram taken at the arrow shows high flow and low pressure. *Abbreviations:* EMG, electromyography; P_{ves}, intravesical pressure; P_{abd}, abdominal pressure; POP, pelvic organ prolapse; VLPP, valsalva leak point pressure; VUDS, videourodynamics.) (Reproduced from Flisser AJ and Blaivas JG, *Urol Clin North Am*, 29(3), 515, August 2002. With permission.)

ABDOMINAL LEAK POINT PRESSURE

Another way to assess urethral function is with the measurement of LPPs. There are two methods of LPP assessment that analyze different functional areas of the lower urinary tract. The detrusor leak point pressure (DLPP), as defined by the ICS, is the lowest detrusor pressure at which urine leakage occurs in the absence of either a detrusor contraction or increased abdominal pressure [19]. It is not a test of urethral function but rather a test examining the relationship of bladder storage function and urethral resistance in patients with neurogenic bladder. In contrast, the abdominal leak point pressure (ALPP) is a measure of urethral function. The ALPP, as defined by the ICS, is the lowest intravesical pressure (P_{ves}) at which urine leakage occurs because of increased abdominal pressure in the absence of a detrusor contraction [19].

McGuire et al. introduced the concept of ALPP in 1993 as a means of differentiating urinary incontinence due to either urethral hypermobility or ISD [20]. This measurement is used to quantify the *stress competence* of the urethra or the ability of the urethra to maintain continence during periods of increased intra-abdominal pressure. McGuire proposed that ALPP is a measure of sphincter strength. In a normally positioned and closed urethral sphincter, increased abdominal pressure does not open the sphincter—thus, there is no normal ALPP. Urine leakage can be caused only by an increase in abdominal pressure when the urethra is abnormal. Low values for ALPP implies less urethral resistance to *protect* against leakage during increased intra-abdominal pressure; thus lower ALPP values suggest *weaker* sphincters. Thus, ALPP cannot be quantified if the subject does not demonstrate SUI during urodynamic testing. In addition, the detrusor pressure at the time of ALPP testing must be low. High detrusor pressure (due to detrusor overactivity, or poor bladder compliance) at the time of ALPP testing may result in the false impression that urethral function is impaired [21].

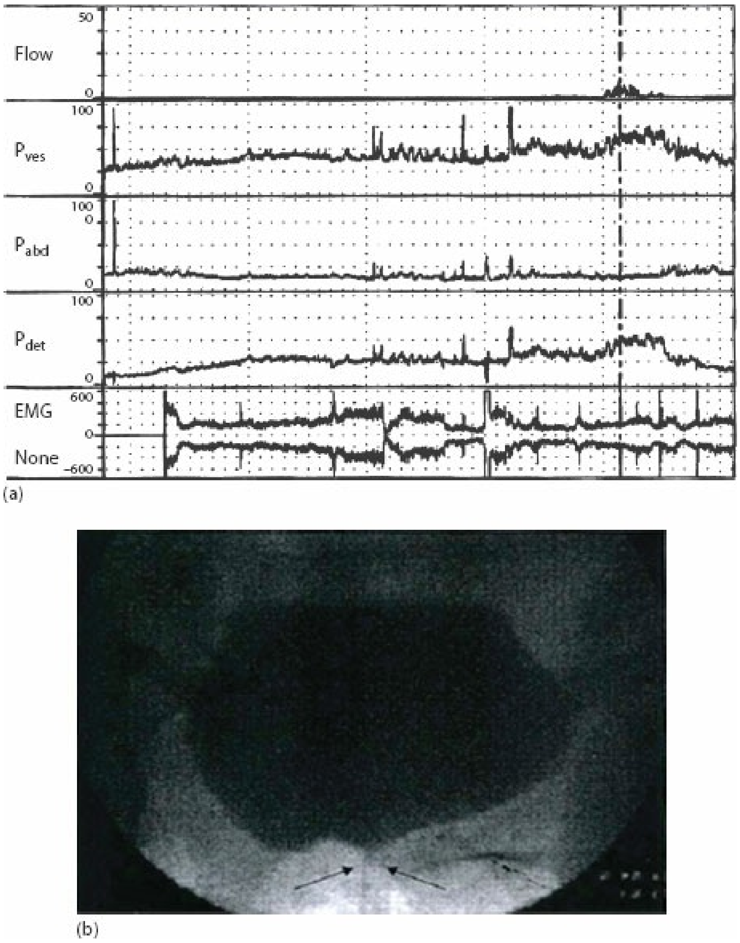


Figure 33.6 Urethral obstruction 5 years status post autologous fascial pubovaginal sling. (a) Urodynamic tracing. P_{det} at Q_{max} = 50 cmH_2O and Q_{max} = 6 mL/s (vertical dashed line). (b) X-ray exposed at Q_{max} shows a narrow urethra just distal to the vesical neck (arrows). *Abbreviations:* EMG, electromyography; P_{ves}, intravesical pressure; P_{abd}, abdominal pressure; P_{det}, detrusor pressure. (Reproduced from Reproduced from Jerry B et al., eds., *Atlas of Urodynamics*, 2nd ed., Blackwell Publishing, Oxford, U.K., 2007. With permission.)

Technique of ALPP

An acceptable technique to measure ALPP involves placing a dual-lumen urodynamic catheter into the bladder. Cystometry then proceeds until the bladder has been filled to 150 cc. The patient is then asked to perform a Valsalva maneuver by gradually increasing his or her intra-abdominal pressure until he or she leaks (Valsalva leak point pressure [VLPP]) (Figure 33.7). The lowest P_{ves} at which leakage occurs is defined as the ALPP. If there is no urine leakage with a bladder volume of 150 mL, the test is repeated at 50 mL increments until maximum cystometric capacity is reached. Measurements at capacity may only be recorded if there is no spontaneous detrusor activity.

If the patient is not able to generate a Valsalva pressure sufficient enough to produce leakage, the patient is asked to cough several times with increasing strength until leakage occurs. Compared to the straining performed with a Valsalva maneuver, coughing generates a faster increase in intra-abdominal pressures. As such, precise measurements are more difficult to obtain with coughing. Once leakage has been observed, the force of the cough is reduced until it generates the minimal amount of abdominal pressure required to produce leakage to determine the P_{ves} at which leakage occurs induced by cough

(cough leak point pressure [CLPP]). Although the term ALPP is often used interchangeably with VLPP, it should not be. The ALPP represents measuring the vesical pressure at which leakage is associated with increasing abdominal pressure. As noted earlier, this may happen by Valsalva (VLPP) or by cough (CLPP). The CLPP is usually measured in the absence of a VLPP, because it is harder to quantify and is usually higher. Thus, VLPP and CLPP are two types of the ALPP. Thus, ALPP is the preferred term for this technique of urethral pressure measurement.

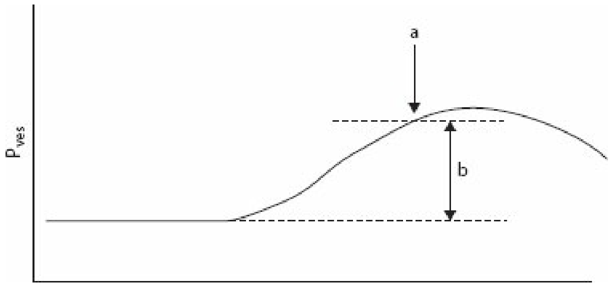


Figure 33.7 Measurement of VLPP: Patient is asked to bear down progressively while holding breath. Leakage is recorded (arrow) at the precise moment that fluid is observed at urethral meatus. The rise on intravesical pressure over baseline (b) represents VLPP. *Abbreviations:* P_{ves}, intravesical pressure; VLPP, valsalva leak point pressure. (Reproduced from Bump RC et al., *Am J Obstet Gynecol*, 173(2), 551, August 1995. With permission.)

Patient position is important. For example, if patients only leak when standing, then the test may need to be done in the standing position. Additionally, in patients who are suspected of having SUI but do not leak during UDS testing with the catheter in place, the AUA Adult Urodynamics Guidelines recommend that stress testing be repeated with the catheter removed. The panel cited studies of patients who leak without the catheter in place despite negative UDS testing—suggesting that the urethral catheter may *mask* the presence of SUI in certain patients [13].

Bladder Volume and ALPP

ALPP testing has been correlated with bladder volume in the majority of clinical studies. Theofrastous et al. performed a study of 120 women with SUI who underwent VLPP testing at bladder volumes of 100, 200, and 300 mL and at maximum cystometric capacity [22]. The authors found that women who leaked with Valsalva maneuvers at lower bladder volumes had worse measures of incontinence compared with women who leaked at higher volumes. Also, they found that the mean VLPP was higher at lower bladder volumes compared to VLPP at maximum cystometric capacity. The authors concluded that VLPP in women with SUI decreases significantly with bladder filling.

Faerber and Vashi also found that VLPP decreased significantly with increasing bladder volumes [23]. Using VUDS, they found that a bladder volume of 250–300 cc allowed for the most appropriate classification of patients. Miklos et al. sought to assess whether ALPP is affected by the method of provocation, the presence of an intravesical catheter, and bladder volume [24]. With respect to bladder volume, they too noted a decrease in ALPP with increasing bladder volume (Figure 33.8). With Valsalva testing, the ALPP decreased by 19 cmH_2O as the bladder volume rose from 150 cc to >400 cc. With coughing, the ALPP decreased by 35 cmH_2O as the bladder volume rose from 150 cc to >400 cc. In contrast, Petrou et al. found no significant difference in VLPP at various bladder volumes [25]. They concluded that the volume in the bladder does not alter the category of SUI or statistically change the VLPP determination.

Urodynamic Catheter Size and Location

Bump et al. also studied the effect of urodynamic catheter size on VLPP [26]. Using an 8 Fr urodynamic catheter, they found that the VLPP was 9.2 cmH_2O higher than when using a 3 Fr urodynamic catheter—$p = 0.01$. Miklos et al. also noted a significant decrease in both CLPP and VLPP at all bladder capacities when removing the transurethral catheter and using only an intravaginal catheter [24]. There is no debate that a transurethral catheter has some effect on the ALPP measurement; however, the precise magnitude of this effect is unclear.

Test–Retest Reliability

Bump et al. found the average pressure differences between the first and second VLPP to be clinically and statistically insignificant, regardless of urodynamic catheter size [26]. The pressure difference between the two consecutive VLPPs was 2.2 cmH_2O using the 8 Fr urodynamic catheter and 1.5 cmH_2O using the 3 Fr urodynamic catheter. Nager et al. published reference urodynamic values for the 655 stress incontinence women that comprised the Stress Incontinence Surgical Treatment Efficacy Trial (SISTEr) [27]. All filling cystometrograms were performed with subjects in the standing position. All vesical pressures were measured with a urodynamic catheter 8 Fr or smaller in size. Each of the 428 patients with measurable VLPPs had reproducible values. For 50% of the women, the VLPP intrapatient range was ≤ 15 cmH_2O. On average, there was only a 10 cmH_2O difference between the mean VLPP (117 cmH_2O) and the minimum VLPP (107 cmH_2O).

Factors Associated with ALPP

Fleischmann et al. studied the relationships between VLPP, urethral hypermobility, and incontinence severity in 65 women with SUI [28]. A linear regression model showed no correlation of VLPP with urethral hypermobility in women with SUI. In addition, no significant difference in incontinence episodes or pad weight was seen in women with urethral hypermobility and a VLPP < 60 cmH_2O compared to women with no urethral hypermobility and a VLPP < 60 cmH_2O. Lemack et al. sought to determine which clinical and demographic factors were associated with women undergoing either Burch colposuspension or autologous rectus fascial sling as part of the SISTEr trial [29]. A multivariate analysis showed that older age, lower body mass index (BMI), smaller bladder capacity, higher maximum flow rate, and lower voiding pressures were all independently associated with lower VLPP. Each 1-year increase in age resulted in a decrease in VLPP of 0.77 cmH_2O. Each one-unit increase in BMI value resulted in an increase in VLPP of 0.66 cmH_2O. Urethral hypermobility, as assessed by cotton swab testing, did not achieve a significant association with VLPP when controlling for POP-Q stage. The authors concluded that cotton swab testing had no role in predicting VLPP in women with urethral hypermobility and SUI. Thus, it appears that there is little reliable correlation of urethral hypermobility with ALPP. However, factors such as advancing age and weight do appear to have some correlation with ALPP measurement.

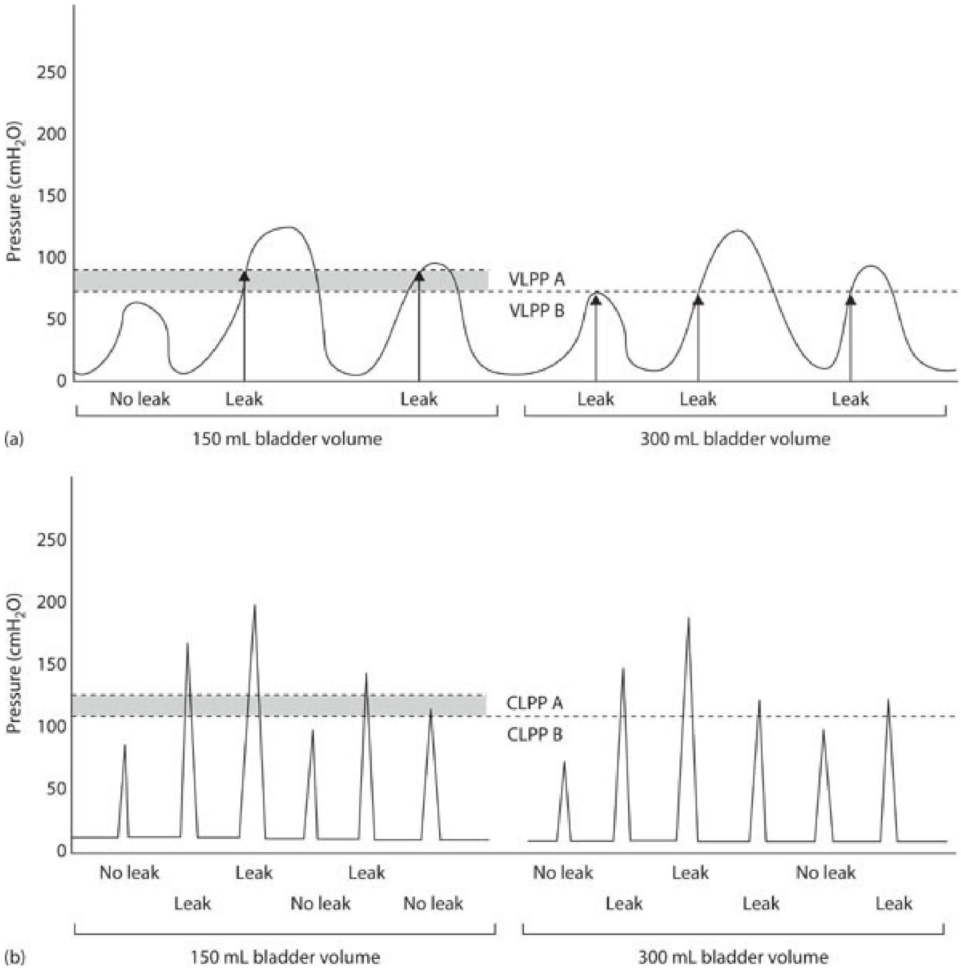


Figure 33.8 Effect of bladder volume on (a) VLPP and (b) CLPP. (Reproduced from Benson J, Electrophysiologic testing, in Walters M and Karram M, eds., *Urogynecology and Reconstructive Pelvic Surgery*, 2nd ed., Mosby, St. Louis, MO, 1999, p. 100. With permission.)

Effect of Pelvic Organ Prolapse on ALPP

POP often artificially elevates VLPP because the prolapse provides a mechanism that dissipates the effect of the increased abdominal pressure on the urethra [21]. As such, it is recommended that VLPP testing be performed with and without prolapse reduction to identify if patients are at risk for occult SUI. Romanzi et al. studied the effect of genital prolapse on voiding in 60 women [30]. All of the women with grade 3 or 4 cystocele who had SUI (either symptomatic or occult) also had ALPP < 60 cmH_2O, which they defined as ISD. Gallentine et al. prospectively evaluated 24 patients with high-grade POP to determine the change in ALPP with reduction of the POP [17]. The prolapse reduction was performed using gauze packing and a speculum blade. The mean decrease in ALPP was 59 cmH_2O after prolapse reduction. The decrease in ALPP with prolapse reduction was much greater in patients with vaginal vault prolapse than in patients with cystocele alone. Gilleran et al. evaluated the effect of cystocele reduction by a vaginal gauze pack on urodynamic studies [31]. Occult SUI was seen in 6% of women, and the mean VLPP of 54 cmH_2O in these women suggested ISD. UDS may be helpful in determining the presence of urethral obstruction or occult SUI associated with POP.

In women with high-stage anterior compartment prolapse, the 2012 AUA Guidelines on Adult Urodynamics recommends that all patients undergoing surgical repair of high-grade anterior compartment prolapse undergo stress testing with the prolapse reduced. In women with high-grade prolapse and associated urinary symptoms, urodynamics with LPP measurement with the prolapse reduced should be performed [13].

Relationship of ALPP to Incontinence Severity

Early studies reported significant correlation between VLPP and measures of incontinence severity. Nitti et al. evaluated 64 women with SUI using the Stress, Emptying, Anatomy, Protection, and Instability (SEAPI) grade [32]. Using VUDS, the authors found that a VLPP of 90 cmH_2O or less did correlate highly with more severe symptoms of SUI. Also, Nager et al. demonstrated significant decreases in VLPP with increasing severity of incontinence as determined by Stamey grade ($p < 0.01$) [33]. However, they found no correlation between VLPP and pad weight or the 16-question QOL questionnaire from the "Q" section of the SEAPI. Albo et al. sought to examine the relationship between severity measures of urinary incontinence in women undergoing either Burch colposuspension or autologous rectus fascial sling as part of the SISTEr trial [34]. Weak-to-moderate correlations were observed between Medical, Epidemiological and Social Aspects of Aging (MESA), incontinence episode frequency, pad weight, Incontinence Impact Questionnaire (IIQ), and Urogenital Distress Inventory (UDI). However, VLPP correlated poorly with all incontinence severity measures. The authors concluded that VLPP is not associated with symptom severity, quantity of urine loss, or QOL impairment. They stated that VLPP neither reflects the bother from incontinence nor takes into account lifestyle activity.

Relationship of ALPP and Stress Continence Outcomes

Rodriguez et al. evaluated the role of prospective VLPP in predicting the outcome of distal urethral polypropylene sling (DUPS) surgery [35]. They divided 174 patients into 4 groups based on VLPP: no leakage, VLPP > 80 cmH_2O, VLPP 30–80 cmH_2O, and VLPP < 30 cmH_2O. The groups were matched with respect to age, number of previous surgeries, and severity of SUI symptoms. When evaluating outcomes based on both daily pad use and patient-driven questionnaires, all groups reported similar success 14 months after DUPS, regardless of preoperative VLPP. The authors concluded that VLPP is more likely a measure of incontinence severity than a test defining the mechanism of incontinence. Nager et al. sought to determine the prognostic value of preoperative urodynamic results in women with SUI as part of the SISTEr trial [36]. Women were eligible for the study if they had predominant SUI symptoms, a positive cough stress test, a bladder capacity > 200 mL, and urethral hypermobility. The association of VLPP and success, controlling for the treatment group, was compared using ANOVA. Women who failed either Burch colposuspension or autologous rectus fascial sling did not have a lower mean VLPP compared to those that achieved success at the 24-month stress-specific outcome assessment (Table 33.1). Note that overall treatment success required a negative pad test, no urinary incontinence on a 3-day diary, a negative stress test, no self-reported SUI symptoms, and no retreatment for SUI. The authors concluded that the level of VLPP did not predict the success of outcomes after either Burch colposuspension or autologous rectus fascial sling procedures in women with pure or predominant SUI. The Value of Urodynamic Education (ValUE) trial reported no improvement in 12-month outcomes between women with stress-predominant urinary incontinence randomized preoperatively to an office evaluation alone and preoperative urodynamic testing, which included LPP testing on all patients. In this study, urethral pressure profiles were performed only if it was a routine of each center. The authors concluded in well-selected women with uncomplicated SUI that UDS did not enhance predicting surgical outcomes [37]. It should be mentioned, however, that after urodynamic testing, women in the urodynamic-testing group were significantly less likely to receive a diagnosis of an overactive bladder with incontinence, an overactive bladder without incontinence, or suspected intrinsic sphincter deficiency, and they were significantly more likely to receive a diagnosis of voiding-phase dysfunction than were those in the evaluation-only group—suggesting that UDS did change the clinician's diagnosis before surgery. In this study, these changes in urodynamic diagnosis did not result in overall changes in surgical treatment [37]. It should be considered that this study group was a highly select group of pelvic surgeons using a rigorous preoperative assessment—and is likely not representative of the overall pelvic surgeon milieu treating women with SUI. In this group, these changes of UDS diagnosis may have induced changes in treatment decisions. Additionally, Zimmern et al., in a follow-up evaluation of the ValUE database, concluded that in the clinical diagnosis of women with SUI, physician confidence increased after doing UDS testing [38].

Table 33.1 VLPP Does Not Predict Success of Either Burch or Pubovaginal Sling

	Burch	**Pubovaginal sling**

Mean cmH_2O (SD)/No.	Overall outcome	
Success	115(40)/57	117(33)/71
Failure	115(37)/104	121(39)/105
Mean cmH_2O (SD)/No.	Stress-specific outcome	
Success	116(40)/80	117(34)/109
Failure	114(37)/87	125(41)/72

Source: Reproduced from Nager CW et al., *J Urol*, 179(4), 1470, April 2008.

Abbreviations:VLPP, valsalva leak point pressure; SD, standard deviation.

URETHRAL PRESSURE PROFILOMETRY

The urethral pressure profile is commonly measured during normal bladder storage and provides information regarding the functional status of the urethra. Most commonly, these measurements are obtained under nonvoiding conditions with the urethra at rest, which is sometimes referred to as the resting urethral pressure profile. However, dynamic measurements may also be obtained during coughing (stress urethral pressure profile) and voiding (micturitional urethral pressure profile) to obtain functional information regarding the urethra during these conditions. Due to the multifactorial nature of this test, it is best to recognize the standardized terminology as it relates to the techniques of UPP being discussed, and the terminology that has been recommended by the International Continence Society is listed in Table 33.2 [39].

Table 33.2 ICS Terminology for UPP Testing

Urethral pressure measurements

Urethral pressure: The fluid pressure needed to just open a closed urethra

Urethral pressure profile: A graph indicating the intraluminal pressure along the length of the urethra

Urethral closure pressure profile: The subtraction of intravesical pressure from urethral pressure

Maximum urethral pressure: The maximum pressure of the measured profile

Maximum urethral closure pressure: The maximum difference between the urethral pressure and the intravesical pressure

Functional profile length: The length of the urethra along which the urethral pressure exceeds intravesical pressure in women

Pressure transmission ratio: The increment in urethral pressure on stress as a percentage of the simultaneously

Abbreviations:ICS, International Continence Society; UPP, urethral pressure profilometry.

Technique of Urethral Pressure Profile

The most commonly utilized methods of urethral pressure measurements are derived from the techniques introduced by Brown and Wickham [40]. This is the most commonly utilized technique to measure urethral pressures. The basic principle of this technique is the measurement of pressure needed to perfuse a pressure-sensing catheter at a constant rate. Thus, it measures the occlusive pressure of the urethral walls by recording the fluid pressure required to *lift* the urethra off the catheter. The catheters are optimally less than 10 Fr in size and contain two opposing side holes, which are some distance from the catheter tip. This can be done using a double- or triple-lumen catheter with separate lumens for recording bladder and urethral pressure. The urethral port of the catheter is connected to a pressure measuring transducer and a motorized syringe pump (usually via a “Y” connector). Constant perfusion at a rate of 2 mL/min to 5 mL/min is maintained. The catheter is then withdrawn at a rate of less than 5 mm/s in order to achieve satisfactory measurements. This may be accomplished manually or more precisely by a mechanical *puller* device (Figure 33.9). Other catheter types can be utilized to measure urethral pressures at rest. Microtransducer tip catheters may be employed. These catheters have the advantage of better resolution and accuracy when compared to perfusion catheters. However, they are expensive, require sterilization, and, most importantly, are prone to rotation artifacts within the urethra. The position of the transducer in the urethral lumen greatly effects the urethral pressure measurements. Balloon catheters have also been utilized. These catheters consist of fluid-filled balloons over the side holes, and the urethral pressures represent the average pressure measured over the length of the entire balloon. This design leads to many distortions in pressure measurement. When a catheter holding a transducer is within the urethra, it is reading the force generated by the walls of urethra, which are not equal in the 360° of the long axis. It has been found that pressures can range from the uppermost range to the lowest by changing the direction of the microtransducer from anterior to posterior. Catheter sizes between 8 and 12 French have been shown not to affect study parameters. This is not the case for bladder volume and patient position, as the pressure within the urethra goes up with increasing volume within the bladder and with a more upright stance. A comparison of air-charged and microtransducer catheters in the evaluation of urethral function showed high concordance for maximum urethral closure pressure (MUCP) and VLPP, but not for functional urethral length [41].

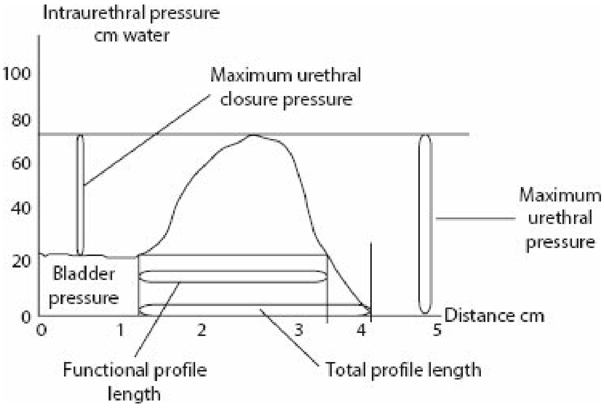


Figure 33.9 Urethral pressure profile: Note the individual parameters of the urethral pressure profile and the relationship to intravesical pressure. (Reproduced from Winters JC and Appell RA, Practical urodynamics, in O'Donnell, P.D., ed., *Urinary Incontinence*, Mosby, New York, 1997, pp. 181–189. With permission.)

The resting urethral pressure profile is usually performed supine. The bladder contains at least 50 mL, and the baseline bladder pressure is recorded. The catheter is then withdrawn at a constant rate (<5 mm/s) and the catheter is perfused at 2 mL/min. Continuous urethral pressure measurement occurs as the catheter is withdrawn, and these measurements should be made with the bladder at resting pressure [42]. The resting urethral pressure profile will produce a characteristic curve. In addition, the urethral pressure measurements can be taken at a fixed site in the urethra by securing the catheter with the urethral pressure sensors in the desired location. This is done fluoroscopically, or by using the measuring landmarks on the catheter. The stress urethral profile is performed in a similar manner. However, during the stress UPP the patient is asked to cough at regular intervals during catheter withdrawal. Alternatively, one may position the catheter at fixed sites along the urethra (0.5 cm intervals) while the patient coughs or performs a Valsalva maneuver. This method of urethral pressure measurement purportedly records the efficiency of pressure transmission into the proximal urethra. The major limitation of stress profilometry is that stress testing can move the profile catheter along the urethra, leading to misleading findings.

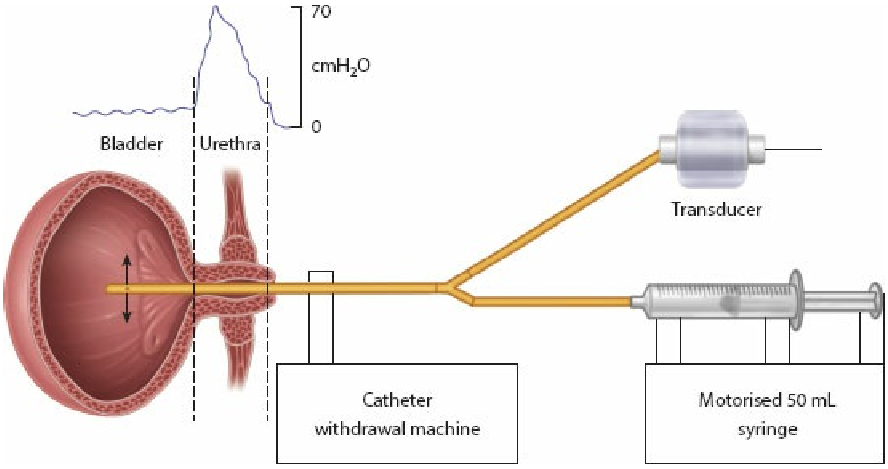


Figure 33.10 Brown–Wickham technique of urethral pressure measurement. (Reproduced from Abrams P, ed., *Urodynamics*, 3rd ed., Springer-Verlag, London, U.K., 2006, pp. 98–110. With permission.)

The catheter withdrawal technique as described generates an infusion profile curve representative of the UPP (Figure 33.10). The parameters obtained are defined by the International Continence Society [19] as

- P_{ves}, the pressure measurement within the bladder.
- Maximum urethral pressure (Pura), the highest pressure obtained during catheter withdrawal.
- UCPmax or MUCP, the difference in pressure obtained when P_{ves} is subtracted from Pura (which represents the pressure gradient from the urethra to the P_{ves}).
- Functional urethral length is the urethral length where the intraurethral pressure exceeds the bladder pressure.
- Total urethral length is the entire length of the urethra as measured using the withdrawal technique.

Thus, urethral length has two aspects, an anatomical one where it is the complete length of the urethra and the functional length, which is the distance of the urethra where urethral pressure exceeds the pressure found within the bladder [43].

Interpretation of Urethral Pressure Profile

In most continent women, the functional urethral length is approximately 3 cm and the MUCP is 40–60 cm water, but there exists considerable variability between studies [44]. It has been suggested that UPP can be helpful in women undergoing stress incontinence surgery. Through the early works of McGuire and Sand, patients with urethral closure pressures less than 20 cm water were noted to have higher failure rates of their incontinence repairs [43,44]. These findings have been supported by other studies showing that a low MUCP is a predictor of poor outcomes for retropubic suspension surgery [45,46]. These findings led surgeons to utilize sling procedures as the anti-incontinence procedure of choice for patients with low urethral closure pressure [47,48]. This change in practice must be taken in the context of a strong trend toward sling procedures (particularly midurethral slings) for all cases of stress incontinence, with or without low urethral pressure, which makes the UPP increasingly irrelevant to the choice of surgical procedure [49]. Weber demonstrated the inherent problems in utilizing UPP measurements in the diagnosis and management of SUI. She pointed out the significant variability within the reported values of urethral pressure measurements [49]. Differences in pressure measurements were seen with different types of catheters, varying positions of the catheter within the urethra, patient position, bladder volume, and the presence of POP. In addition, detrusor overactivity can affect urethral function resulting in decreases in functional urethral length and pressure transmission ratio (PTR) with bladder filling [50]. Although the investigator can control technical factors, there are still substantial differences in interoperator and per patient reproducibility. These factors account for widespread differences in reported values across urodynamics laboratories. As one examines the reported values of urethral pressure among investigators, there is considerable variability between investigators with the MUCP varying from 36 to 101 cm water in non–stress incontinent patients. In addition, there are large standard deviations of reported data, suggesting significant variability within the reported values [49]. Despite these differences however, there is a trend among studies that the urethral closure pressures are lower in stress incontinent women. However, in many of these studies, the differences are not statistically different and the overlap is so great that it is impossible to select a cutoff value that discriminates continent and incontinent patients [49].

If the urethra and the bladder were thought of as a continuous system free of the muscular activity that surrounds it, then the PTR can be thought of as the sequential increase in urethral pressure during a concurrent increase in bladder pressure [42]. This proportion can exist at a solitary location, or several points can be determined at distinct locations to produce a pressure transmission profile. Although it has been reported that stress incontinent women with urethral hypermobility generally have lower PTRs than stress continent women [51], other studies have questioned the validity of pressure transmission profiling, and the value of this test has been called into question [52]. The PTR also cannot discriminate between stress incontinent patients and controls [53]. As a result of such divergent data, the ICS has stated that the clinical utility of urethral pressure measurement is unclear [54]. Given the fact that UPP deals with urethra in a nonphysiological state of rest, it provides little information regarding incontinence as a result of anatomic derangement. Furthermore, no single parameter of the UPP is useful in diagnosing stress incontinence [55]. These reports have prompted the International Consultation on Incontinence Committee on Dynamic Testing to make the following recommendations regarding UPP [56]: First, investigators and clinicians should recognize the poor sensitivity and specificity of urethral pressure measurements and their normal test–retest variation. In addition, the committee does not recommend urethral pressure measurements as the only urodynamic test of incontinence. If performed, these measurements should be judged in relationship to other elements of the examination.

In conclusion, the clinical role of urethral pressure and the urethral closure pressure is questionable as there is no urethral pressure measurement that can discriminate urethral incompetence from other disorders, provide a measure of the severity of the condition, or provide a reliable indicator of surgical success after intervention [56]. Although attempts have been made to correlate a low MUCP with the presence of stress incontinence and with the presence of ISD (MUCP < 20 cm H_2O), the test proves to lack both sensitivity and specificity. Additionally, there are many continent women with low MUCPs and conversely incontinent women with a high MUCP [57]. To date, the preponderance of evidence demonstrates that the diagnostic accuracy of the urethral pressure profile is poor. This test, if utilized, should be interpreted in the entire clinical context of SUI in order to assess incontinence severity and not as a stand-alone evaluation of urethral function [54].

ELECTROMYOGRAPHY

Electric activity produced by a cell is a result of the interaction of various ions of opposing charge separated by a lipoprotein bilayer. Unequal distributions of ions on either side of the bilayer cause a gradient that leads to a difference in electric potential across the membrane. The motor unit is comprised of an anterior horn cell, its axon, and terminal branches (all of which make up the motor neuron), the neuromuscular junctions, and all the individual muscle fibers the cell innervates. The size of the motor unit, that is, the number of muscle fibers innervated by a single anterior horn cell, varies with each muscle. In general, muscles exhibiting fine motor control have low innervation ratios (e.g., 10 to 20:1 in the extraocular muscles), whereas big, bulk-supporting muscles have high innervation ratios (e.g., 1500 to 2000:1 in the gastrocnemius muscle) [58]. When an anterior horn cell is activated, all muscle fibers belonging to that motor unit are depolarized, and the electrical activity from these muscle fibers summate to generate a motor unit action potential (MUAP) [59]. Such activity produces a characteristic triphasic wave with distinct components, detectable by an electrode placed in close proximity. There is a positive (downward) deflection as the electrical impulse moves along the muscle fiber membrane toward the extracellular recording electrode. This is then followed by a negative (upward) deflection when the impulse reaches the electrode. Finally, another positive (downward) deflection results as the impulse moves away from the electrode (Figure 33.11). There are numerous types of electrodes, broken down into two distinct groups—surface and needle electrodes, all having their positive attributes, as well as negative characteristics.

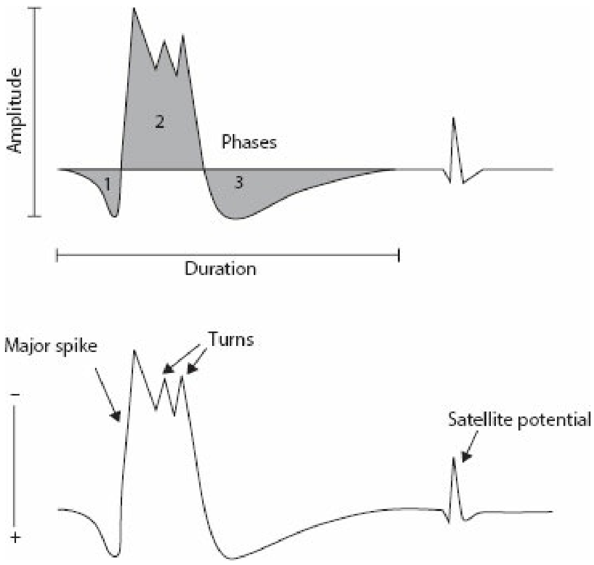


Figure 33.11 Duration is measured as the time from the initial deflection of the MUAP from baseline to its final return to baseline. It is the parameter that best reflects the number of muscle fibers in the motor unit. Amplitude reflects only muscle fibers very close to the needle and is measured peak to peak. Phases (shaded areas) can be determined by counting the number of baseline crossings and adding 1. MUAPs are generally triphasic. Serrations (also called turns) are changes in direction of the potential that do not cross the baseline. The major spike is the largest positive-to-negative deflection, usually occurring after the first positive peak. Satellite, or linked, potentials occur after the main potential and usually represent early reinnervation of muscle fibers. (Reproduced from Preston DC and Shapiro BE, *Electromyography and Neuromuscular Disorders*, Butterworth-Heinemann, Boston, MA, 1998, pp. 541–560. With permission.)

Skin patch electrodes are usually self-adhesive and have the benefit of being less invasive, with a patch being placed on the perineum. However, some contend that the signal may be inferior [60]. In preparation for a study using such electrodes, the skin should be shaved and prepared with alcohol to reduce surface resistance and the electrode placed directly on the skin overlying the muscle of interest [61]. With surface electrodes, EMG pattern recordings depict the net electrical activity occurring in the muscle. Surface electrodes therefore demonstrate an electronically generated summation of muscular electrical activity but are incapable of distinguishing individual motor unit potentials. This can be seen in the area of the striated urethral sphincter and levator ani, which are located in close proximity, but anatomically and neurologically discontinuous [62]. Thus, such perineal surface measurements may not reflect the true striated sphincter activity, but rather compounding of motor unit signals from all the muscles of the pelvic floor. In a comparison of patch vs. needle electrodes during pressure flow studies, needle electrode EMG was more often interpretable and showed motor unit quiescence of the external sphincter more often, suggesting that the signal obtained from the pelvic floor musculature in the region may mask the actual signal obtained from the external sphincter [63]. Needle electrodes are able to isolate electrical activity from specific muscle fibers within a 0.5 mm radius of the tip [63]. Such accurate information of course does come with a drawback of being more invasive and operator dependent.

Needle electrodes can be either monopolar, concentric, or single fiber in type varying in dimensions and the type of metal that is used. Monopolar electrodes are thin needles coated with an insulating material that have an exposed tip. A reference electrode is needed, such as a surface stick or subcutaneous needle attached to the skin near the muscle being examined. Concentric electrodes have a hollow cannula serving as the reference electrode. An insulated fine wire extends through the cannula exiting as a beveled tip and is the active electrode. The advantage of concentric electrodes is a more predictable surface area, producing more reliable measurements of MUAPs [64].

To obtain representative EMG studies of the pelvic floor, electrodes may be placed into the bulbocavernosus muscle through the perineum in men and the superficial anal sphincter in women. In women, the superficial anal sphincter is accessed with an electrode placed through the perineum at the 12 o’clock position, which is advanced just under the skin at the mucocutaneous junction to obtain an

EMG signal [65]. To obtain activity of the external urethral sphincter in women using these types of electrodes, a needle is placed lateral to the urethral meatus and advanced parallel to the urethra to a distance of about 1–2 cm. This of course may be difficult and painful for women, and meticulous attention to detail is required. The technical precision of needle placement is important in order to accurately record the activity within the true urethral sphincteric complex. If localized properly, *noise* from the adjacent pelvic floor can be eliminated, resulting in a true measurement of isolated sphincter function.

Normal EMG findings imply a lack of neurological basis for a patient's voiding dysfunction, whereas an abnormal EMG study indicates a need for further work-up. Findings must be taken in relation to the subject's concurrent action. In patients free of pathology, the EMG activity is low at rest, and it increases in amplitude and frequency with increases in pressure of the abdomen, such as coughing, laughing, and with bladder filling [60].

Due to the complex neurophysiological process of micturition, there is synergic coordination of the urethral sphincter mechanism and bladder. During voiding, the urethra should be relaxed, so as to permit the passage of urine. Focused EMG studies utilizing surface or needle electrodes can be carried out on the distal sphincter of the urethra. During a void, the urethra should be in a relaxed state, which would correspond to silence on the EMG, whereas during filling an increase in electrical activity should be observed [66]. The goal of EMG during UDS is to determine whether the external urethral sphincter complex is coordinated or uncoordinated with the bladder during voiding [67]. During the study, the absence of urethral relaxation during a void may signify an abnormality in urethral function. Such an abnormality in the context of a known neurological condition is termed detrusor external sphincter dyssynergia [68]. However, constant urethral tension during voluntary micturition in the absence of known neurological pathology is called dysfunctional voiding, which may represent a learned behavior [15].

EMG: Clinical Interpretation

Urethral sphincter EMG is used to make the diagnosis of DESD, and it is used to distinguish the 3 types of DESD (Figure 33.12). In type 1 DESD, there is a sudden and complete relaxation of the striated sphincter at the peak of the detrusor contraction, and unobstructed voiding occurs. Type 2 DESD is characterized by sporadic involuntary contractions of the striated sphincter throughout the detrusor contraction. Voiding occurs in bursts during sphincter relaxation. With type 3 DESD, there is a crescendo–decrescendo pattern of sphincter contraction, which results in urethral obstruction throughout the entire detrusor contraction. In all 3 types of DESD, the involuntary sphincter contraction precedes the involuntary detrusor contraction. In contrast, with AVD, the sphincter EMG activity diminishes just prior to the detrusor contraction and then sporadically increases as the patient contracts and relaxes the striated sphincter (Figure 33.13). The 2012 AUA Guidelines on Adult Urodynamics recommend that EMG be performed with cystometrogram in patients with relevant (at risk for upper tract complications) neurological disease at risk for neurogenic bladder, or in patients with other neurological disease and increased postvoid residuals or urinary symptoms.

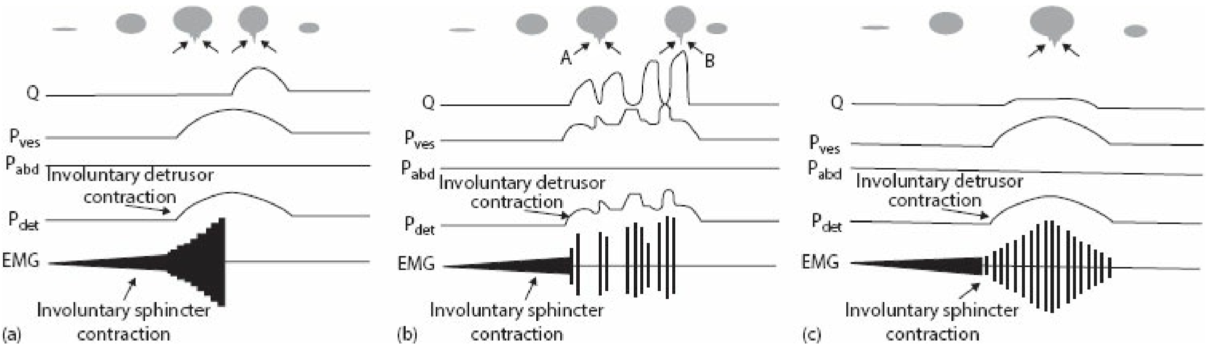
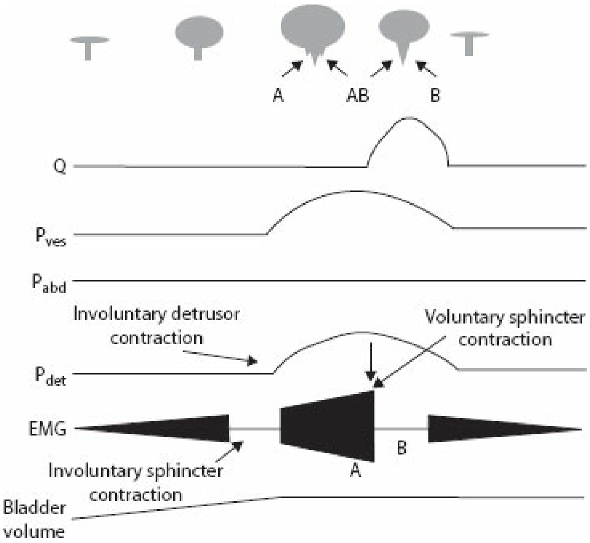

Q
P_{ves}
P_{abd}
Involuntary detrusor contraction
P_{det}
EMG
Involuntary sphincter contraction
(a)
A
B
(b)
(c)

Figure 33.12 Three types of DESD: (a) type 1 DESD, sphincter relaxes at peak of detrusor contraction; (b) type 2 DESD, sporadic sphincter contractions throughout detrusor contraction; (c) type 3 DESD, crescendo–decrescendo pattern of sphincter contraction. *Abbreviations:* DESD, detrusor external sphincter dyssynergia;

EMG, electromyography; P_{ves}, intravesical pressure; P_{abd}, abdominal pressure; P_{det}, detrusor pressure. (Reproduced from Jerry B et al., eds., *Atlas of Urodynamics*, 2nd ed., Blackwell Publishing, Oxford, U.K., 2007. With permission.)



A
AB
B
Q
Pves
Pabd
Involuntary detrusor contraction
Voluntary sphincter contraction
Pdet
EMG
B
A
Involuntary sphincter contraction
Bladder volume

Figure 33.13 Acquired voiding dysfunction. An involuntary detrusor contraction is heralded by complete relaxation of the sphincter electromyography (EMG). As the patient senses the detrusor contraction, she contracts her sphincter (increased EMG activity) in an attempt to prevent incontinence (arrows A). Once the sphincter fatigues, the urethra opens and incontinence ensues (arrows B). *Abbreviations:* EMG, electromyography; P_{ves}, intravesical pressure; P_{abd}, abdominal pressure; P_{det}, detrusor pressure. (Reproduced from Reproduced from Jerry B et al., eds., *Atlas of Urodynamics*, 2nd ed., Blackwell Publishing, Oxford, U.K., 2007. With permission.)

Fowler syndrome was first described in 1985 in young women with urinary retention [69]. The sphincter EMG signal in these women contains repetitive discharges and decelerating bursts. This impairs sphincter relaxation and leads to obstructed voiding with either incomplete emptying or retention. The development of the sphincter abnormality may be under the influence of estrogens, as suggested by the high association of polycystic ovaries in these women [70]. Sacral neuromodulation has a rapid effect in restoring voiding function in some of these women, which may work by reversing the inhibitory effect of the sphincter contraction on the voiding reflex. The abnormalities of sphincter function (abnormal EMG activity and high MUCP) are not reversed with neuromodulation [71].

It is clear that EMG measurements (particularly patch EMG technique) are nonspecific *generalizations* of sphincteric function. In essence, these studies represent an assessment of pelvic floor activity to determine if the appropriate relaxation/coordination in function is present. As in all urodynamic tests, these findings must be taken in global context, including history and physical examination (neurological disorder or not), fluoroscopy ("spinning top" appearance of the posterior urethra), and urinary flow to correlate the EMG activity to the other urodynamic events. These studies are not to be interpreted in isolation. Needle EMG may provide more precise detail regarding sphincteric activity, but patient discomfort appears to greatly restrict its use.

Urethral pressure reflectometry is a technique that uses the acoustic patterns detected in a polyurethane bag placed in the urethra, enabling measurement of the pressure needed to open the closed urethra and giving estimates of pressure and cross-sectional area in the entire length of the urethra [72,73]. The procedure appears to be less uncomfortable than conventional UPP and provides a more detailed and flexible approach to assessing various parameters of urethral function [74]. Reflectometry indicates that urethral opening pressure at rest is unchanged after TVT and that TVT brings increased resistance against the dilation of the urethra [75]. The technique is comparatively new and continues to be subject to ongoing improvements in methodology [76,77].

SUMMARY

The 2012 AUA Guidelines on Adult Urodynamics recommend urethral function tests (ALPP and/or UPP) in women who are undergoing urodynamics for the evaluation of SUI. In addition, EMG studies are recommended in patients with certain neurogenic disorders. These tests are not standardized in technique, are nonspecific, and lack diagnostic accuracy. In 2013, the International Consultation on Incontinence Research Society performed a critical assessment of the techniques of urethral function measurements and reached several notable conclusions. First, it was noted that the severe limitations of urethral function testing techniques confound a proper assessment of a fundamental element of maintaining continence. Second, there is a considerable gap between symptomatic realities we need to address in practice and the variables that our current tests can assess. Lastly, the significant need for research in improving our assessment of urethral function was noted [78].

Clearly, there is a need for better diagnostic accuracy in measuring urethral function. Whether it is through improvements in existing technology or emerging new technologies is yet unclear. What is clear is that the assessment of urethral function is through a comprehensive assessment including history and physical examination, diary assessment, and multiple urodynamic testing techniques (if needed). Urethral function tests are only one component of a comprehensive urodynamic examination and should not be used in isolation to obtain a diagnosis of urethral dysfunction.

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34 Special Urodynamic Tests: Videourodynamics

Ilias Giarenis and Marcus J. Drake

INTRODUCTION

Urodynamics (UDS) is the umbrella term for any test giving a dynamic evaluation of lower urinary tract (LUT) function. The test in most widespread use is cystometry, in which abdominal and bladder pressure are measured synchronously with urine flow during bladder filling (filling cystometry) and voiding (pressure flow studies), as described in Chapter 32. Conventional UDS is informative in well-defined circumstances, but many women have additional complications in their symptomatology or past medical history. This can make the ability to obtain extra information important for full insight into underlying pathophysiology and consequently for making safe treatment recommendations.

Videourodynamics (VUDS) allows synchronous imaging during cystometry, and this enables the urodynamicist to elicit additional information at crucial times during the test. Cystometry was first synchronized with cinefluoroscopy in the early 1950s through the pioneering efforts of ER Miller [1] and further developed through the 1960s in the United States by Tanagho [2] and in the United Kingdom by Turner-Warwick [3]. Improvements in imaging technology, pressure transducers, digital signal processing, and computing have led the evolution of the original technique to the modern VUDS. The term videocystourethrography can be used interchangeably and is used in the most recent joint International Urogynecological Association/International Continence Society (ICS) terminology document [4]. VUDS is also referred to as fluorourodynamics mainly in North America.

While VUDS offers the most comprehensive means of assessment of LUT dysfunction, it constitutes a comparatively small proportion of urodynamic testing overall (6% in a cohort of 1.4 million female U.S. Medicare beneficiaries) [5]. Nevertheless, it is an essential measure for assessing complex cases by adding high-resolution anatomical details to the physiological (urodynamic) data. VUDS allows direct observation of the effects of bladder events, the position and conformation of the bladder neck in relation to the pubic symphysis, bladder neck closure during rest and stress, diverticula of the bladder and urethra, vesicovaginal and urethrovaginal fistulae, vesicoureteric reflux, and voiding events [4]. The current chapter describes how VUDS is undertaken, placing emphasis on the additional requirements and technique alterations compared to simple cystometry. The indications and limitations for VUDS are outlined, and the potential risks and benefits of gaining further insight into individual cases are discussed.

SPECIFIC REQUIREMENTS FOR VUDS

The ICS defined best urodynamic practice in a standards document published in 2002 [6], and, more recently, the Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction published relevant guidelines [7]. The ICS document states that a good urodynamic practice comprises three main elements:

1. A clear indication for, and appropriate selection of, relevant test measurements and procedures
2. Precise measurement with data quality control and complete documentation
3. Accurate analysis and critical reporting of results

Specifically for VUDS, a typical arrangement includes a fluoroscopy unit with an image intensifier, a multichannel urodynamic recorder, and a flowmeter. Some companies offer special equipment where computerized systems mix urodynamic signals with x-ray images in order to produce a combined superimposed image on a computer screen.

Fluoroscopy is performed using either a fixed x-ray unit with a table that can be positioned in the supine and upright position or a C-arm image intensifier. In fixed units, a radiotranslucent commode seat attachment to the table facilitates fluoroscopic screening of voiding in the seated position, which is ideal for women. While a C-arm image intensifier provides inferior image quality to fixed x-ray units, it enables patients to sit or stand in a natural position, ensuring the least inhibition to voiding. The use of a C-arm gives also some independence from the x-ray department and the ability to create a less daunting atmosphere, by performing VUDS in a purpose-built urodynamic suite [8]. Provision of a suitable environment is crucial, stipulating that the walls of the screening room are not permeable to x-rays, to ensure radiation does not spread into the adjacent environment. The VUDS room has to have suitable alerts when radiological screening is being undertaken, such as illuminated alert screens at the doorway when screening is happening to avoid unexpected entry of unprotected individuals into the x-ray environment.

Since the study is a radiological procedure, there are several key safety aspects, in addition to the preparation for conventional urodynamic tests:

- Steps should be taken to ensure radiation exposure of pregnant women is avoided.
- Women with prior allergic reactions to radiological contrast medium or iodine should be excluded.
- Compliance with national and international ionizing radiation medical exposure regulations.

For protection of patients, it is necessary to ensure there is adequate justification for doing the test, checking of patient identity, and screening mechanisms for pregnancies and allergies. Within the unit, a specific person has to take responsibility for compliance with the required legislation and ensure equipment maintenance is undertaken according to the manufacturer recommendations. All the urodynamicists should attend a structured radiation protection course and clinical skills, and competencies need to be assessed following training under an identified preceptor with a minimum of 40 cases and regular attendance at videourodynamic clinics and multidisciplinary meeting (MDM) relevant to the clinical areas covered [9].

Contrary to conventional cystometry, where the fluid used is saline, VUDS requires the use of radiological contrast medium for bladder filling, so that the bladder can be visualized with x-ray imaging. A low-concentration, low-osmolality nonionic contrast medium (e.g., Iohexol, Omnipaque^{TM} 140, GE Healthcare) is ideal for VUDS. As the contrast medium is of different density from urine, adjustments may have to be made to the flowmeter, which would otherwise record falsely high readings because of the greater weight of the voided fluid [8].

Every attempt should be made to minimize exposure to an “as low as reasonably achievable” (ALARA) level without sacrificing the diagnostic accuracy of the examination. A number of radiation exposure reduction techniques could be applied using the ALARA principles. The performance of fluoroscopy by trained urodynamicists allows tailoring of the examination to patient symptoms and past medical and surgical history and limiting parts of the examination that are not expected to offer valuable information, such as prolonged imaging during the voiding phase. Pulsed or low-dose setting continuous fluoroscopy with spectral beam filtration and optimal selection of the tube current and high voltage by an automatic brightness control system could further reduce the radiation exposure [10]. Minimization of the primary radiation field to include only the anatomical region of interest and an attempt to spare the ovaries also reduce the detrimental risks [11].

Staff also need to be protected, with x-ray-opaque (lead) aprons or shielding and body-worn dose monitoring detectors. During screening, all individuals present need to move to a location as far as practicable from the x-ray source and the source of scattered x-rays (notably the patient receiving the x-rays will scatter part of the dose). Indeed, remote monitoring from outside the room is increasingly realistic.

BASIC PRINCIPLES OF VUDS

When commencing a cystometry appointment, the urodynamicist needs to review the clinical presentation, treatment received thus far, medical history, and physical examination findings. The patient’s symptom scores and bladder diary are reviewed, so that the crucial aspects are clearly understood. Thereby, the urodynamicist can ensure there is the best chance of understanding contributory mechanisms and potential adverse aspects, so that a treatment recommendation can factor in correction of causative factors and avoidance of complications.

Filling cystometry is performed according to the ICS standards [6]. Overall, the major distinctions of

VUDS from conventional UDS are the use of contrast as the bladder filling medium and the adaptations of the patient positioning. Positioning during filling and voiding has to be considered, in order to enable placement of the anatomical areas into the line of the imaging equipment.

Fluoroscopy is performed at key points as deemed relevant by the urodynamicist and depending on the urodynamic question:

- After filling with about 50 mL of contrast. This serves as a “baseline” for comparison with x-ray screening performed at other times.
- When the patient first reports sensation. This is used to assess whether the bladder neck has opened (since stimulation of urethral receptors can give a sensation of urgency) and whether the bladder has changed shape (suggesting the occurrence of bladder contraction).
- During stress provocation tests. Pelvic floor support is assessed by noting the position of the base of the bladder at rest and during the cough series or straining. At rest, it should be level with the pubic symphysis, and when straining, only a low-amplitude transient downward movement should be observed. Activating the imaging equipment for a short time (<2 seconds) allows the urodynamicist to assess the state of pelvic floor support (Figure 34.1) and observe the presence of stress urinary incontinence (SUI) (Figures 34.1 and 34.2).
- When the cystometric capacity is reached. It is performed to assess the bladder shape and outline and the presence of vesicoureteric reflux (VUR).
- During voiding to assess the urethral shape and outline. Screening during voiding should reveal a urethra of 2–3 cm length and an even caliber. The presence of proximal urethral dilation may indicate obstruction (Figure 34.3), and descent of the bladder base may indicate straining to initiate or maintain the urinary stream.
- During a voluntary stop test. An optional inclusion that can be performed to re-evaluate the presence of VUR.
- After completion of voiding to assess for residual contrast medium.

Screening is usually done in the anteroposterior and oblique plane, both during filling and voiding. Sometimes, other planes can be helpful in cases of suspected structural abnormalities. For example, a lateral viewpoint can be useful in mapping the location of a bladder diverticulum.

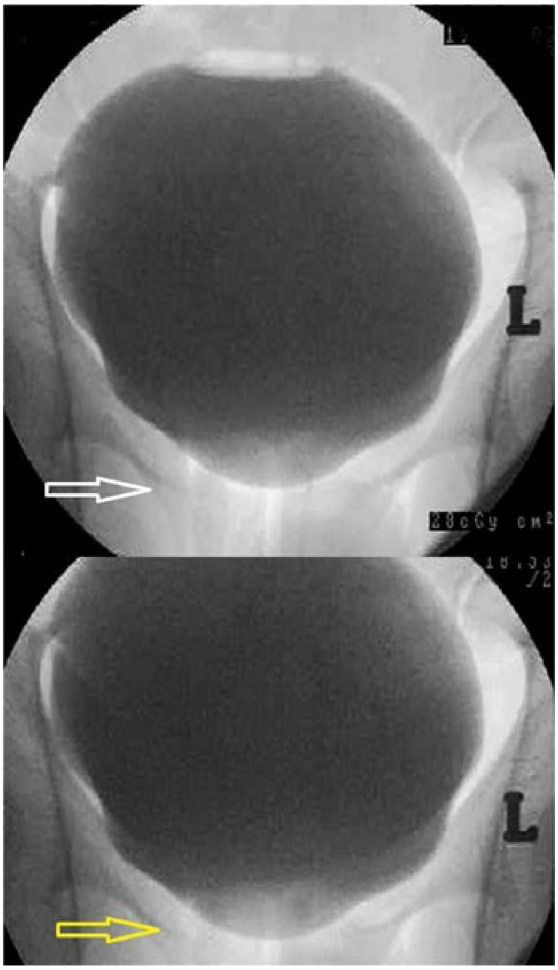

Figure 34.1 A woman with a well-supported pelvic floor. At rest, the base of the bladder lies slightly above the lower border of the pubis (upper image, white arrow). When she coughed (lower image), the bladder base was only fractional lowered at maximum cough amplitude (yellow arrow).

In a continent woman, only the bladder should fill, but contrast filling of other structures should be noted:

- *Urethra*: During the filling phase, urethral visualization suggests SUI.
- *Vagina*: Vaginal visualization indicates either that the bladder filling line was misplaced or displaced, vaginal pooling of contrast (due to dribbling or spraying stream, SUI, or perineal intrusion into the urinary stream) (Figure 34.4), or the presence of a vesicovaginal fistula (VVF).
- *Ureter*: During the filling or voiding phase, ureteric visualization indicates retrograde flow of liquid from lower to upper urinary tract, i.e., VUR (Figure 34.5).
- *Bowel*: A rare event that results either from a fistula or wrongly connected urodynamic lines.

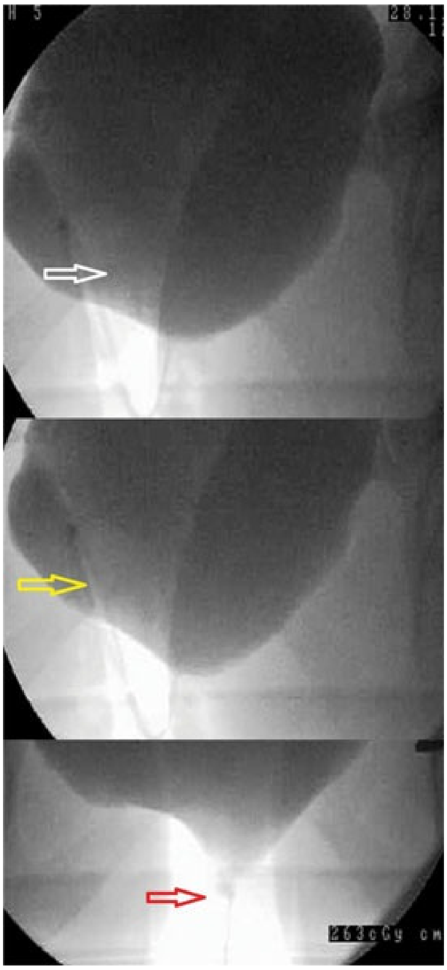

Figure 34.2 A woman with a poorly supported pelvic floor (anterior compartment POP). At rest, the base of the bladder lies below the lower border of the pubis (upper image, white arrow). When she coughed (middle image), the bladder base was further lowered at maximum cough amplitude (yellow arrow indicates base of pubis). With a series of coughs, urodynamic stress incontinence (bottom image, red arrow) was seen on the third cough.

WHO SHOULD UNDERGO VUDS

In most units, invasive evaluation is undertaken following full urological and gynecological assessment and conservative treatment. Only if refractory bothersome symptoms remain in a patient willing to undergo more interventional treatment would cystometry be undertaken. The specific urodynamic approach to understanding the patient's problems has to be derived from the clinical context and potential treatment options. While simple subtracted cystometry is usually sufficient in parous women complaining of primary SUI who have no major medical history of note, assumptions about responsible pathophysiology are not appropriate in other complex cases since there is a greater variety of potential mechanisms underlying. Use of VUDS is needed where the pathophysiology is difficult to predict.

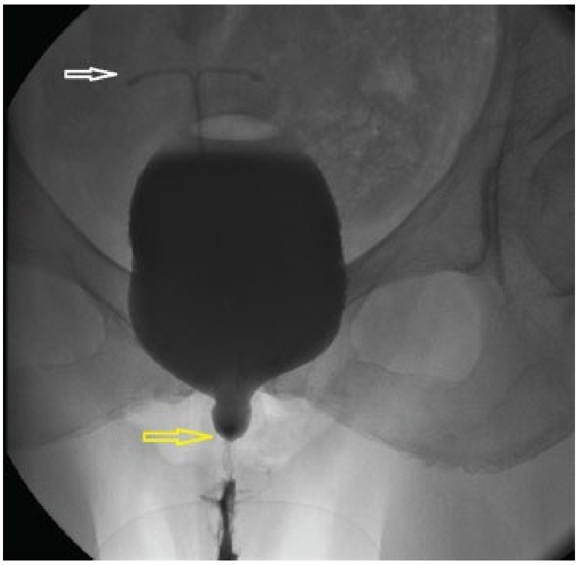

Figure 34.3 A woman with a previous midurethral tape operation, causing partial urethral obstruction (yellow arrow). Note the urethra is dilated proximally. An intrauterine contraceptive device is also present (white arrow).

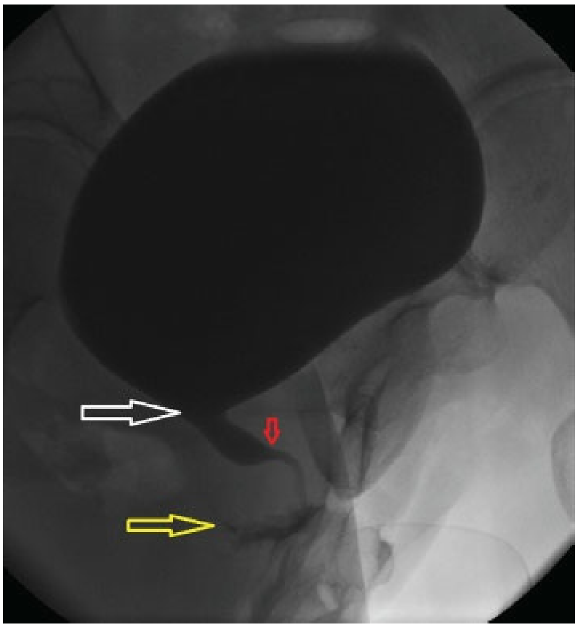

Figure 34.4 A woman with vaginal pooling of voided contrast (yellow arrow). The white arrow indicates a well-opened bladder neck. There is some sphincter contraction visible on this image (red arrow).

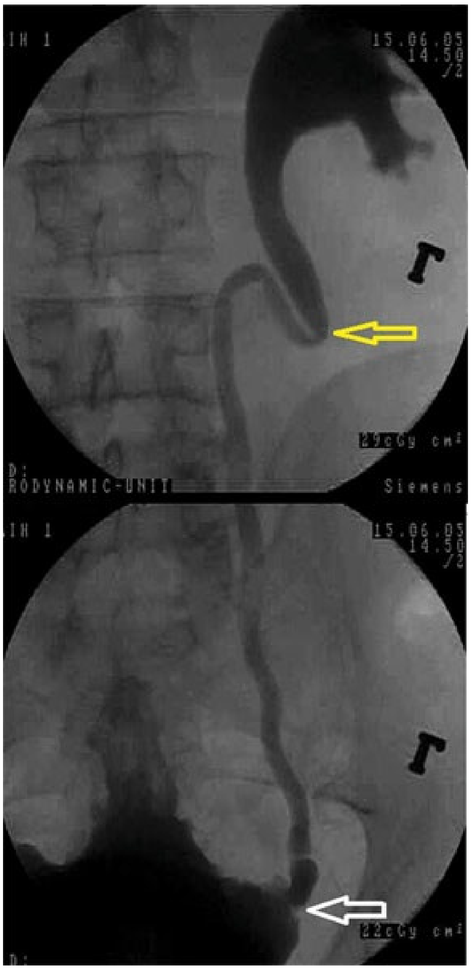

Figure 34.5 Vesicoureteric reflux (VUR). Contrast has passed retrogradely all the way to the kidney. The white arrow marks the ureterovesical junction. Chronic VUR is often associated with an abnormally tortuous proximal ureter (yellow arrow).

Due to the lack of robust scientific evidence, indications for VUDS are based on expert opinion. The International Consultation on Incontinence (ICI) [12,13], the American Urological Association [7], and the European Association of Urology (EAU) [14] have recently reviewed the available evidence and developed relevant guidelines. When available, VUDS should be considered:

- For women with relevant neurological disease at risk of neurogenic bladder (NGB) or in patients with other neurological diseases and elevated postvoid residual (PVR) or urinary symptoms (EAU, Grade of Recommendation A; ICI and AAU, Grade of Recommendation C)
- In the preoperative evaluation of women with persistent or recurrent UI after continence surgery (ICI: Grade of Recommendation C)
- For women with UI after complicated pelvic surgery and high suspicion for VVF
- In the assessment of women with complex incontinence where the history does not fit the findings on preliminary investigations
- For women with coexisting lower urinary tract symptoms (LUTS) and recurrent urinary tract infections in order to rule out structural anomalies [15]

WHAT INFORMATION CAN BE DERIVED DURING VUDS

During the filling phase, the following diagnoses may be identified:

- Urodynamic stress incontinence (USI) (Figure 34.2); this is defined as involuntary leakage of urine, associated with increased intra-abdominal pressure, in the absence of a detrusor contraction [4]. It can be a consequence of urethral hypermobility or intrinsic sphincter deficiency (ISD). The two often coexist but sometimes can be distinguished using VUDS, since USI from ISD is seen to arise with only minimal descent of the pelvic floor (Figure 34.6). ISD is an important possibility in women who have had previous pelvic or incontinence surgery and those with neurological disease. Distinguishing the type of USI is important since it may affect the chance of a successful outcome after operative intervention especially in the challenging group of women with persistent or recurrent USI after failed continence surgery [16]. VUDS is also more sensitive in detecting USI compared to conventional UDS as even minimal loss of contrast can be detected during screening [17].

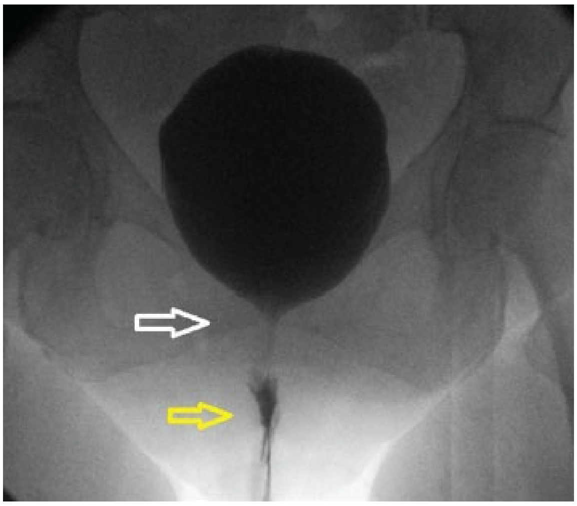

Figure 34.6 A woman with urodynamic stress incontinence caused by intrinsic sphincter deficiency. At rest, the base of the bladder lies level with the lower border of the pubis (white arrow). When she coughed, the bladder base did not move any lower and the urethra opened, i.e., stress incontinence (yellow arrow).

- Detrusor overactivity (DO): A urodynamic observation characterized by involuntary detrusor contractions during the filling phase, which may be spontaneous or provoked [4]. The presence of DO is routinely diagnosed from the pressure trace. However, in the presence of an incompetent urethral sphincter, a change of the bladder shape during VUDS might suggest the occurrence of a bladder contraction without simultaneous rise of the detrusor pressure.
- Increased filling sensation: Patients reporting urgency sensations where no DO occurs on the pressure trace may benefit from x-ray imaging during the urgency episode, as opening of the bladder neck or low-grade stress incontinence may be detected; the contact of urine on the urethral receptors can give a strong sensation.
- Structural abnormalities such as VUR (Figure 34.5), VVF, and bladder diverticula. Bladder hernias through the rectus sheath could be detected in women with multiple lower abdominal/pelvic surgery (Figure 34.7). Extrinsic pressure from pelvic masses (e.g., uterine fibroids, adnexal masses) might also be visualized (Figure 34.8).
- Quality of pelvic floor support: If poorly supported, the pelvic floor can bulge downward at rest or during a rise in abdominal pressure.
- Occult USI on prolapse reduction. Screening during VUDS can confirm successful reduction of a large cystocele after insertion of a pessary. This test has high specificity (93%) and negative predictive value (98%) in predicting SUI after prolapse surgery [18].

The following diagnoses may also be identified during or after the voiding phase:

- *Bladder outlet obstruction* (*BOO*). Voiding with high detrusor pressure but only a low flow rate indicates that there is an obstruction impeding urine flow. For women, there is no standardized diagnostic criterion for establishing BOO, despite the description of various approaches [19]. VUDS can be used to classify a woman as having partial BOO if there is radiographic evidence of obstruction between the bladder neck and distal urethra in the presence of a sustained detrusor contraction [20]. The location of BOO can often be seen clearly since the urethra proximal to the obstruction will typically be dilated (Figure 34.6). However, inclusion of urodynamic testing does not necessarily lead to influence on clinical outcomes of treatment, if voiding symptoms or retention is the reason for intervention [21].

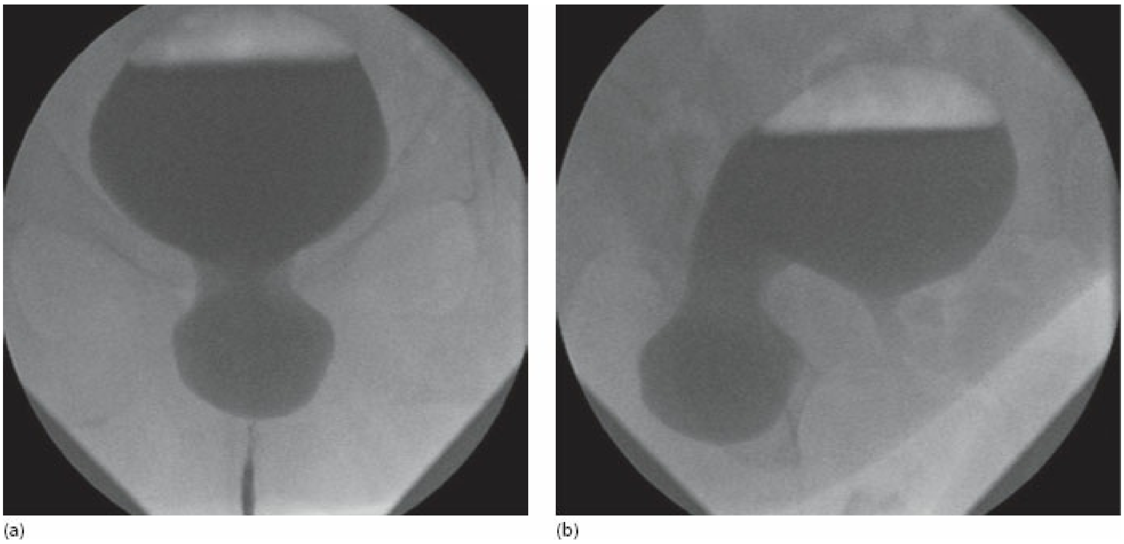

Figure 34.7 Bladder hernia through a rectus sheath defect in anteroposterior (a) and oblique (b) plane.

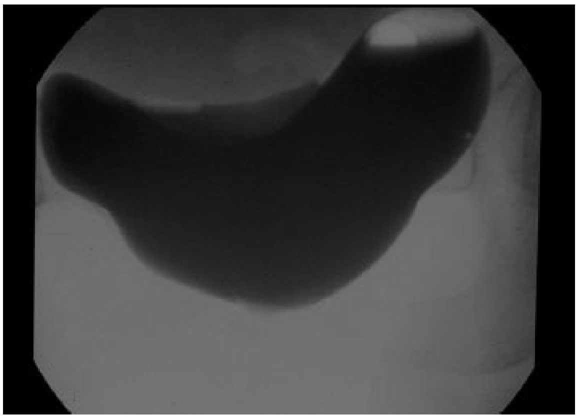

Figure 34.8 Extrinsic bladder pressure from a large fibroid uterus.

- Detrusor underactivity is a contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or a failure to achieve complete bladder emptying within a normal time span [4]. Detrusor underactivity is more prevalent in older women. VUDS can be useful as it helps exclude the presence of BOO.
- Dysfunctional voiding may be diagnosed if persistent sphincter contractions are seen during voiding in neurologically normal women; these can be visualized with VUDS. A similar picture of incoordination between detrusor and sphincter during voiding due to a neurological abnormality is suggestive of detrusor sphincter dyssynergia.
- Structural abnormalities such as urethral diverticula (Figure 34.9) and urethrovaginal fistulae.
- Incomplete bladder emptying: x-ray screening after the void can rapidly ascertain whether bladder emptying is complete or whether there is a “postvoid residual.” Particular care should be taken if there is a bladder diverticulum since a narrow neck may slow draining of the diverticulum, leaving contrast still present, even if voiding managed to empty the bladder efficiently. Care is also needed in the presence of VUR, as return of the refluxed contrast from the upper urinary tract to the bladder can falsely give the impression that bladder emptying was incomplete.

Overall, VUDS provides extra information, which could alter patient diagnosis and management. A case series in a tertiary referral center has shown that in 7.5% of patients, the correct diagnosis was made only with VUDS [17]. Especially in patients with NGB, it permits the diagnosis of abnormalities due to a variety of different neurological conditions and in some cases may help distinguish the etiology of NGB with respect to the underlying neurological disease [7]. Finally, video and sound recording allows review of complex cases during multidisciplinary meetings.

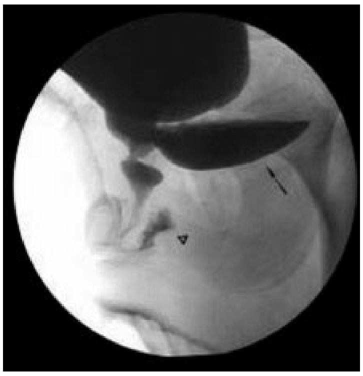

Figure 34.9 Urethral diverticulum filled during the voiding phase with typical air–fluid level (arrow). Contrast medium pooling in the vagina (arrowhead).

LIMITATIONS OF VUDS

Radiation

Although awareness of the radiation exposure from diagnostic radiology has been gradually increasing, there are limited data regarding the radiation effective dose of VUDS in the literature [22]. The variety of examination protocols has led to a wide range of reported radiation doses. The mean effective dose of VUDS varies between 0.34 mSv for a protocol using fluoroscopy only [23] and 4.3 mSv for a protocol requiring routine static image acquisition [24]. Among the organs, the bladder and uterus receive the highest absorbed doses with 1.57 and 1.39 mGy, respectively [24]. Based on the current ICRP recommendations (ICRP 103) [25] with a mean effective dose of 0.34 mSv, VUDS could result in approximately 1 in 75,000 cases of fatal cancer and have a total detriment risk (including fatal and nonfatal cancers as well as severe hereditary effects) of 1 in 50,000.

Despite the very low radiation risk, every attempt should be made to minimize exposure to an ALARA level without sacrificing the diagnostic accuracy of the examination. The decrease in the number of the voiding radiographs has been shown to reduce the radiation dose without compromising the quality of testing in VUDS [26]. A quality assurance protocol is also able to reduce the radiation exposure by decreasing the number of the spot films and fluoroscopy time [27]. Routine documentation of fluoroscopy time and dose area product by the urodynamicist is advisable as it raises radiation awareness and reduces the radiation dose [28].

Anaphylactic Reaction

Anaphylactic reaction is a recognized complication of administration of radiographic contrast media. Immediate severe reactions can lead to laryngeal edema, hypotension, and very rarely even death. After excluding women with a history of allergic reaction to contrast medium, the risk of an anaphylactic reaction due to contrast after VUDS is less than 0.01% [29]. Almost all reported cases of contrast reactions occur in the presence of Grade II or above VUR, as the urothelium forms an effective barrier against contrast absorption, whereas the renal pelvices may allow small quantities of contrast to enter the circulation [30]. In the absence of VUR, a reaction may still be possible if extravasation of contrast occurs following an injury to the urothelium. The selection of contrast agents might influence the anaphylactic risk as low-osmolality nonionic contrast medium is associated with lower rate of severe reactions than conventional high osmolar ionic agents (0.04% vs. 0.22%) after intravenous administration [31].

Other Factors

VUDS is more expensive compared to conventional UDS, as it is more time-consuming and requires the use of expensive equipment, along with the cost of contrast medium. It also requires operators with specialized training and adequate workload to maintain their competence [9]. Therefore, it is an investigation limited usually to large tertiary referral centers.

The quality of imaging may also be poor with obese patients and those with anatomic limitations to their positioning. It could also be difficult for some patients to void in front of the camera, with catheters in the bladder and rectum and observers watching them in an unnatural laboratory environment.

FUTURE DEVELOPMENTS

Alternative imaging modalities have been explored in light of concerns regarding x-ray radiation hazards associated with VUDS and the lack of soft tissue imaging. Two-dimensional and three-dimensional pelvic floor ultrasound offer supplementary information about bladder neck position and mobility, urethral sphincter volume, pelvic organ descent, morphology of the levator ani, diameters of the genital hiatus, and location and functional impact of a preimplanted tape [32]. However, simultaneous performance of ultrasound with cystometry is challenging. Standardization of pelvic floor ultrasound imaging and well-designed and adequately powered multicenter studies are required before its introduction into routine clinical practice.

Dynamic magnetic resonance imaging (MRI) offers an alternative option for imaging in patients with complex pelvic floor dysfunction [33]. Despite the advantage of the lack of radiation, MRI is an expensive investigation, not always available, requiring specialist radiological interpretation and cannot be performed with synchronous multichannel cystometry.

Due to the minimal data in the literature, there is an outstanding need to evaluate further the role of preoperative VUDS especially prior to redo surgery, with studies assessing how these tests influence decision making and/or improve surgical outcome [13]. Future prospective studies could also explore the diagnostic value of the different phases of VUDS and the associated radiation risk.

CONCLUSIONS

VUDS is a useful test for more complex cases in women who are still symptomatic after conservative treatment. Additional safety measures and training are needed compared with conventional UDS. Nonetheless, imaging can provide valuable anatomical and functional information relevant for decision making in individual cases.

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35 Special Urodynamic Test: Ambulatory Urodynamics

Kevin L.J. Rademakers and Gommert A. van Koeveringe

INTRODUCTION

Urodynamic investigations are an important tool in the diagnostic route of patients with lower urinary tract (LUT) dysfunction. Apart from the generally used conventional urodynamic studies (conventional UDS), certain centers conduct ambulatory UDS additionally for specific indications. In contrast to conventional UDS, in which artificial filling is used, ambulatory urodynamic monitoring is based on diuresis-induced natural filling of the bladder [1]. Herewith, ambulatory UDS mimics the situation in which the patients have their urinary symptoms close to what they experience in real life. This is important as incontinence is a benign condition but can diminish quality of life significantly and can influence everyday life. In addition, the argument of conventional UDS being nonphysiological is bypassed by ambulatory urodynamics through the use of natural filling. Furthermore, the laboratory situation in which conventional urodynamics are performed can give psychological inhibition of the bladder [2].

Natural (orthograde) fill cystometry was described for the first time in 1957 by Comarr [3]. In 1959, Mackay [4] reported about bladder pressure measurement in an ambulant patient using radiotelemetry. In the first systems, telemetry was used [5,6]. The technique has evolved ever since, and many methods have been developed [1,7,8]. As time progressed, tape recording systems have been used, with the disadvantage of limited recording capacity [9]. In 1989, Griffiths et al. [10] developed an ambulatory system using microtip pressure transducers and a digital solid-state recorder. This made transfer of data and review of the data at the end of the assessment possible.

At present, ambulatory UDS is a reliable and well-tolerated cystometry tool. The technique is particularly valuable in recording bladder filling and voiding phases (Figure 35.1), combined with the amount and timing of urinary incontinence in a near-normal situation (Figure 35.2) [2,11–15]. This makes ambulatory UDS a useful tool in patients with troublesome urinary tract symptoms [1].

Despite the advantages of ambulatory UDS, conventional UDS is the “gold standard” for the investigation of LUT symptoms as it is a highly standardized and validated measurement tool [16,17]. Validation of ambulatory urodynamic monitoring has proven to be difficult. Validating a sensitive diagnostic tool (ambulatory UDS) based on a less sensitive gold standard (conventional UDS) is arguable. Therefore, validation of ambulatory UDS should be based on the correlation with patient-related treatment outcome. However, studies comparing ambulatory urodynamics to the patients’ treatment outcomes have not been described yet.

This chapter will focus on the indication and procedure of ambulatory UDS. In addition, the use of ambulatory UDS with respect to voiding and storage symptoms will be discussed [8,18,19].

INDICATIONS

- LUT symptoms that conventional UDS fails to reproduce or explain
- Overactive bladder syndrome without detrusor overactivity on conventional UDS
- Incontinence of unclear primary origin
- Voiding dysfunction without detrusor contractility on conventional UDS

EQUIPMENT

A guideline on urodynamic equipment performance was published by a specific International Continence Society (ICS) working group in 2014. This paper covers the technical aspects and considerations of urodynamic equipment. In this chapter, we will include relevant parts of these guidelines [20].

Ambulatory urodynamic equipment consists of an abdominal (usually rectal) and bladder pressure catheter (connected to a transducer system), a recording unit, and the analyzing system. The catheters generally used in conventional urodynamic measurements are water filled and connected to an external transducer. Water-filled systems respond reasonably well to fast pressure changes and are recommended by the ICS for the use in conventional urodynamics [16,21]. However, in ambulatory urodynamics, water-filled catheter systems are not recommended, as pressures measured are dependent on the patients' positioning and are prone to movement artifact [20].

Air-filled catheter systems are also mounted to an external transducer, with the difference that the catheter is filled with air instead of water. Because of the low density of air, the measured pressure is transmitted directly from the catheter tip to the transducer, making it functionally more similar to a catheter-tip transducer. However, responses to rapidly changing pressures can be delayed and diminished in air-filled catheter systems [21]. Air-filled catheters were used for ambulatory UDS in the 1980s [9]. However, based on the limited recording capacity available at that time, a recording threshold was determined. Consequently, small pressure differences were missed, and diagnosis based on the measurement could not reliably be provided.

Currently, microtip pressure transducers are often used for ambulatory UDS. In this system, the transducers are mounted in the tip of the five to eight French catheters inserted in the bladder and rectum. The catheter inserted in the bladder contains a second transducer measuring pressure at the urethral level. The registered pressure signal is converted to a voltage, which is then amplified. Compared to water-filled catheter systems, microtip transducers are less prone to movement artifact, with the additional advantage of fast response to pressure differences. A major disadvantage of microtip catheters is the positioning of the catheter tip since, like the air-filled catheters, there is uncertainty of positioning of the microtip transducers [20]. This can result in pressure differences between measurements. Therefore, pressure values should be clearly displayed at the start of the assessment. Microtip transducer drifting during the measurement can be an issue; however, this is usually only within a small range [22].

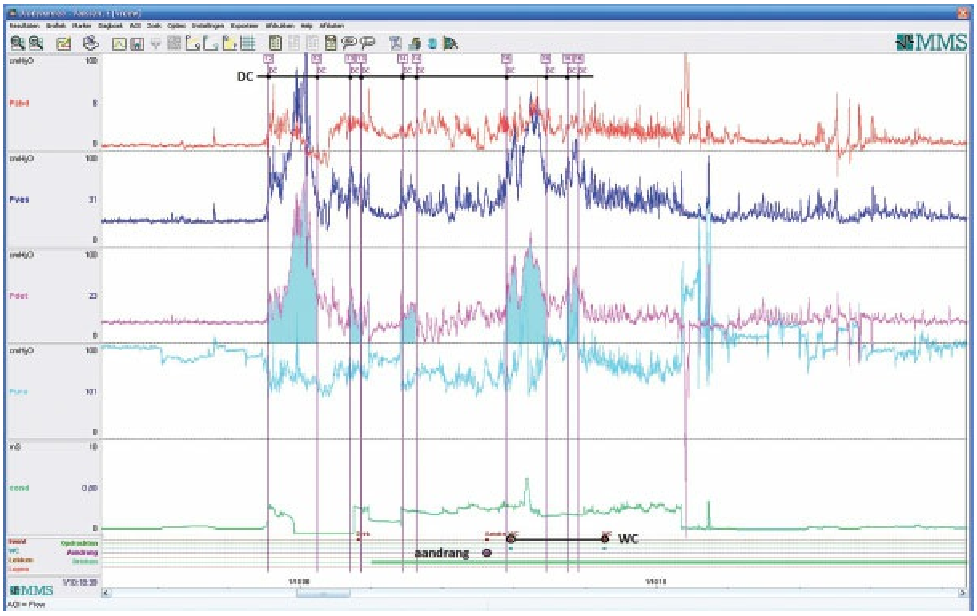
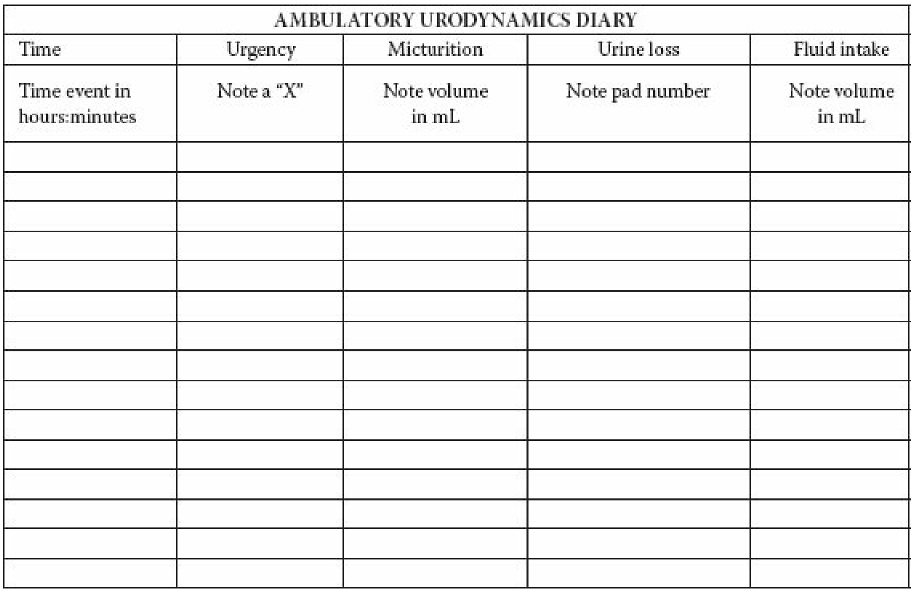


Figure 35.1 Ambulatory urodynamic trace showing detrusor overactivity (with high detrusor pressure), in the presence of the used "urgency" event button. "DC" marker: detrusor contraction, indicating the start and end of a detrusor contraction (detrusor overactivity if during the filling phase). "Aandrang" marker: represents the urgency event. "WC" marker: indicating start and end of the toilet visit.



AMBULATORY URODYNAMICS DIARY				
Time	Urgency	Micturition	Urine loss	Fluid intake
Time event in hours:minutes	Note a "X"	Note volume in mL	Note pad number	Note volume in mL

Figure 35.2 Ambulatory urodynamic diary.

During ambulatory UDS, physiological signals and other behavioral indicator parameters are measured and stored in a portable digital recording unit. Currently, several comparable ambulatory urodynamic systems are available, including Luna (MMS), Blue Runner (Memphis), and Medkonsult's UroPress Salsa (information obtained April 2014). Besides recording pressure signals, the recording device contains several event buttons. Patients are instructed to use these buttons at specific events, for example, in case of an urgency episode, a toilet visit, drinking, or involuntary leakage of urine. At present, the registration of these events is connected to a timer incorporated into the recording unit. The event buttons should be simple and easy to interpret as event timings are essential for interpretation of the ambulatory UDS, along with urodynamic trace and detected urine leakage [1]. In patients needing to perform clean intermittent self-catheterization (CISC), an additional eight French catheter might be inserted via the urethra during the assessment. Postvoiding residual urine can then be drained after voiding attempts, in case of incomplete voiding.

Pressure traces are transferred to a computer and via specific software translated to a measure of detrusor and urethral function (Figure 35.1). Wireless Bluetooth techniques have the advantage of instant pressure–flow trace viewing while recording [23].

For evaluation of incontinence, urine loss measurement during ambulatory UDS is essential. There are several options for measuring urine leakage. First, the loss can be measured by using an electronic pad or electronic diaper (Urilos). The electronic pad has elongated, interleaved electrodes embedded in absorbent material. A 50 mV (low voltage) alternating current is passed between the two electrodes. The current increases as the urine loss increases, depending on the extent of contact between the electrodes and the conducting medium (urine). Because of this, the pad has to be preloaded with a known volume of electrolyte solution. The electronic pad is only suitable for volumes between 1 and 100 mL, which makes this method useful in only a proportion (20%) of the patients.

A second option is measuring perineal temperature. Urine has a higher temperature than that of the body surface. In case of urine leakage, the temperature steadily rises above skin surface temperature after which temperature rapidly falls. This allows urine loss episodes to be identified. The rate of temperature rise may correlate well with the amount of urine leaked. However, this measurement technique is dependent on the position of the detector in relation to the leaked urine as well as the position of the patient. Perineal temperature rises when a patient sits, meaning explicit instructions are necessary.

The third method is measurement of urine leakage by using a weighed pad. When used as a separate method, this test gives a rough estimation of the amount of urine that has been lost, but it gives little information about the timing of urine leakage. However, combining this with placing a conductance catheter gives the necessary additional information on the episode of urine leakage. A conductance catheter contains two electrodes and is placed within the urethra. A current is passed between both electrodes. In the event of urine passage, there is an increased conduction and a larger current passes across the electrodes. However, exact localization is key and should be monitored closely at the start of the assessment.

STANDARDIZATION OF AMBULATORY URODYNAMIC STUDIES

A standardization report on ambulatory UDS was published by a working group of the ICS in 2000 [1]. This document covers different aspects such as technical considerations and suggestions and both clinical and scientific reports for ambulatory urodynamics. In this chapter, we will discuss the parts of this report most relevant for clinical purposes.

Terminology

The ICS standardization working group advises the use of terminology during ambulatory UDS, which is consistent with that used during conventional UDS [24].

Methodology

Signals

The following signals are (have been) recorded by ambulatory UDS:

- Pressure: intravesical, abdominal, and urethral
- Flow rate
- Micturition volume
- Residual urine (e.g., with a bladder scan), in those cases where preassessment CISC was undertaken
- Urinary leakage episode
- Leakage volume
- (Urethral electrical conductance)
- (Perineal integrated surface electromyography)

Additional Event Marker Information

Event marker information should be recorded during any ambulatory UDS to include the following phenomena:

- Initiation and cessation of voluntary voids
- Episodes of urgency
- Episodes of discomfort or pain
- Provocative maneuvers
- Time and volume of fluid intake
- Time and volume of urinary leakage
- Time of pad change

Signal Quality

Ambulatory UDS is more versatile and represents a more natural situation compared to conventional urodynamics. The versatility of ambulatory urodynamics is associated with a greater risk of losing signal quality. Therefore, although all signals should be recorded as outlined in the ICS recommendations on “good urodynamic practices” [16], there are a number of cautions that apply specifically to ambulatory UDS, as described in the following text.

Intravesical and Abdominal Pressure Measurement

Although it is possible to measure intravesical and abdominal pressures using fluid-filled lines (water or air), the use of catheter-mounted microtip transducers allows greater mobility during ambulatory UDS. In the absence of continuous supervision, stringent checks on signal quality should be incorporated in the measurement protocol. At the start of monitoring, these should include testing of recorded pressure online by coughing and abdominal straining in the supine, sitting, and erect positions. The investigator must be convinced that signal quality is adequate before proceeding with the ambulatory phase of the investigation.

Prior to termination of the investigation, and at regular intervals during monitoring, similar checks of signal quality such as cough tests should be carried out. Such tests will serve as a useful retrospective quality check during the interpretation of traces. The following considerations must be taken into account when using microtip transducers:

- Transducers should be calibrated before every investigation.
- The “zero point” is atmospheric pressure. All transducers must be “zeroed” at atmospheric pressure before insertion of the catheters.
- Water-filled pressure catheters have a fixed reference point at the upper edge of the symphysis pubis, whereas catheter-mounted microtip pressure transducers have no fixed reference point.
- Microtip transducers will record direct contact with solid material (the wall of a viscus or fecal material) as a change in pressure. The use of multiple transducers may eliminate this source of artifact.
- Under some circumstances, the pressure measured at the transducer surface will result in a discrepancy equal to the difference in a vertical height between the two transducers. This can result in the estimated detrusor rest pressure being <0 (i.e., negative) with, for instance, the patient in supine position.

Urethral Pressure and Conductance

The recording of urethral pressure is a qualitative measurement with emphasis on changes in pressure rather than absolute values. The use of urethral electrical conductance to identify leakage in association with pressure monitoring facilitates interpretation of urethral pressure traces. Precise positioning and secure fixation of catheters are essential to maintain signal quality (Figures 35.3 through 35.5). The orientation of the transducer should be documented. (The use of multiple pressure transducers facilitates identification of movement artifact but increases catheter stiffness and thereby deformation of the urethra during recording.)

Catheter Fixation

Securing catheter fixation is essential to maintain signal quality. Methods that have been used include adhesive tape, suture fixation, and specially designed silicone fixation devices.

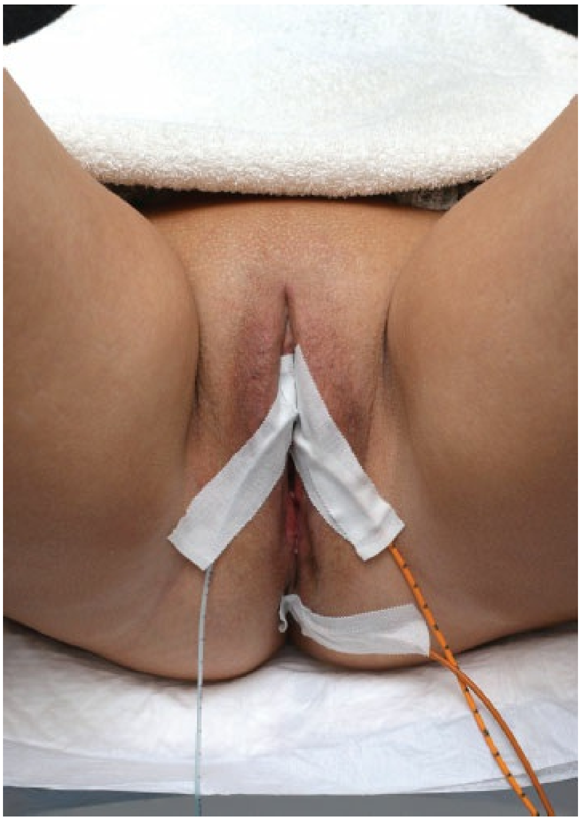


Figure 35.3 Positioning and fixation of the urodynamic catheters in a woman who is unable to void to completion. The blue catheter represents one to empty the bladder after micturition. The yellow catheter on the top is used for measuring intravesical and urethral pressures. The lower catheter, fixated to the buttock, is used to measure rectal pressure.

Recording of Urinary Leakage

The method of urine leakage determination should be recorded. It should be stated whether the urinary leakage is recorded as a signal with the pressure measurements or is dependent on the subject pressing an event marker button or completing a urinary or leakage weight diary (Figure 35.2).

Instructions to the Patient

Detailed instructions as to recording of symptoms, identification of catheter displacement, and hardware failure should be given to the patient. It is the recommendation that such verbal instructions should be reinforced by written instructions, and, in addition to the hardware built into the system, the patient is provided with a simple diary to record events. This allows correlation of the test observations with symptoms.

Analysis

Quality Assessment

The first step in the analysis of an ambulatory UDS trace is the assessment of the quality of data recorded. The specific points that should be addressed with regard to pressure measurement are as follows:

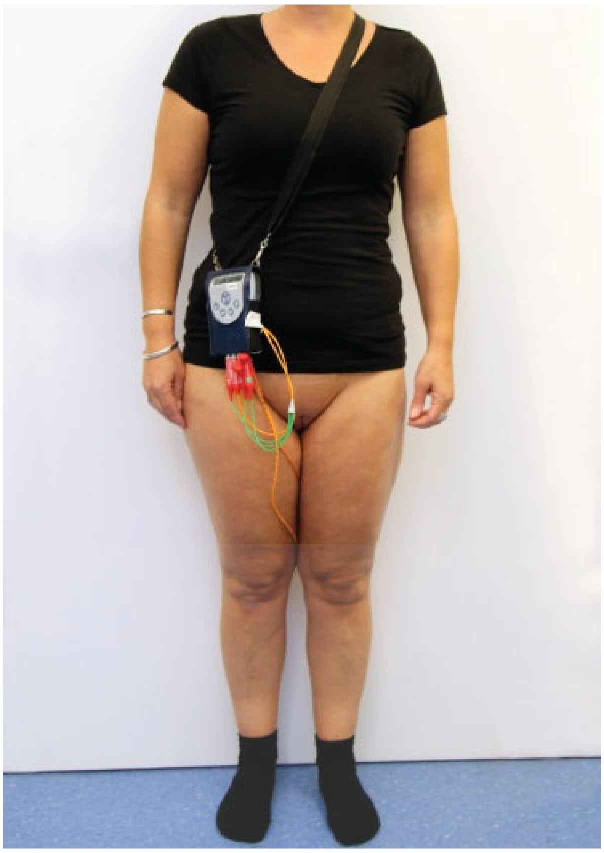


Figure 35.4 Overview on how the catheters are connected to the portable recording unit during a four to seven hour measurement.

- Is the trace "active," i.e., fine second-to-second variation in pressure is visible (indicating breathing and body movement), rather than a completely flat line?
- Is the baseline static or highly variable?
- Are the cough tests or other activities causing abdominal pressure changes that can be used for signal plausibility check regularly present?
- Is the subtraction adequate, e.g., minimal change in subtracted detrusor pressure with coughing?

If the technical quality of the traces is less than perfect, then, although the investigation may yield valuable clinical information, the information that can still be derived from the traces is very much dependent on the experience of the team and the person responsible for the interpretation of the assessment.

Phase Identification

Depending on the purpose of the investigation, markers must be placed to identify voluntary voids and allow differentiation of such events from involuntary events, which may be associated with changes in recorded pressure. The protocol of the investigation should state specifically the point at which the markers identifying commencement and cessation of a voluntary void are placed. Analysis of the voiding phase follows the same principles and terminology used during conventional pressure–flow investigation.

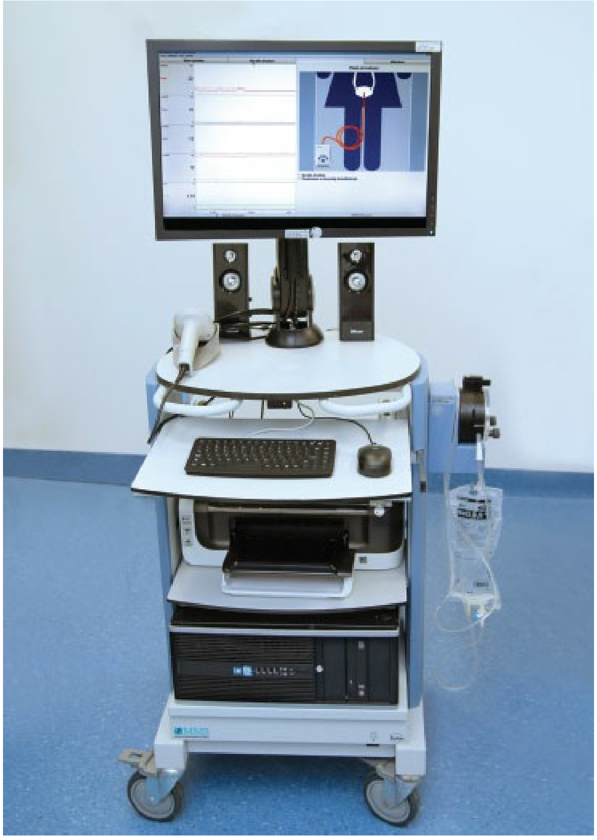


Figure 35.5 General urodynamic filling, recording, and monitoring system. The system is used to check catheter position before fixation and connection to the portable unit. In addition, data from the portable recording unit are transferred to this system after the ambulatory measurement has ended.

Events

The use of a patient diary considerably improves the detailed analysis of events occurring during ambulatory UDS and is a necessity for adequate interpretation. In addition, it has proven very valuable as a double check for both patient and equipment compliance. Typical events occurring during the filing phase are detrusor contractions, urethral relaxation, and episodes of urgency and incontinence.

CLINICAL REPORT

The report should be tailored to the urodynamic indication(s) and can include the following:

- Whether symptomatic complaints were reproduced during the test
- Duration of recording
- Filling rate, timing, method, and volume of any retrograde filling before commencing ambulatory UDS
- Dose and timing of diuretics, if administered
- Volume of fluid intake during the assessment
- Number of voids
- Total and range of voided volumes and postmicturition urinary residual
- Episodes of urgency, urinary incontinence, and pain
- Detrusor activity during the filling phase (frequency, time, duration, amplitude, area, form)
- Pressure–flow analysis
- Results of provocative maneuvers employed during the test
- In case of premature termination, reason for termination of recording

COMMENTS

Additional to the ICS standardization report, there are several recommendations to ensure quality control during ambulatory urodynamics, as follows.

Patient Preparation

- The patient should be instructed before the assessment on the following:
  - Reasons of execution of ambulatory UDS.
  - Duration of the assessment (in general between 4 and 7 hours) [2].
  - How to fill out the diary, in detail (Figure 35.2). This will provide information on activity during the assessment, which is essential for optimal performance of the ambulatory UDS.
  - Behavior during the assessment (this should be as in the normal, daily situation).
  - Wearing loose comfortable separate clothing.
- Catheters are inserted using an aseptic technique. Catheters are placed in the bladder, urethra, and rectum and brought into optimal position.
- After insertion, the catheters are taped to the inner thigh (sometimes also to the pubic region for optimal fixation), close to the labia (as close to the urethra as possible) using several pieces of 5 cm medical tape. After fixation, catheter positions should be checked again and, in case necessary, corrected for optimization of the pressure–flow traces.

Procedure

- The patient should use the timer on the ambulatory box, not her own watch.
- The patient is instructed how to use the event button. In the event of a toilet visit, the button is pressed when entering the bathroom or at the starting point of voiding and pressed again once voiding has finished. When fluids are consumed, or during an episode of urgency, the relevant buttons are used. Instructions for the use of the event buttons should be included on the diary sheet, as should the instructions on how to fill out the diary.
- In case of problems or discomfort, the patient should be able to contact the coordinator easily. This is also important for the quality of the assessment.
- At the end of the assessment, the patient should be asked to perform a series of activities, such as coughs, which can improve diagnostic yield. After this, the patient is asked to void.
- After completion, the patient’s diary is checked and, if necessary, discussed with the patient present. The traces and diary can be interpreted with the patient still present or at a later stage. If the traces are interpreted in a later stage, the diary must have been filled out correctly by the patient and event markings been recorded correctly. This is important for linking symptoms to the ambulatory urodynamic outcome.
- After the test, the patient is warned that she may have an irritative feeling in the urethra and bladder for up to 24 hours and is advised to maintain optimal fluid intake. If symptoms suggesting cystitis are persistent or urine becomes offensive, the patient should seek advice from her doctor. Anders et al. [25] showed that there is no indication for antibiotic prophylaxis for patients who undergo an ambulatory UDS and had no positive urine culture prior to the assessment. However, in case of known residuals, vesicoureteric reflux or recurrent urinary tract infections (UTIs), antibiotic prophylaxis should be given.

CLINICAL APPLICATION

Patient Bother

In general, conventional UDS is well tolerated in women [26]. Compared to conventional urodynamics, ambulatory UDS has a longer duration (4–7 hours), making it more prone to bother. However, two studies of Oh et al. in 40 patients (33 women and 7 men) showed that conventional UDS appeared to have a higher degree of anxiety than ambulatory UDS ($p = 0.045$), while boredom was significantly more during ambulatory UDS ($p = 0.013$), with no significant difference in embarrassment or bother between both assessments [27]. In addition, the degree of intolerance decreased significantly at second ($p = 0.016$) and third ($p = 0.049$) ambulatory urodynamic assessments [28].

Ambulatory UDS and Storage Dysfunction

Poor Correlation between Symptoms and Conventional UDS

Several studies already showed that urinary symptom diagnosis and conventional urodynamic diagnosis differ [29–31]. A study in 209 nonneurogenic patients (92 women and 117 men) with persistent OAB symptoms showed detrusor overactivity (DO) on conventional urodynamics in only 58.7% [32]. Haylen et al. [33] showed that none of the OAB symptoms alone can accurately predict DO on conventional urodynamics. Sekido et al. [34] retrospectively evaluated 50 patients (38 women and 12 men) with OAB symptoms in relation to the presence or absence of DO. The overall incidence of DO was 36.8% in the female patient group, making the bladder an unreliable witness for predicting detrusor overactivity on conventional UDS [35].

Ambulatory UDS versus Conventional UDS in Storage Dysfunction

Although ambulatory UDS is a relatively elaborate and time-consuming investigative tool to perform and to analyze, it is thought to be a more accurate tool for diagnosing LUT dysfunctions in both children and adults [23,36]. In case of DO, ambulatory UDS has been reported to have a higher sensitivity compared to conventional UDS [8,11]. Patravali et al. showed that ambulatory UDS can diagnose urinary dysfunction in 77% of symptomatic women with inconclusive conventional urodynamics. These results are in line with earlier results from Anders et al. in 475 symptomatic women [37]. Radley et al. [13] compared ambulatory UDS and conventional videocystometry findings in 106 women with OAB symptoms. They showed a significant difference ($p < 0.001$) in the detection of DO, with a higher prevalence detected using ambulatory UDS. No significant difference was seen when comparing stress incontinence rates in both groups ($p = 0.629$).

The difference in observations between both assessment types could be explained by the technique used. The retrograde, rapid bladder filling and the shorter time span of conventional urodynamics may very well lead to an underestimation of DO. However, it cannot be excluded that the vesical catheter itself is a nonphysiological trigger resulting in a higher incidence of detrusor overactivity during ambulatory urodynamics [38]. In addition, a previous study in healthy female volunteers showed DO on ambulatory UDS in 68% of the cases, compared to 18% after conventional UDS [39]. Salvatore et al. [40] showed that the symptom diary and potentially also the placement of two transducers in the bladder can decrease the finding of pathological detrusor activity on ambulatory UDS by minimizing possible artifacts.

There still remains a lot of controversy regarding the clinical implications of using urodynamics in OAB patients [41]. Giarenis et al. [42] recently showed that women with OAB and additional DO on conventional or ambulatory UDS experience a more significant impairment to their quality of life and have a greater degree of bladder dysfunction compared to OAB patients without DO on urodynamics.

In clinical practice, ambulatory urodynamics can be of additional value in the specific group of treatment of refractory OAB patients without DO on conventional UDS. The fact that the bladder produces involuntary detrusor contractions in response to the small flexible catheters during an ambulatory urodynamic measurement itself might indicate a higher excitability of the bladder sensory function or a decreased central inhibition of the urethra–detrusor facilitative reflex contractions in the filling phase [43]. This might even serve as a biomarker of pathology. To accomplish this, quantification and characterization of DO on ambulatory UDS is necessary. In the past, van Waalwijk van Doorn and Ambergen [44] started with characterization of DO by development of the detrusor activity index. However, this method is used seldom in clinical practice.

Ambulatory UDS and Incontinence

In case of urinary incontinence with uncertainty about the underlying cause, conventional urodynamics in general does not give sufficient additional information on the pathophysiological background. The advantages of ambulatory UDS having a longer recording period, multiple micturition cycles, additional stress testing, and the observation of urinary leakage combined with pressure–flow traces make it more suitable for potential detection of the predominant cause of the urinary incontinence (Figure 35.6).

Robinson et al. [45] assessed whether ultrasound bladder wall thickness measurement could replace ambulatory urodynamics in 128 patients women with a conventional urodynamic diagnosis not explaining their urinary symptoms. The authors concluded that in women with stress incontinence ambulatory urodynamics remains the investigation of choice.

There is currently only limited literature on the specific role of ambulatory UDS in the identification of the origin of incontinence with attention to DO as well as the stress component. However, the available literature suggests that ambulatory UDS improves the ability to detect an underlying pathophysiology compared to conventional urodynamics [15].

Pharmacological Treatment Monitoring

Ambulatory urodynamics can be used for the evaluation of pharmacological OAB treatment and potentially has advantages over conventional UDS based on the design of the ambulatory assessment. The optimal duration to yield useful information appears to be 6 hours [46] (Figure 35.7). A study by Chapple and Abrams comparing darifenacin and oxybutynin in patients with OAB showed that ambulatory UDS can potentially be a useful investigative tool in the evaluation of therapeutic agents [47].

The topic of ambulatory UDS pharmacological treatment evaluation is still heavily under discussion [48] as Oh et al. published a study suggesting that ambulatory UDS does not take into account the patient perception of bladder condition after treatment [49]. In addition, correlations between the patient view of treatment outcome and urodynamic measures are poor [49]. However, most studies have a small sample size, emphasizing the need for larger studies to evaluate the usefulness of ambulatory UDS to this respect.

Effective Evaluation of Invasive OAB Treatment: Sacral Neuromodulation and OnabotulinumtoxinA

There is currently only one study presenting results on treatment evaluation using ambulatory UDS as a diagnostic outcome tool. Scheepens et al. [50] published a study in OAB patients treated with sacral neuromodulation (SNM) and described a correlation between reduction in involuntary detrusor contractions and clinical outcome after treatment. This, together with clinical experience, shows that ambulatory urodynamics is potentially a useful diagnostic tool in the evaluation of SNM treatment.

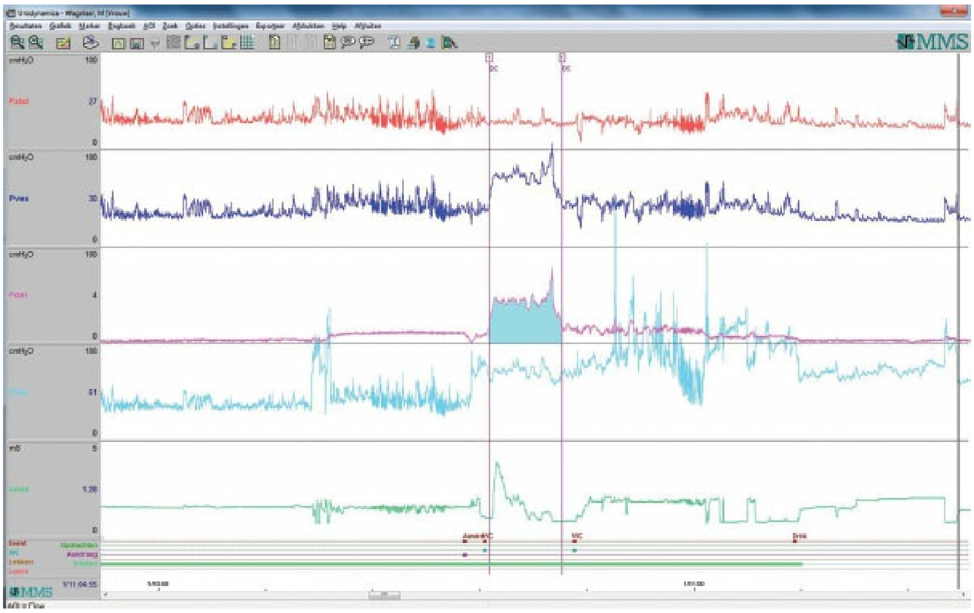


Figure 35.6 Ambulatory urodynamic trace showing bladder contractility in a patient after sacral neuromodulation (SNM) test phase. This specific patient had bladder acontractility before SNM testing. Additionally, there is a lack of urethral relaxation. “DC” marker: detrusor contraction, indicating the start and end of a detrusor contraction (detrusor overactivity if during the filling phase). “Aandrang” marker: represents the urgency event. “WC” marker: indicating start and end of the toilet visit.

In contrast, there are no data available on ambulatory urodynamic evaluation of onabotulinumtoxinA treatment. However, a study analyzing conventional UDS showed that results after intradetrusor injections of onabotulinumtoxinA in idiopathic OAB patients were not predicted by the presence of detrusor overactivity on pretreatment conventional UDS [51].

Ambulatory UDS and Spinal Cord Injury Patients

Spinal cord injury (SCI) patients routinely have a urodynamic follow-up to detect poor compliance, high-pressure storage, or neurogenic DO, which can lead to incontinence, bladder stones, UTIs, or upper urinary tract deterioration. In the context of SCI patients, there have been new ambulatory system developments recently. In 28 patients, a new system, with abdominal pressure measurement using surface EMG patches, was tested [52]. These patches appeared to be able to replace the use of a rectal catheter.

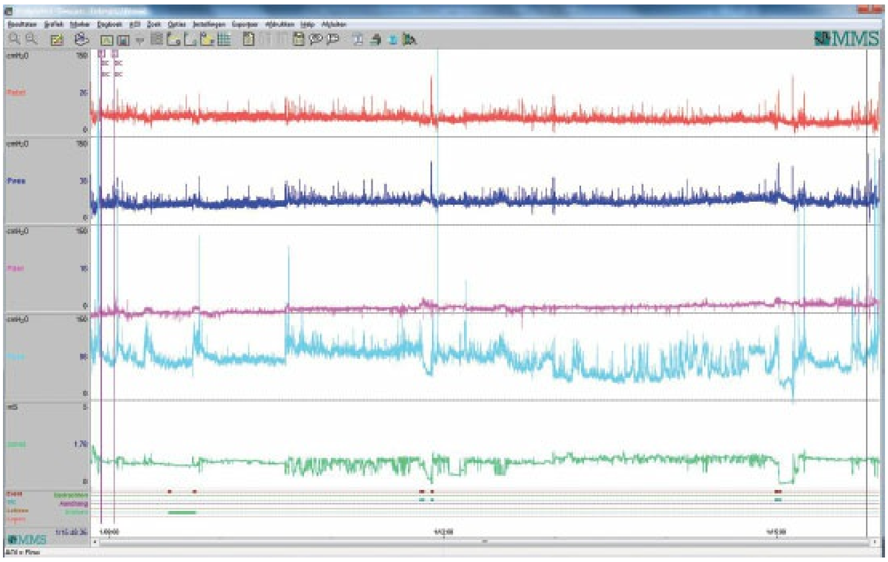


Figure 35.7 Ambulatory urodynamic trace overview in a 6 hour measurement.

Despite these developments and the reliability for reproducible results [36], a recent study of Martens et al. concluded there is no primary role for ambulatory urodynamics in SCI patients [17]. All included patients underwent conventional and ambulatory UDS, resulting in a larger number of patients diagnosed with DO after ambulatory UDS. However, there was no significant difference in bladder pressure measured during DO. According to the authors, the higher DO rate on ambulatory UDS was based on artifacts. Although conventional UDS might underdiagnose NDO, a good clinical assessment combined with video urodynamics is sufficient in making an accurate diagnosis of NDO in SCI patients [17,53].

AMBULATORY UDS AND VOIDING DYSFUNCTION

Voiding dysfunction can have different causes related to the bladder outlet or intrinsic bladder characteristics. Causality can vary from bladder outlet obstruction (in women, e.g., strictures or previous surgery) or dysfunctional voiding to detrusor underactivity or an acontractile bladder.

Detrusor underactivity is defined by the ICS as a contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or a failure to achieve complete bladder emptying within a normal time span [24]. Bladder acontractility is characterized by an inability to empty the bladder completely, without a visible contraction on cystometry. Clinically, these patients present with the inability to void to completion and/or with recurrent UTIs or urinary retention. Both detrusor underactivity and bladder acontractility can be caused by dysfunction at various levels in the CNS–bladder axis, from damage to the detrusor muscle or its autonomic nerve supply to dysfunction at spinal or brain level [54].

Bladder acontractility represents a heterogeneous urological entity, and the etiological variety forces us to search for different therapeutic approaches. A first step in this process is finding the most optimal diagnostic tool in diagnosing true bladder acontractility. Currently, there is only limited evidence relating ambulatory urodynamics and bladder acontractility. Van Koeveringe et al. [2] pointed out the value of ambulatory UDS in differentiating LUTS etiology. In a subgroup of 25 patients, suspected of having acontractility based on conventional UDS, bladder acontractility was confirmed in only 16% of the cases after ambulatory UDS. All other patients (21 out of 25) still had contractions present on during ambulatory UDS and therefore were not diagnosed with bladder acontractility [2]. This initial pilot study highlighted the potential of ambulatory UDS in diagnosing detrusor underactivity and bladder acontractility (Figure 35.8).

Current treatment options for restoring voiding effectiveness in patients with complete ambulatory UDS–confirmed bladder acontractility are limited. Bladder and sphincter reflex modulation techniques such as SNM can only be used if there is little or no damage to the CNS–bladder axis, in combination with intact function of the detrusor contractile apparatus. Therefore, in the right selection of patients (with at least some contractile function present on ambulatory UDS), this therapeutic option can be effective [55,56]. Moreover, a reconstructive surgical procedure such as latissimus dorsi detrusor myoplasty is only feasible in a highly selected group of patients with an acontractile bladder [57,58]. This means that the majority of patients are left with no other options than performing lifelong CISC [59].

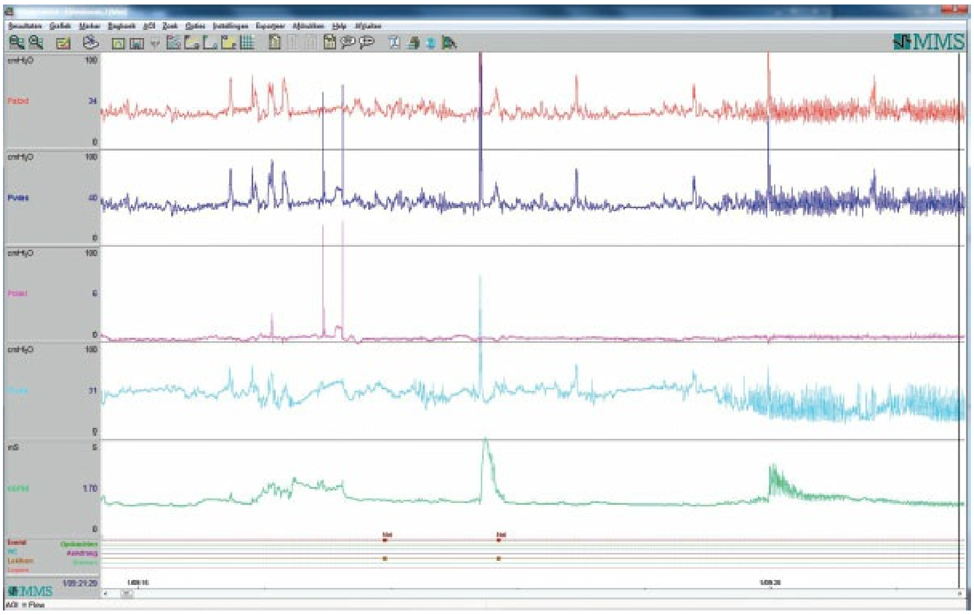


Figure 35.8 Ambulatory urodynamic trace indicating stress urinary incontinence by simultaneously steep peaking of the abdominal and vesical pressure with coinciding raised conductance and marker use. “DC” marker: detrusor contraction, indicating the start and end of a detrusor contraction (detrusor overactivity if during the filling phase). “Aandrang” marker: represents the urgency event. “WC” marker: indicating start and end of the toilet visit. “Nat” marker: indicating urinary loss objectified by the patient.

In order to increase the success rate of the invasive, limited, and more expensive therapeutic options such as sacral neuromodulation, there is a need for a valid diagnostic tool in patients with suspected bladder acontractility. Hence, ambulatory UDS is expected to gain a more prominent role in the diagnostic algorithm for detrusor underactivity and the differentiation of this entity from true bladder acontractility [60].

CONCLUSIONS

Ambulatory urodynamic monitoring is a valuable discriminating diagnostic tool in patients with various LUT complaints, particularly when conventional urodynamics fail to explain the symptoms. Ongoing research focuses on extending the application possibilities, particularly increasing attention to the role of ambulatory urodynamics in the assessment of bladder contractility or mixed urinary incontinence.

ACKNOWLEDGMENTS

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36 Basic Neurological Evaluation and Referral

David B. Vodušek and Jalesh N. Panicker

INTRODUCTION

Recordings of bioelectrical activity from muscles and the nervous system have been found clinically useful and named “clinical neurophysiology tests.” (Sometimes, tests other than electrophysiological investigations of nervous functions are listed as “neurophysiology,” but these other tests will not be described in this chapter.)

Clinical neurophysiology tests are many and are grouped together into subcategories according to different criteria. It is practical to distinguish recordings from muscle (electromyography) and tests of nerve and nervous pathway function (conduction studies). Typically, the different tests are referred to with disconcerting capital letter abbreviations, and even professionals close to the field have some difficulty in understanding the terminology and complex physiological and technical background of the methods, and distinguishing the different types of information provided by different tests. This chapter aims at clarifying these issues.

Recording Electrical Muscle Activity: Electromyography

Electromyography (EMG) is the extracellular recording of bioelectrical activity generated by muscle fibers. Modern EMG started with the introduction of the concentric needle electrode (CNE) in 1929 [1], the design of which has endured ever since, almost unchanged (Figure 36.1) [2]. Clinical EMG studies of the pelvic floor were sparse till the 1970s; since then, EMG has been used increasingly in urogynecology, neurourology, and proctology research. Nowadays, it is used as a routine diagnostic investigation.

EMG may be performed for two quite distinct, although complementary, purposes. On the one hand, it can reveal the “behavior” (i.e., patterns of activity) of a particular muscle; on the other hand, it can be used to demonstrate whether a muscle is normal, myopathic, or denervated/reinnervated. The former can be called “kinesiological EMG” and the latter “motor unit” EMG, but usually, this division is not specified and both types of examination are just called “EMG,” which can confuse the uninitiated. There are, of course, anatomical, physiological, and practical specificities of pelvic floor and perineal EMG, but the techniques are intrinsically the same for all striated muscles.

Testing Conduction across Nerves and Nervous Pathways

Conduction studies examine the capacity of a nerve (or nervous pathway) to transmit a test volley of depolarization elicited by a stimulus along its length. Tests have been as a rule introduced for limb nerves (and their central connections) and only later modified by workers in pelvic (uro-) neurophysiology [2].

Conduction along a nerve (or central nervous system pathway) depends on the anatomical integrity of the structure. In finer detail, the velocity of conduction depends on the thickness of constituent axons and their myelin sheath. All these may be altered by pathology and reflected as changes in either the latency of the recorded response (or velocity of conduction) or the amplitude (and configuration). It needs to be appreciated that “pure” conduction via nervous pathways is only measured where there is no synapse between the stimulated and the recorded sites (such as in stimulating a nerve and recording from the same nerve). The “conduction” across several synapses (as in recording a reflex response) is not only “longer” because of synapses but also variable (dependent on various additional factors, not only anatomical integrity and myelination).

Testing a nerve with a motor function, its responsiveness can be measured by the electrical stimulation of the nerve and recording the elicited muscle response (Figure 36.2). Both the time taken to muscle activation (latency) and the amplitude of the muscle response (known as the compound muscle action potential or “M” response) can be measured [2]. The latter depends on the number of intact individual motor fibers, whereas measures of motor latency (i.e., time to onset of response) and motor conduction velocity (CV) reflect the conduction speed of the fastest nerve fibers. For this reason, measures of latency are a poor guide to the integrity of innervation. The amplitude of the evoked muscle response gives a better guide, but because this measurement depends so heavily on the configuration of the electrodes employed, amplitude is not as valuable as might have been expected on a theoretical basis. Ideally, to measure compound muscle action potential amplitude, the reference electrode should be placed over the tendon and the active recording reference over the motor end plate (i.e., point of entry of nerve into muscle). For a strap-shaped muscle, this can be identified as midway along its anatomic length, but in more anatomically complex muscles such as those in the pelvis, the motor end plate region has not been identified and recording well-formed compound muscle action potentials is difficult.

The nerve roots carrying nerve fibers for particular muscles can be stimulated over the spinal column, thus testing the conduction over the whole length of the peripheral motor axons. The stimulation of the motor cortex area for particular muscle groups can be achieved from the scalp, thus testing the whole motor pathway (both central and peripheral). The muscle responses obtained by such stimulation are called motor evoked potentials (MEPs).

If the peripheral nerve being tested is accessible over sufficient length, so that stimulating and recording electrodes can be placed at some distance from each other (at least 10 cm is recommended to lessen stimulus artifact), it may be possible to record nerve activity directly. This response is called a “compound nerve action potential.” The amplitude of a compound nerve action potential is related to the number of nerve fibers being depolarized by the stimulating impulse and is a good measure of the number of active nerve fibers.

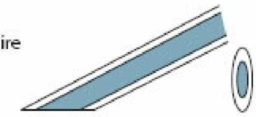
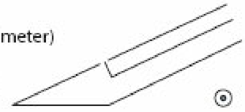
Needle recording electrode	Needle tip and recording surface	Pick-up	Needle diameter	Filter settings	Activity recorded
Concentric needle electrode: central insulated platinum wire inside a steel cannula		Hemisphere radius 0.5 mm	0.3–0.65 mm	5–10 kHz	Motor units
Single-fiber needle electrode: fine platinum wire (25 μm diameter) inside steel cannula which records from a side aperture		Hemisphere radius 250–300 μm	0.5–0.6 mm	500–10 kHz	Individual muscle fibers of motor units. In health the potentials are either singles or pairs: after reinnervation the potentials have multiple components

Figure 36.1 The concentric needle electrode and the single-fiber needle electrode, their physical characteristics, the filter settings required for use, and the nature of the activity that each records. (Modified from *Clinical Neurophysiology: EMG, Nerve Conduction and Evoked Potentials*, Vol. 1 (revised and enlarged edition), Fowler C and Tedman B, Electromyography: Normal and pathological findings. Copyright 2004, with permission from Elsevier.)

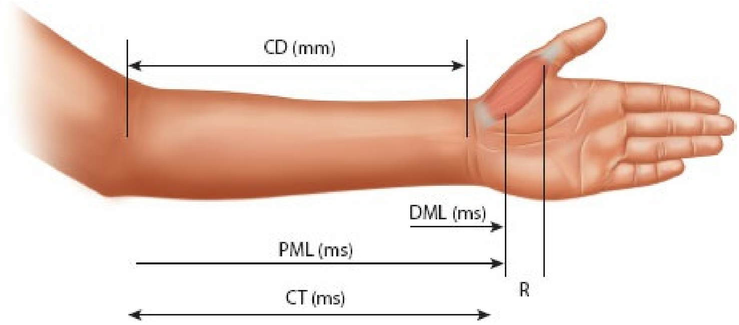


Figure 36.2 Measurements to be made in calculating motor conduction velocity (CV). (CD, conduction distance; CT, conduction time; DML, distal motor latency; PML, proximal motor latency; R, recording

electrodes. CV = CD/CT.)

If the stimulated nerve is purely sensory, as may be the case for some peripheral cutaneous branches, the compound nerve action potential is called the sensory neurogram (sensory nerve action potential). Such recordings are not routinely practical in the pelvis for anatomic reasons.

On stimulation of sensory nerves or the innervated skin or mucosa, an "electrical" response from the central nervous system (i.e., from the spinal cord and the brain) can be recorded. The recorded potentials are called somatosensory evoked potentials (SEPs).

On stimulation of sensory receptors in the skin or mucosa, or stimulation of sensory nerves, reflex responses are also elicited and can be recorded (for instance, the bulbocavernosus reflex). The commonly adopted technique is to apply a series of single electrical stimuli via surface electrodes to the dorsal clitoral nerve (above the clitoris) and record the consecutive reflex responses from the anal sphincter with a concentric needle EMG electrode.

Motor Unit

Knowledge of the structure and function of the motor unit is fundamental to understanding the application of EMG methods.

"Muscle electrical activity" is generated by depolarization of single muscle fibers (i.e., consisting of muscle fiber action potentials). But the innervation of muscle is such that a single muscle fiber does not contract on its own, but rather in concert with other muscle fibers that are part of the same motor unit, i.e., innervated by the same motor neuron.

Motor neurons that innervate striated muscle lie in the anterior horn of the spinal cord. Their cell bodies are relatively large and their axonal processes correspondingly of large diameter and myelinated to allow rapid conduction of impulses, although the neurons that innervate the sphincters are relatively smaller than those innervating the skeletal limb and trunk muscles. Within the muscle, the motor axon tapers and then branches to innervate muscle fibers that are scattered throughout the muscle (Figure 36.3). The innervation of muscle is such that it is unlikely that fibers that are part of the same motor unit will be adjacent to one another. The number of muscle fibers innervated by an axon is known as the "innervation ratio." There is no simple neurophysiological method for estimating this parameter, and the number of motor units per muscle is also difficult to estimate by clinical neurophysiological means.

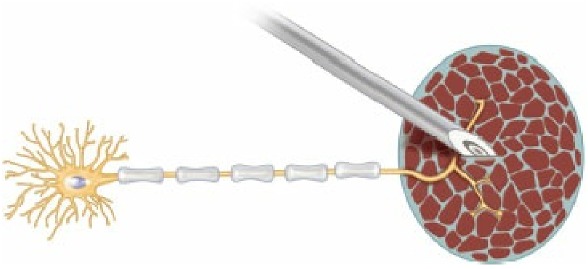


Figure 36.3 Diagram of a motor unit showing the motor neuron that is located in the anterior horn of the spinal cord, Onuf's nucleus in the case of the sphincters, and the motor axon that travels in the peripheral nerve to the muscle. Here, it divides, innervating a number of muscle fibers, most of which are not adjacent. (Modified from *Clinical Neurophysiology: EMG, Nerve Conduction and Evoked Potentials*, Vol. 1 (revised and enlarged edition), Fowler C and Tedman B, Electromyography: Normal and pathological findings. Copyright 2004, with permission from Elsevier.)

The contraction properties of a motor unit depend on the nature of its constituent muscle fibers. Muscle fibers can be classified according to their twitch tension, speed of contraction, and histochemical staining properties. The fatigue-resistant type 1 fibers constitute motor units that fire for prolonged periods of time at lower firing frequencies, i.e., "tonically" (see in the succeeding text). Type 2 fibers make up motor units that fire briefly and rapidly in bursts, i.e., "phasically." Unfortunately, there is no clinical electrophysiological method that can estimate the proportion of motor units of different muscle fiber types. In the pelvic floor and sphincters, the majority of muscle fibers are type 1 (with some regional variation).

ELECTROMYOGRAPHIC METHODS

Kinesiological EMG

Method

By prolonged recording of bioelectrical activity of a muscle, a qualitative and quantitative description of its activity over time is obtained. Such techniques are used in rehabilitation and sports medicine to study movement. Meaningful kinesiological EMG can, of course, only be performed from an innervated muscle. If the lower motor neuron integrity of a particular muscle is questioned, "motor unit" EMG analysis (see succeeding text) has to be performed first.

The choice of muscle for EMG examination depends on the aims of the investigation. Routine EMG as part of urodynamic testing usually employs a single channel for recording from the urethral or anal sphincter muscle. The sphincters being small circular muscles, it is assumed that the two sides react in a similar fashion, although this may not always be the case, as was shown for the levator ani [3].

When we are interested in the pattern of activity of an individual muscle, the technique should ideally provide a selective recording, uncontaminated by neighboring muscles on one hand and a faithful detection of any activity within the source muscle on the other hand. Unfortunately, both objectives are difficult to achieve simultaneously and the purpose of the investigation will suggest an acceptable compromise. Overall detection from the bulk of a muscle can only be achieved with nonselective electrodes; selective recordings from small muscles can only be made with intramuscular electrodes with small detection surfaces. Nonselective recordings carry the risk of contamination with activity from other muscles; selective recordings may fail to detect activity in all parts of the source muscle. Meaningful recordings from deep muscles can only be accomplished by invasive techniques.

Considering the aforementioned, truly selective recording from sphincter muscles can probably only be obtained by intramuscular electrodes; in clinical routine, often, the CNE is used. This electrode has the advantage of being widely available, easy to introduce, and adjustable in position and has a standardized active surface. It is, however, painful to have inserted and subsequent movement of the source muscle can be uncomfortable and the needle then easily dislodged. Instead, two thin isolated/bare tip wires (with a hook at the end) can be introduced into the muscle with a cannula; the latter is then withdrawn, and the wires stay in place. The advantage of this type of recording is good positional stability and painlessness once the wires are inserted, although their position cannot be much adjusted.

To make EMG recording less invasive, various types of surface electrode have been devised; also, there are alternatives for intravaginal placement [4], anal plug electrodes, and catheter-mounted ring electrodes [5] to record from the urethral sphincter (Figure 36.4).

Recordings with surface electrodes are more artifact prone and, furthermore, the artifacts may be less easily identified. Critical online assessment of the "quality of the EMG signal" is mandatory in kinesiological EMG, and this requires either auditory or oscilloscope monitoring of the raw signal. Integration of high-quality EMG signals may help in quantification of results, as can automatic analysis of the interference pattern [6].

Findings in Normal and Abnormal Conditions

The normal kinesiological sphincter EMG shows some continuous activity at rest (which may be increased voluntarily or reflexly) (Figure 36.5); such activity could be recorded for up to 2 hours and even after a subject has fallen asleep during the examination [7]. This physiological spontaneous activity may be called "tonic." It consists of prolonged firing of tonic motor units, not rapidly interchanging activation and inactivation of different motor units [7].

The "amount" of recorded activity depends on the uptake area of the electrode (Figure 36.1). Using a CNE, activity from 1 to 5 motor units is usually recorded per detection site in the anal sphincter at rest. "Tonic" activity is encountered in many but not all detection sites of the levator ani muscle [8]. Typically, it consists of low-amplitude motor unit potentials (MUPs) that fire fairly regularly at low frequencies. In a study of 39 such motor units from the anal sphincter in 17 subjects (inclusion criterion was rhythmic spontaneous firing for 2 minutes before onset of measurement), the range of discharge rates was found to be 2.5–9.4 Hz. Any reflex or voluntary activation procedure is mirrored first by an increase in the firing frequency of the motor units; then, with any stronger activation or increase in abdominal pressure, the new so-called phasic motor units are recruited (Figure 36.5). These are usually of higher amplitude and their discharge rates are higher and irregular. A small percentage of motor units with an “intermediate” activation pattern can also be encountered. Both the urethral and anal sphincters show short-lasting voluntary activation times (typically below 1 minute), which is also the case for pubococcygeus muscles [8].

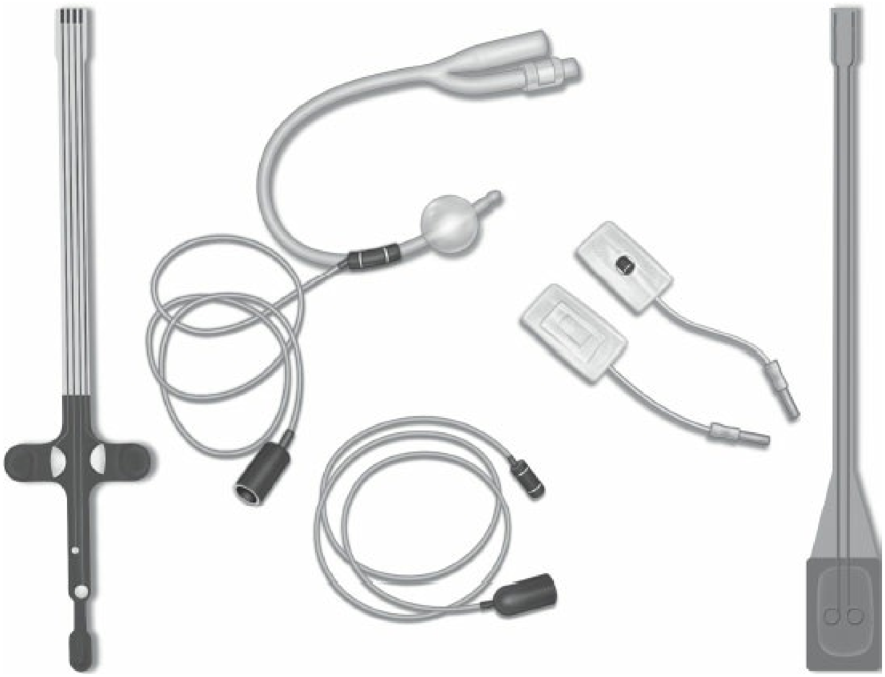


Figure 36.4 Electrodes used to record sphincter activity. (Reproduced from *Clinical Neurophysiology: EMG, Nerve Conduction and Evoked Potentials*, Vol. 1 (revised and enlarged edition), Fowler C and Tedman B, Electromyography: Normal and pathological findings. Copyright 2004, with permission from Elsevier.)

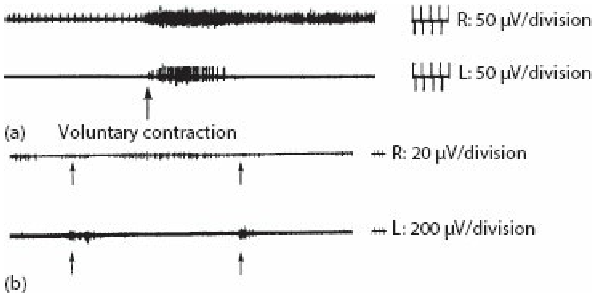


Figure 36.5 Kinesiological EMG recordings from the pubococcygeus muscles (recording with intramuscular wires: right, upper traces; left, lower traces). (a) Recordings from a 33-year-old nulliparous woman. Continuous firing of motor unit potentials is seen on the right with a gradual recruitment on voluntary contraction. On the left, no ongoing activity is present. Symmetrical recruitment on voluntary contraction is present. (b) Recordings from a 52-year-old stress urinary incontinent woman. Some ongoing muscle activity can be seen in both pubococcygeal muscles. On voluntary contraction, recruitment can only be seen on the left. On the right, there is actually a decrease in firing of motor units on “voluntary contraction.”

On voiding, all EMG activity in the urethral sphincter ceases prior to a detrusor contraction. Coordinated detrusor/sphincter activity is lost with lesions between the lower sacral segments and the upper pons (the pontine micturition center); detrusor contractions are then accompanied by an increase in sphincter EMG activity [9]. This pattern of activity is called “detrusor sphincter dyssynergia.” On the basis of the temporal relationship between urethral sphincter and detrusor contractions, three types of dyssynergia have been described [10]. This neurogenic uncoordinated sphincter behavior has to be differentiated from “voluntary” contractions that may occur in the so-called nonneuropathic voiding disorders that may be a learned abnormality of behavior [15] and may be encountered in women with dysfunctional voiding [11].

Failure of relaxation of urethral sphincter contraction during detrusor contractions has also been reported in patients with Parkinson's disease [12]. The normal physiological behavior of the striated anal sphincter is characterized by its relaxation with defecation [13]; a paradoxical sphincter activation during defecation has been described in Parkinson's disease, the so-called anismus [1].

The pubococcygeus in the healthy female reveals patterns of activity similar to those found in the urethral and anal sphincters at most detection sites, i.e., continuous activity at rest, some increase in activity during bladder filling, and a reflex increase in activity during any activation maneuver such as talking, deep breathing, and coughing. It relaxes during voiding, and in health, the muscles on both sides act in concert [8]. Timely activation of the levator ani muscle has been demonstrated to be an important aspect of stable bladder neck support; its activation precedes activity of other muscles in the cough reflex [14]. In stress-incontinent women, the physiological patterns of activation, as well as the coordination between the two sides, may be lost [3] (Figure 36.5). A delay in muscle activation on coughing has also been demonstrated, as compared to continent women [15].

Little is known about the normal complexity of activity patterns of different pelvic floor muscles (i.e., urethral sphincter, urethrovaginal sphincter, anal sphincter muscle, different parts of the levator ani), but it is generally assumed that they act as one, in a coordinated fashion. Differences have, however, been demonstrated even between the intra- and periurethral sphincter [16]. Coordinated behavior is often lost in disease states, as has been shown, for example, for the levator ani and the urethral and anal sphincters [17]. Disturbances of pelvic floor muscles activity have been modified by using the kinesiological EMG recording as a biofeedback signal [18].

Diagnostic Usefulness of Kinesiological EMG

The demonstration of voluntary and reflex activation of pelvic floor muscles is indirect proof of the integrity of respective neural pathways. Kinesiological EMG recordings of sphincter muscles, either urethral or anal, are obtained in selected patients in urodynamic laboratories to ascertain sphincter behavior during bladder filling and voiding. Such simultaneous studies of detrusor and sphincter activity are, as a rule, obtained only in patients with suspected detrusor–sphincter dyssynergia. External anal sphincter EMG is recorded in some laboratories in the assessment of anorectal dysfunction [13].

Other than the polygraphic urodynamic recordings to diagnose detrusor–sphincter dyssynergia, the diagnostic contribution of kinesiological EMG is yet to be established and is now rarely recorded for several reasons. It is often technically difficult to obtain a good quality EMG signal from a site that is as inaccessible as the urethral sphincter. The best signal is obtained using a needle electrode, but the discomfort from the needle itself is likely to impair normal relaxation of pelvic floor muscles including the urethral sphincter. The alternative of surface recording electrodes has been used, but they record activity from other muscles as well, which makes interpretation of the results difficult. With the advent of video-urodynamics, which permits multichannel cystometry and pressure/flow studies of voiding with synchronous fluoroscopic screening, much of this information about the outflow tract is obtained from a less-invasive investigation.

EMG Methods to Differentiate Normal from Pathological Muscle

Needle EMG may help to differentiate between normal, denervated, reinnervated, and myopathic muscle. Such EMG has also been called "motor unit" EMG to distinguish it from "kinesiological" EMG.

The needle electrode needs to be placed appropriately in the target muscle. The levator ani muscle can be located by transrectal or transvaginal palpation and reached transcutaneously. The anal sphincter is easily located. The urethral sphincter is anatomically separate from the pelvic floor musculature and can be approached either perineally with a needle insertion 0.5 cm laterally to the urethral orifice (the authors suggest one single skin insertion per side) or it can be reached transvaginally using a Sims speculum to retract the posterior vaginal wall. The latter approach has been estimated as less uncomfortable [19], but is not used by many. The position of the needle should be adjusted in a systematic way so that the same muscle area is not repeatedly sampled.

The needle electrode most commonly used in diagnostic EMG is the single-use disposable CNE; it consists of a central insulated platinum wire encased within a steel cannula and the tip ground to give an elliptical area of 580–150 μm (Figure 36.1). This type of electrode has the recording characteristics necessary to record spike or near activity from about 20 muscle fibers. The number of motor units recorded therefore depends both upon the local arrangement of muscle fibers within the motor unit and the level of contraction of the muscle [2].

The other EMG technique (using a different needle electrode) to differentiate between normal and neuropathic muscle is single-fiber EMG (SFEMG). This method has often been used in research, particularly by British authors, but is not routinely applied in diagnostics.

Recently, surface EMG recording using noninvasive electrode arrays and multichannel EMG amplifiers was introduced to the EAS and puborectalis. Although observations in normal and pathological conditions have been published [20], the clinical value of this method in diagnosing neurogenic sacral disorders has not yet been demonstrated.

Normal Findings in Concentric Needle EMG Electrode

CNE EMG can provide information on insertion activity, abnormal spontaneous activity, MUPs, and interference pattern [2].

In healthy skeletal muscle, initial placement of the needle elicits a short burst of “insertion activity” that is due to mechanical stimulation of excitable membranes. This phenomenon may also be seen in the sphincters; however, because of the reflex, pain-induced burst of motor units that occurs, insertion activity may be difficult to discern. Insertion activity is recorded at a sensitivity setting of 50 μV/division, which is also the gain used to record spontaneous activity. The absence of insertion activity with an appropriately placed needle electrode usually indicates a complete denervation atrophy of the examined muscle.

There are two distinct patterns of electrical activity reported in the sphincter muscle. One is the tonic discharge observed at rest characterized by regular firing of MUPs. The degree of tonic discharge from the sphincter muscles varies in each individual and with posture. During sleep, this continuous firing diminishes but never disappears. The number of continuously active MUPs during relaxation can be estimated by counting the number of continuously firing low-threshold MUPs. In partially denervated sphincter muscle, there is—by definition—a loss of motor units (MUs). In patients with cauda equina or conus medullaris lesions, for instance, fewer MUPs fire continuously during relaxation, probably due to partial axonal loss.

The other is the phasic bursts of MUPs that may occur reflexly and evoked by various stimuli such as eliciting the anal reflex and by voluntary efforts such as coughing. Thus, in addition to continuously firing low-threshold motor units, new (high-threshold) MUPs are recruited (voluntarily or reflexly). Normally, MUPs should intermingle to produce an “interference” pattern on the oscilloscope during voluntary muscle contraction and during a strong cough.

It has been shown that the two MUP populations (the “tonic” and the “phasic”) differ in their characteristics, reflexly or voluntarily activated high-threshold MUPs being larger than continuously active “low-threshold MUPs.” As a consequence, a standardized level of activity at which a template-based multi-MUP analysis obtains between three and five MUPs on a single muscle site was suggested [21]. The main obstacle to qualified assessment of a reduced number of activated MUs, and activation of MUs at increased firing rates (as occurs in limb muscles), is a lack of concomitant measurement of the level of contraction of the examined muscle (this can be readily assessed when studying limb muscles).

MUPs should be analyzed at a sensitivity setting that allows their full display. The commonly used time scale is 5 or 10 ms/division, with an amplitude gain of 50–500 μV/division (Figure 36.6). The commonly used amplifier filter settings for concentric needle EMG (CN EMG) are 10–10,000 Hz. The amplitude of a MUP is largely determined by the activity of those muscle fibers closest to the recording electrode. Other fibers within a 0.5 mm radius of the recording electrode contribute little to the amplitude, but in a normal motor unit, there are unlikely to be more than two or three fibers belonging to the same motor unit. Amplitude is highly sensitive to needle position and very minor adjustments of the electrode will result in major changes, i.e., a change in position by 0.5 mm alters the amplitude 10- to 100-fold [2].

The duration of a motor unit is the time between the first deflection and the point when the waveform finally returns to the baseline. This will depend on the number of muscle fibers within the motor unit and is little affected by the proximity of the recording electrode to the nearest fiber. The difficulty with this measurement is defining the exact point of return to the baseline. The phases of a MUP are defined by the number of times the potential crosses the baseline. A unit that has four phases or more is said to be polyphasic. A related parameter is a "turn," which is defined as a shift in direction of a potential of greater than a specified amplitude.

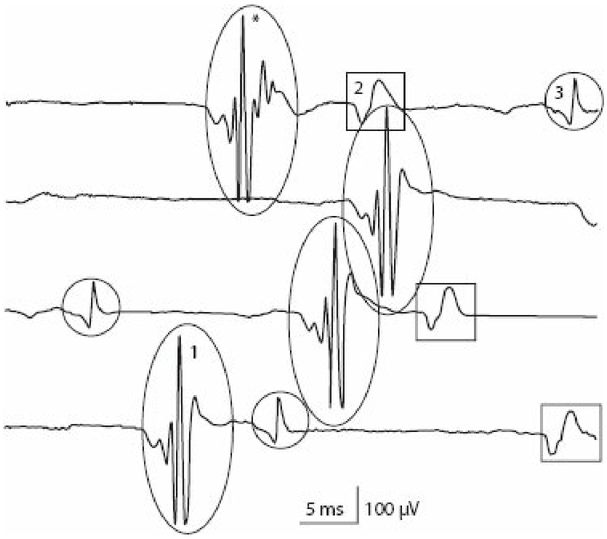


Figure 36.6 Concentric needle EMG recording of motor unit potentials from the urethral sphincter of a 35-year-old stress incontinent female, several years after second vaginal delivery. At this detection site, three motor unit potentials are firing continuously and can be analyzed. It can be seen that the motor unit potential (MUP) with the asterisk is different from the others of similar overall shape. Further analysis of such a signal is needed to ascertain whether it is a superimposition of two individual MUPs or an instability within a complex of MUPs. The use of trigger and delay facility is advantageous to solve such questions.

Using the standard recording facilities available on all modern EMG machines, individual MUPs can be captured and their amplitude and duration measured. To allow identification of MUPs and to be certain the late components of complex potentials are not due to superimposition of several MUPs, it is necessary to capture the same potential repeatedly (Figure 36.7). MUPs are mostly below 1 mV in the normal urethral sphincter and below 2 mV in the normal anal sphincter. Most are less than 7 ms, and few (less than 15%) are above 10 ms in duration. Additionally, most are bi- and triphasic, but up to 15%–33% may be polyphasic. Normal MUPs are stable—their shape on repetitive recording does not change [16,22].

There are two approaches to analyzing the bioelectrical activity of motor units quantitatively: either individual MUPs are analyzed or the overall activity of intermingled MUPs (the "interference pattern," or IP) is analyzed. Generally, three techniques of MUP analysis ("manual-MUP," "single-MUP," and "multi-MUP") and one technique of IP analysis (turn/amplitude, or T/A) are available on advanced EMG systems. By either method, a relevant sample of EMG activity needs to be analyzed for the test to be valid. In the small half of the sphincter muscle collecting 10 different MUPs has been accepted as the minimal requirement for using single-MUP analysis.

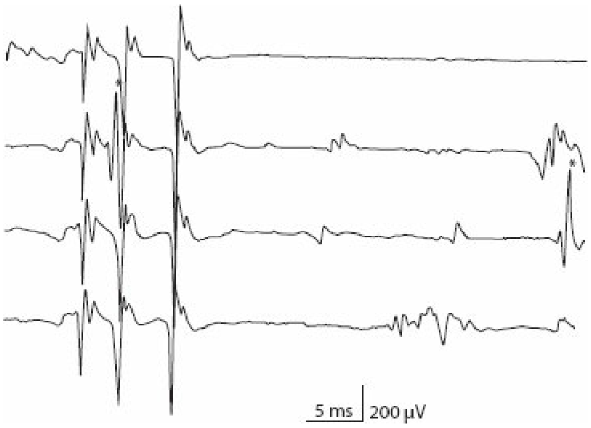


Figure 36.7 A concentric needle EMG recording from the urethral sphincter of an 18-year-old nulliparous female 4 years after a partial cauda equina injury. A trigger and delay facility is used. A complex motor unit potential (MUP) with prolonged duration is shown. Superimposition of another individual MUP (asterisk) may be falsely interpreted as instability of the potential.

Using manual-MUP and multi-MUP techniques, sampling of 20 MUPs (standard number in limb muscles) from each external anal sphincter (EAS) presents no difficulty in healthy controls and most patients. Normative data obtained from the EAS muscle by standardized EMG technique using all three MUP analysis techniques (manual-MUP, single-MUP, multi-MUP) have been published [23,24]. The technical differences in the methods are many and no in-depth description is attempted here. The more technical issues of quantitative EMG, the relevance and usefulness of various parameters, etc., are discussed in neurophysiological sources.

MUPs are identified either using a trigger and delay line (“single-MUP”) or appearing repeatedly in a prolonged recording of EMG activity (“manual-MUP”). Both approaches favor identification of relatively larger MUPs and become less reliable on stronger activation of muscle. Both methods are relatively slow and subject to examiner bias. The template-based multi-MUP analysis and the T/A analysis of IP (both run by automated computer analysis) are fast (5–10 and 2–3 minutes/muscle, respectively) and easy to apply and allow little opportunity for examiner bias [24]. Use of quantitative MUP and IP analyses of the EAS is facilitated by the availability of normative values that can be introduced into the EMG system’s software. It has been shown that normative data are not significantly affected by age, gender, number of uncomplicated vaginal deliveries, mild chronic constipation, and the part of the EAS muscle (i.e., subcutaneous or deeper) examined [25–27]. This makes quantitative analysis much simpler and results from different laboratories easily comparable.

The main drawback of the multi-MUP method is its tendency to chop up long polyphasic MUPs (such as occur in anal sphincter of MSA patients) into “components,” thus “missing” these highly abnormal MUPS. If the electromyographer checks the native EMG and observes such MUPs, the “collected MUPs” should be carefully scrutinized, and possibly, a “manual-MUP” analysis performed for a quality check.

Similar in-depth analyzed normative data from standardized techniques for other pelvic floor and perineal muscles are not yet available, but individual laboratories use their own normative data.

Single-Fiber Electromyography

SFEMG is used in general clinical neurophysiological laboratories to diagnose disturbed neuromuscular transmission (as in myasthenia gravis). The original recording needles are specially constructed (with a small recording area oriented “sideways” on the thin cannula; Figure 36.1) and very expensive and disposable versions are not available. An adapted method using disposable CNEs is being used in many laboratories as it is becoming unacceptable not to use disposable needles. When recording SFEMG, the amplifier filters are set so that low-frequency activity is eliminated (500 Hz to 10 kHz). Thus, the contribution of each muscle fiber appears as a biphasic positive–negative action potential.

In the past, SFEMG has been used to record not only the neuromuscular “jitter” (a measure of neuromuscular transmission) but also “fiber density” (FD), which is the mean number of muscle fibers belonging to an individual motor unit per detection site (a parameter that reflects motor unit morphology). To measure FD, recordings from 20 different detection sites are necessary (Figure 36.8) and the number of component potentials to each motor unit is recorded and averaged. The normal fiber density for the anal sphincter is below 2.0 [28,29]. Small changes with age have been reported; women have significantly greater fiber density than men [28].

Due to its technical characteristics, a SFEMG electrode is able to record even small changes that occur in motor units due to reinnervation, but is less suitable to detect changes due to denervation itself, i.e., abnormal insertion and spontaneous activity. SFEMG has indeed never been used in "routine uro-neurophysiological diagnostics," only in research.

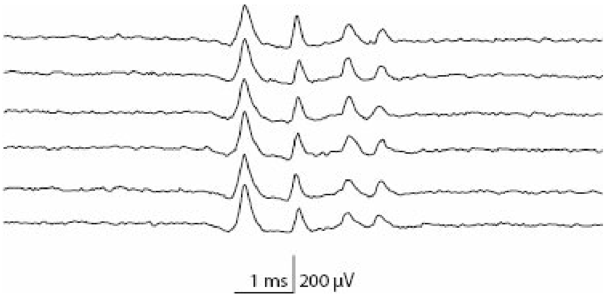


Figure 36.8 Single-fiber EMG recording from the anal sphincter of a 51-year-old nulliparous female with an extrapyramidal syndrome and recent development of poor bladder emptying accompanied by stress incontinence. The fiber density in the anal sphincter was found to be 3.7 and a diagnosis of possible multiple system atrophy was suggested. Further development of the clinical picture supported the diagnosis.

EMG Findings due to Denervation and Reinnervation

After complete denervation, all motor unit activity ceases and there may be electrical silence for several days. Between 10 and 20 days after a denervating injury, "insertion activity" becomes more prolonged and abnormal spontaneous activity in the form of short biphasic spikes ("fibrillation potentials") and biphasic potentials with prominent positive deflections ("positive sharp waves") appear [38]. In perineal muscles, complete denervation can be observed after traumatic lesions to the lumbosacral spine and damage to the cauda equina. Most lesions will, however, cause only partial denervation. In partially denervated muscle, some MUPs remain and mingle eventually with abnormal spontaneous activity. As the MUPs in sphincter muscles are also short and mostly bi- or triphasic, it requires considerable EMG experience to recognize abnormal spontaneous activity in the presence of surviving motor units. In long-standing partially denervated muscle, a peculiar abnormal insertion activity appears, the so-called repetitive discharges. These are made up of repetitively firing groups of potentials with so little jitter between the potentials that it is assumed the activity must be due to ephaptic or direct transmission of impulses between muscle fibers [30]. However, this activity may be found in the striated muscle of the urethral sphincter without any other evidence of neuromuscular disease and it has been hypothesized that it causes impaired relaxation of the muscle when spontaneous and profuse [31].

Abnormal spontaneous activity has also been described as a marker for degeneration of Onuf's nucleus occurring in patients with multiple system atrophy (MSA) [32].

After complete denervation, axonal reinnervation may occur and MUPs appear again, first short bi- and triphasic, soon becoming polyphasic, serrated, and of prolonged duration.

In partially denervated muscle, there is a certain loss of the number of motor units; some MUPs remain; however, the amount is difficult to estimate as the amount of motor unit activity recorded depends on needle position and voluntary activation. In partially denervated muscle, collateral reinnervation takes place; surviving motor axons will sprout and grow out to reinnervate those muscle fibers that have lost their nerve supply, resulting in a change in the arrangement of muscle fibers within the unit. Whereas in healthy muscle, it is unusual for two adjacent muscle fibers to be part of the same motor unit, following reinnervation several muscle fibers all belonging to the same motor unit come to be adjacent to one another. Early in the process of reinnervation, the newly outgrown motor sprouts are thin and therefore conduct slowly so that the time taken for excitatory impulses to spread through the axonal tree is abnormally prolonged. This is reflected by prolongation of the waveform of the MUP that may have small, late components (Figure 36.7). Neuromuscular transmission in these newly grown sprouts may also be insecure so that the motor unit may show “instability.” In skeletal muscle, with time and provided there is no further deterioration in innervation, the reinnervating axonal sprouts increase in diameter and thus increase their CV so that activation of all parts of the reinnervated motor unit become more synchronous. This has the effect of increasing the amplitude and reducing toward normal the duration of the MUPs measured with a CNE. This phenomenon may be different in the sphincter muscles where long duration motor units seem to remain a prominent feature of reinnervated motor units [33]. There are several conditions in which gross changes of reinnervation may be detected in motor units of the pelvic floor.

Sphincter EMG in the Evaluation of Suspected Cauda Equina Lesions

Injury to the cauda equina most commonly occurs following trauma, disc prolapse, and tumors. Sacral root damage results in pelvic floor dysfunction and patients present with lower urinary tract dysfunction (LUTD) and often sexual and bowel dysfunction as well. Concentric needle EMG of the external anal sphincter, innervated by the sacral 2, 3, and 4 roots, often demonstrates changes of chronic reinnervation, with a reduced interference pattern and enlarged polyphasic motor units (>1 mV amplitude), and is characteristic of long-standing cauda equina syndrome [34,35]. Though EMG may demonstrate pathological spontaneous activity 3 weeks or more after injury, these changes of moderate to severe partial denervation or complete denervation often become lost in the tonically firing motor units of the sphincter, and rather, an EMG of the bulbocavernosus muscle might detect these changes.

Sphincter EMG in the Diagnosis of Multiple System Atrophy

MSA, a variant of Parkinson’s disease, is a progressive neurodegenerative disease, which often, particularly in its early stages, is mistaken for Parkinson’s disease but is poorly responsive to antiparkinsonian treatment. Autonomic failure causing postural hypotension and cerebellar ataxia causing unsteadiness and clumsiness may be additional features. Urinary incontinence in both women and men occurs early in this condition, often appearing some years before the onset of obvious neurological features, and not uncommonly, patients may present to the urologist [36]. As part of the neurodegenerative process, selective loss of anterior horn cells occurs in Onuf’s nucleus so that partial but progressive denervation of the sphincter occurs and recorded motor units show changes of reinnervation, becoming markedly prolonged. Sphincter EMG has been demonstrated to be of value in distinguishing between idiopathic Parkinson’s disease and MSA [33,37]. The anal sphincter is once again most often studied and changes of chronic reinnervation in MSA tend to result in prolonged duration motor units and these changes can be detected easily [38].

The value of sphincter EMG in the differential diagnosis of Parkinsonism has been widely debated over the years. Technically, the MUPs recorded in MSA are quite prolonged and adopting a multi-MUP method results in a tendency to chop up these long polyphasic MUPs into individual components. Thereby, the late components might be missed when measuring the motor unit duration and the duration of the MUP may be erroneously noted as being normal. It is preferable therefore to identify MUPs manually when performing the EMG for a patient with suspected MSA to avoid this pitfall. Moreover, the changes are not specific to MSA and similar changes of chronic reinnervation may be found in long-standing Parkinson’s disease, other parkinsonian syndromes such as progressive supranuclear palsy [39] and dementia with Lewy bodies, and other neurodegenerative conditions such as spinocerebellar ataxia type 3, following obstetric injury with sphincter damage and cauda equina damage. Nevertheless, a body of opinion exists that maintains that a highly abnormal result in a patient with mild Parkinsonism is of value in establishing a diagnosis of probable MSA [40]. A highly abnormal EMG in the absence of other obvious causes in a patient with suspected MSA in first 5 years is significant [41].

EMG Changes after Vaginal Delivery: EMG in Idiopathic Incontinence

Electrophysiological methods have played a major role in establishing the neuromuscular lesion due to vaginal delivery as a risk factor for incontinence and pelvic organ prolapse (in addition to histopathological findings) [42]. Studies using computer-assisted quantified and less operator-biased techniques have confirmed older findings [43,44] of at least subtle neurogenic pelvic floor muscle changes in parous women [25,45].

It is a common experience that EMG changes are more pronounced in the urethral sphincter and in women with complicated vaginal deliveries. The finding of decreased intramuscular nerve density in the female urethral sphincter, which correlates with decreased muscular tissue, provides validation for the reported EMG abnormalities [46]. The abnormalities demonstrated in external anal sphincter and pudendal nerves have been suggested to be of pathogenetic significance and also for idiopathic fecal incontinence [47]. The development of imaging techniques has improved the diagnosis of postpartum structural (anatomical) damage to pelvic floor structures (including sphincters), which has put the importance of the postpartum neurogenic electrophysiological changes in perspective, which, when minor, may have little functional consequences.

The neurogenic damage caused by vaginal delivery is acknowledged to be, to a large extent, repaired by regenerative processes, but may then recur in the long run [47]. Repetitive straining at stool due to constipation has been the main implicated pathogenetic mechanism for such chronic progression of the neuromuscular lesion. Indeed, prolongation of pudendal nerve terminal latency has been demonstrated after 1 minute of hard straining [48]. Cumulative damage to the pudendal nerve may occur in severe chronic constipation; our study in patients with mild chronic constipation failed, however, to reveal any neurogenic anal sphincter changes, as compared to nonconstipated controls [27].

On the other hand, myogenic changes in pelvic floor muscles after vaginal delivery were also reported [49].

The usefulness of EMG in individual patients with idiopathic incontinence is limited as its predictive value for treatment outcome has not been established. In routine diagnostics, CN EMG of pelvic floor muscles in women after vaginal delivery and/or with undefined urinary incontinence should be restricted to the rare cases in whom a substantial pudendal nerve or sacral plexus involvement is suspected [50].

EMG Changes in Women with Urinary Retention and Obstructed Voiding

For many years, it was said that isolated urinary retention in young women was due to psychogenic factors or was the first symptom of onset of multiple sclerosis. However, CN EMG in this group has demonstrated that many such patients have profuse complex repetitive discharges (CRDs) and decelerating burst (DB) activity in the urethral sphincter muscle [51]. The CRDs have a very characteristic sound quality over the loudspeaker on the EMG machine, similar to a helicopter or motorcycle engine. It is the DBs that produce the myotonic-like sound, which has been likened to underwater recordings of whales. The jitter between the CRD potentials is very small [30].

It was proposed that this pathological spontaneous activity leads to sphincter contraction, which endures during micturition and causes obstruction to flow. Positive proof of this has been demonstrated by combined CN EMG and kinesiological EMG analysis of a group of females with dysfunctional voiding [11].

The syndrome described by Clare Fowler is associated with polycystic ovaries (Fowler's syndrome) [51]. There may be some (as yet unidentified) hormonal susceptibility of the female striated urethral sphincter, which causes a loss of stability of the muscle membrane and permits ephaptic transmission to develop, manifest as CRDs. Sustained contraction of the urethral sphincter has an inhibitory effect on bladder afferents and efferents, resulting in loss of bladder sensation and urinary retention.

Although urethral sphincter EMG may indicate the presence of an abnormality, it is inevitably only a sample and it is difficult to know whether the abnormality is sufficient to account for the clinical finding of complete or partial urinary retention. The investigations that have proved to be useful as adjuncts to the EMG are measurement of the urethral pressure profile (UPP) and volume of the sphincter muscle estimated with ultrasound [52]. Young women with urinary retention due to the sphincter abnormality regularly have UPPs in excess of 100 cm H_2O.

The typical clinical presentation of this syndrome is of a young woman with either spontaneous onset of urinary retention or retention following some sort of operative intervention. The mean age of a series of women with this problem was 27 years; spontaneous onset appears to be more common in women under 30 [52]. Characteristically, the women present with a bladder capacity in excess of 1 L, and, although this may cause painful distension, they lack any expected sensations of urinary urgency. There may or may not be a history of infrequent voiding prior to the onset of urinary retention. These women are taught to do clean intermittent self-catheterization and commonly experience difficulties with this technique, in particular pain and difficulty in removing the catheter. Patients with Fowler's syndrome respond well to sacral neuromodulation [53]. The stimulation does not, however, cause a cessation of the abnormal EMG activity [54].

A strong association with opiates and the onset of urinary retention is something that has become apparent recently, and an important observation was that of all the women, tests showed that one third did have FS, but a quarter of the women with Fowler's syndrome were taking opiate medications [55]. A recent hypothesis is that the abnormal sphincter EMG activity (cause remains unknown) probably causes neurotransmitter changes in the spinal cord, which are brought about by the effect of naturally occurring opiates, and that Fowler's syndrome is the result of spinal cord intoxication by the body's endorphins or enkephalins.

Because CN EMG will detect changes of both denervation and reinnervation as occur with a cauda equina lesion, as well as abnormal spontaneous activity, it has been argued that this test is mandatory in women with urinary retention [56]. It should certainly be carried out before stigmatizing a woman as having "psychogenic urinary retention."

EMG Changes in Primary Muscle Disease

CN EMG changes reflect pathological changes in the structure of the motor unit but also changes due to disease of the muscle fibers. With degeneration of muscle fibers, the motor units loose them; the number of motor units, however, may not change. The "typical" CN EMG features of myopathy of skeletal muscle are abundant small, low-amplitude polyphasic units recruited at mild effort. Such changes have not been reported in the pelvic floor, even in patients known to have generalized myopathy [57]. Pelvic floor muscle involvement in limb-girdle muscular dystrophy in a nulliparous female has been reported, but concentric needle EMG of her urethral sphincter was reported as normal [58]. Myopathic changes were observed in the puborectalis and the EAS in patients with myotonic dystrophy.

Little is currently known about what might be expected of an EMG recording from traumatized muscle that has been subject to a severe stretch injury—as occurs during childbirth—but there may well be changes reflecting rupture of individual muscle fibers and injury to small intramuscular nerves.

Diagnostic Usefulness of EMG Methods

Both CN EMG and SFEMG have been employed in neurourological, urogynecological, and proctological research. In routine diagnostics, using CN EMG, an experienced examiner can quickly come to a conclusion regarding normality or abnormality of the muscle examined simply by "observing" the abnormal spontaneous activity and the motor unit activity on the oscilloscope screen. This is one reason why quantified determination of MUP parameters by CN EMG is not as widely used as would be expected. If quantification is desirable, quantified CN EMG does provide the same information on reinnervation changes in muscle as the SFEMG parameter of "fiber density" [7,59]. An ideal quantitative EMG method has not been found yet, however, and expertise is required from the electromyographer to allow good quality control.

CN EMG is the electrophysiological method of choice in routine examination of skeletal muscle. It should be logical to extend an "EMG examination" from, for example, lumbar and upper sacral myotomes to the lower sacral myotomes in, say, a child with myelomeningocele or an adult after a cauda equina lesion. Furthermore, the concentric electrode can be employed at the same diagnostic session for recording motor evoked responses and/or reflex responses [21].

CONDUCTION STUDIES OF THE SACRAL MOTOR SYSTEM

Measurement of motor CV is routinely carried out to evaluate limb motor nerves. However, the technique requires access to stimulation of the nerve at two separated points and measurement of the distance between them (Figure 36.3)—a requirement that cannot be practically met in the pelvis. An electrophysiological parameter that requires a shorter length of motor nerve to be accessible is measurement of the terminal motor latency of a muscle response [2].

Terminal motor latency of the pudendal nerve can be measured by recording with a CNE from the bulbocavernosus, anal, or urethral sphincter muscles in response to bipolar stimulation placed on the perianal or perineal surface. The latencies of MEPs from the perineal muscles obtained by this means are between 4.7 and 5.1 ms [60]; similar latencies have been obtained for the same method of stimulation and recording from the anal sphincter [61,62].

The more widely employed technique of obtaining the pudendal terminal motor latency relies on stimulation with a special "surface electrode assembly" fixed on a gloved index finger [63], often referred to as the "St Mark's" device. It consists of a bipolar stimulating electrode fixed to the tip of the gloved finger with the recording electrode pair placed 5 cm proximally on the base of the finger. The finger is inserted into the rectum or vagina and stimulation is performed close to the ischial spine. A "rounded" response is recorded from the surface electrodes at the base of the finger (which is claimed to be the M wave from the external anal sphincter) with a typical latency around 2 ms. This test is usually referred to as the "pudendal nerve terminal motor latency (PNTML) test." If a catheter-mounted electrode is used, responses from the urethral sphincter can also be obtained. In studies, as a rule only latencies have been studied as amplitudes of the "M wave" response have not proved contributory. From studies using this test, it was concluded that occult damage to the pudendal innervation of the external anal sphincter occurs after vaginal delivery, and the conditions worsen over many years by abnormal straining patterns of defecation [47]. It was said to be of pathogenetic importance for idiopathic stress urinary incontinence, fecal incontinence, and pelvic floor prolapse [44]. Sultan et al. [64] also demonstrated a small but statistically significant increase in pudendal nerve latency following vaginal delivery, but, more importantly, they demonstrated a defect of either the internal or external anal sphincter, or both, in 35% of women after vaginal delivery using anal endosonography and a strong association between these defects and the development of bowel symptoms. The prolonged latency and the muscle defect were thought to reflect a common traumatic cause.

Although no correlation of PNTML to parity was found in some studies [28], the term "pudendal neuropathy" has become established in the literature for a while, and authors less familiar with clinical neurophysiology theory tended to equate a prolongation of pudendal motor latency with pelvic floor denervation. This however, is mistaken, as prolongation of latency is a poor measure of denervation. In fact, experts now mostly doubt the validity of the test. A lack of correlation to sphincter pressure measurements has been demonstrated: in one study, approximately 50% of patients with PNTML had normal anal canal squeeze pressures [65]. In contrast to earlier studies, more recent work suggests the test does not predict improvement, or the lack of improvement, after surgical repair of anal sphincter defects [66]. A prospective evaluation of anorectal physiological tests in 90 patients with fecal incontinence did not find that pudendal terminal latency test results changed treatment decisions [67]. Indeed, the American Gastroenterological Association statement indicated that "pudendal terminal latency cannot be recommended for evaluation of patients with fecal incontinence" [68]. Recording of PNMTL is no longer recommended in the investigational workup of the patient with suspected pudendal neuralgia. There are several reasons for this. Nerve entrapment initially results in axonal excitability and excessive ectopic spike discharges that is followed by central sensitization, which plays an important role in maintaining chronic pain. These functional changes cannot be identified by clinical neurophysiology and only when entrapment is severe enough do abnormalities appear. Segmental demyelination results in conduction block with focal nerve conduction slowing, which may not be identified in the short length of the pudendal nerve measured. Also, these techniques investigate motor functions, whereas symptoms and signs are mainly due to sensory dysfunction [69]. Currently, measuring pudendal nerve latencies in incontinence is not recommended [70].

A selective needle recording of a (sphincter or pelvic floor) muscle response (M wave) on appropriate electrical stimulation may be informative in selected patients with suspected "lower motor neuron–type" lesions.

Anterior Sacral Root (Cauda Equina) Stimulation

Transcutaneous stimulation of deeply situated nervous tissue became possible with the development of special electrical [71] and magnetic [72] stimulators. When applied over the spine, these stimulators stimulate mainly the roots at the exit from the vertebral canal [73]. There have been reports of these techniques applied to the sacral roots [74]. Parasympathetic efferents most probably cannot be stimulated using magnetic stimulation: while it has been claimed that MPEs from detrusor can be produced following magnetic stimulation of the cauda equina [75], others have demonstrated inhibition of detrusor hyperreflexia following sacral root stimulation [76], which is expected after depolarization of perineal afferents.

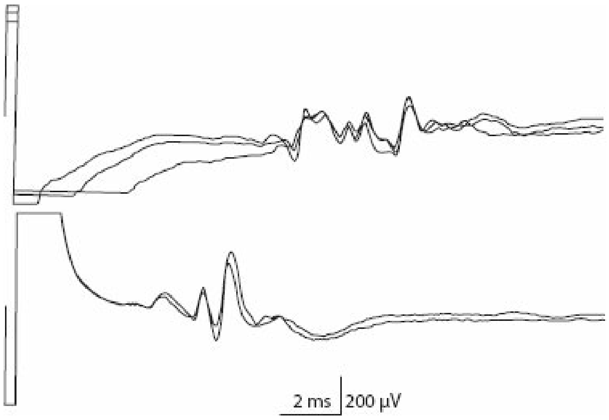


Figure 36.9 Concentric needle EMG recording from the anal sphincter showing responses on "strong" electrical stimulation with surface electrodes over the back (upper trace at level L1; lower trace at level S3). Digitimer stimulator: stimulus duration 50 µs, stimulus amplitude 50%. Three and two consecutive responses are superimposed, respectively.

Needle EMG electrodes rather than nonselective surface electrodes should be used to record MEPs to electrical or magnetic stimulation because both depolarize underlying neural structures in a nonselective fashion and there may be activation of several muscles innervated by lumbosacral segments. It has been shown that responses from gluteal muscles may contaminate attempts to record from the sphincters and lead to error [77].

Recording of MEPs with magnetic stimulation has been less successful, at least with standard coils [78,79], than with electrical stimulation, and there is often large stimulus artifact. Positioning of the ground electrode between the recording electrodes and the stimulating coil should decrease the artifact (Figure 36.9). Stimulation of the roots may be used to obtain a peripheral conduction time so that a central conduction time (see next section) can be calculated [79].

Demonstrating the presence of a perineal MEP on stimulation over the lumbosacral spine and recording this with a concentric needle (CN) EMG electrode may occasionally be helpful; however, an absent response has to be evaluated with caution and the clinical value of the test has yet to be established.

Assessment of Central Motor Pathways

Using the same magnetic or electrical stimulation as mentioned earlier, it is possible to stimulate the motor cortex and record a response from the pelvic floor. Magnetic stimulation is less unpleasant; electrical cortical stimulation is nowadays only used intraoperatively in anesthetized patients.

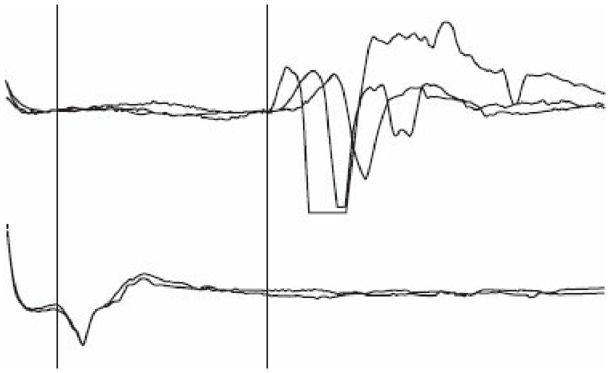


Figure 36.10 Recording from the urethral sphincter with a concentric needle electrode (CNE) in response to magnetic stimulation of the lower lumbar spine (lower trace; latency 6.5 ms) and the motor cortex (upper trace; latency 25.4 ms). The effect of "facilitation" (i.e., a slight voluntary contraction) on shortening the latency of the response following cortical stimulation is evident.

By electrical stimulation over the motor cortex of healthy subjects, MEPs in anal and urethral sphincters and in the bulbocavernosus [77] muscles were reported. The mean latencies were between 30 and 35 ms if no "facilitatory maneuver" was used. If, however, stimulation was performed during a period of slight voluntary contraction of the muscle, the latencies of MEPs shortened significantly (for up to 8 ms) (Figure 36.10).

By applying stimulation both over the scalp and in the back (at level L1), and subtracting the latency of the respective MEPs, a "central conduction time" can be obtained. Central conduction times of approximately 22 ms without and about 15 ms with the facilitation (i.e., slight voluntary contraction) have been reported [79].

Substantially, longer central conduction time in patients with multiple sclerosis and spinal cord lesions as compared to healthy controls have been found [1], but all those patients had clinically recognizable cord disease.

Normative values for the urethral sphincter and the puborectal muscle in adult women have been reported for transcranial magnetic stimulation [80,81]. The necessity to use concentric needle EMG for recording has been reconfirmed [82].

MEPs have opened an avenue of research on excitability of the motor cortex. It has been demonstrated that in comparison to the motor area for hand muscles, the anal sphincter motor cortex has less intracortical inhibition [83].

Because of the significant influence of voluntary contraction, there is a possibility of variability of both total conduction times and central conduction times. A well-formed sphincter MEP with a normal latency in a patient with a functional disorder or a medicolegal case may on occasion be helpful.

MEP on cortex stimulation may be useful for intraoperative monitoring, and indeed, this may be the only routine application of this test at present [84].

CONDUCTION STUDIES OF THE SACRAL SENSORY SYSTEM

Cerebral Somatosensory Evoked Potentials (SEPs)

The pudendal evoked response is easily recorded following electrical stimulation of the clitoral nerve [79,85,86]. This SEP is of highest amplitudes at the central recording site ([Cz –2 cm: Fz] of the International 10–20 EEG System) and is highly reproducible. Amplitudes of the P40 measure between 0.5 and 12 μV [86] (Figure 36.11). Later negative (at around 55 ms) and then further positive waves are interindividually quite variable in amplitude and expression and furthermore have little known clinical relevance.

Pudendal SEP recordings have been widely employed in patients with neurogenic bladder dysfunction due to multiple sclerosis [78], but it has since been shown that the tibial cerebral SEPs are more often abnormal than the pudendal SEP, and only in exceptional cases is the pudendal SEP abnormal but the tibials normal, pointing to an isolated conus involvement [87]. Cerebral SEPs on clitoral stimulation were reported as a possibly valuable intraoperative monitoring method in patients with cauda equina or conus at risk of a surgical procedure [88,89].

Special techniques of stimulation isolate each dorsal clitoral nerve and may be more sensitive at locating the precise site of pathology [90]. Following spinal cord injury, tibial and pudendal SEPs have been claimed to predict recovery in bladder control [91]. Pudendal SEPs were used to study the mechanism of sacral neuromodulation [92].

A study that looked at the value of the pudendal evoked potential when investigating urogenital symptoms for detecting relevant neurological disease found it to be of lesser value than a clinical examination looking for signs of spinal cord disease in the lower limbs, i.e., lower limb hyperreflexia and extensor plantar responses [93]. There may, however, be circumstances in routine diagnostics—such as when a patient is complaining of loss of bladder or vaginal sensation—that it is reassuring to be able to record a normal pudendal evoked response.

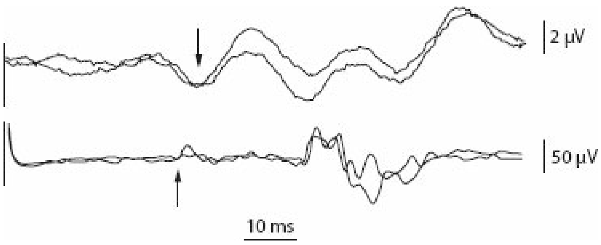


Figure 36.11 Cerebral somatosensory evoked potential (SEP) (above) and bulbocavernosus reflex (below) on dorsal clitoral nerve stimulation (rectangular pulses, 0.2 ms long at 1 Hz) in a 37-year-old woman with a compressive fracture of L1, complaining of difficulties in initiation of micturition. SEP is recorded with surface electrodes (Cz –2 cm: Fz); the bulbocavernosus reflex is recorded from the anal sphincter with surface electrodes. Two consecutive averages of 128 responses are superimposed. The P40 of the SEP and the first component of the bulbocavernosus reflex are indicated. The first reflex component is spurious at the applied stimulation strength, which was two-times sensory threshold; the second (late) reflex component is obvious.

Pudendal SEP may be useful for intraoperative monitoring, and indeed, this may be the only routine application of this test at present [84].

Electrical Stimulation of the Urethra, Bladder, and Anal Canal

Cerebral SEPs can also be obtained on stimulation of the bladder urothelium [94]. When making such measurements, it is of utmost importance to use bipolar stimulation in the bladder or proximal urethra; otherwise, somatic afferents will be depolarized [95,96]. These cerebral SEPs have been shown to have a maximum amplitude over the midline (Cz –2 cm: Fz) [95]; but the potential is of low amplitude (1 µV or less) and of variable configuration and may be difficult to identify in some control subjects [95,97]. The typical latency of the most prominent negative potential (N1) is approximately 100 ms [95,97]. The responses were claimed to be of more relevance to neurogenic bladder dysfunction than the pudendal SEP, as the Aδ delta sensory afferents from bladder and proximal urethra accompany the autonomic fibers in the pelvic nerves [95].

Another stimulation site in the perineal region is the anal canal, following which cerebral SEPs with a slightly longer latency than those obtained following stimulation of the clitoris have been reported, but it is not possible to record this response from all control subjects. The rectum and sigmoid colon have also been stimulated, and cerebral SEPs of two types recorded. One was similar in shape and latency to pudendal SEP and the other to SEP recorded on stimulation of bladder/posterior urethra [98].

SACRAL REFLEXES

Physiological Background, Methods, and Terminology

“Sacral reflexes” refer to electrophysiologically recordable responses of perineal/pelvic floor muscles to (electrical) stimulation in the urogenitoanal region. There are two reflexes—the anal and the bulbocavernosus—that are commonly clinically elicited in the lower sacral segments; both have the afferent and efferent limb of their reflex arc in the pudendal nerve and are centrally integrated at the S2–S4 cord levels (Figure 36.11). Electrophysiological correlates of these reflexes have been described. EMG recording of the sacral reflex has been shown to be more reliable than the clinically assessed response (e.g., observing and palpating the contraction) in males and particularly in females [99].

It is possible to use electrical [60], mechanical [100], or magnetic stimulation. Electrical stimulation can also be applied perianally [60]. The pudendal nerve itself may be stimulated by applying needle electrodes transperineally [101] or by using “St Mark’s electrode” [102]. As a rule, reflex responses are recorded as EMG activation of target muscles, but responses of the external urethral sphincter have also been recorded with a microtip transducer catheter as pressure rises, with latencies between 27 and 41 ms [103].

Bladder neck/proximal urethra can be stimulated using a catheter-mounted ring electrode [96] and reflex responses obtained from perineal muscles. These reflexes have been referred to as “vesicourethral” and “vesicoanal,” depending from which muscle the reflex response is recorded. With visceral denervation (e.g., following radical hysterectomy), the viscerosomatic reflexes (from both bladder and urethral stimulation) may be lost while the bulbocavernosus reflex is preserved. Loss of bladder–urethral reflex with preservation of bladder–anal reflex has been described with urethral afferent injury after recurrent urethral surgeries [104].

Reports of sacral reflexes obtained following electrical stimulation of clitoral nerve give consistent mean latencies of between 31 and 38.5 ms [60]. Sacral reflex responses obtained on perianal or bladder neck/proximal urethra stimulation have latencies between 50 and 65 ms [60]. This more prolonged response is thought to be due to the afferent limb of the reflex being conveyed by thinner myelinated nerves with slower conduction velocities than the thicker myelinated pudendal afferents. The longer latency "anal reflex"—the contraction of the anal sphincter on stimulation of the perianal region—may also have thinner myelinated fibers in its afferent limb as it is produced by a nociceptive stimulus. On stimulation perianally, a short latency potential can also be recorded as a result of depolarization of motor branches to the anal sphincter [60,61] (being an "M wave").

Sacral Reflex on Electrical Stimulation of Penis or Clitoris

The nomenclature of the various reflex responses that can be recorded from pelvic structures in response to electrical stimulation was recently rationalized so that the term used gives an indication as to the site of stimulation and recording. The penilo-cavernosus/clitoro-cavernosus reflex, formally known as the "bulbocavernosus" reflex, assesses the sacral root afferent and efferent pathways. The dorsal nerve of penis (or clitoris) is electrically stimulated and recordings are made from the bulbospongiosus (previously called bulbocavernosus) muscle (or the EAS) usually with a concentric needle. This reflex was shown to be a complex response, often formed by two components [60,105]. The first component (with typical latency of about 33 ms) is the response that has been most often called the bulbocavernosus reflex. It is stable, does not habituate, and is thought to be an oligosynaptic reflex response, as the variability of single motor neuron discharges within this reflex is similar to that of the first component of the blink reflex [105]. The second component has a similar latency to the sacral reflexes evoked by stimulation perianally or from the proximal urethra. The variability of single motor neuron responses within this component is much larger, as is typical for a polysynaptic reflex [105]. The second component is not always demonstrable as a discreet response. The two components of the reflex may behave somewhat differently in control subjects and in patients: whereas in normal subjects it is usually the first component that has a lower threshold, in patients with partially denervated pelvic floor muscles, the first reflex component cannot be obtained with single stimuli, but on strong stimulation, the later reflex component does occur. This can cause confusion, and very "delayed" reflex responses may be recorded in patients without recognizing the possibility that it is not a delayed first component but an isolated second component of the reflex. The situation can be clarified by using double stimuli that facilitate the reflex response and may reveal the first component, which was not obvious on stimulation with single stimuli [106].

Sacral reflex responses recorded with needle or wire electrodes can be analyzed separately for each side of the anal sphincter; this is important because unilateral or asymmetrical lesions are common. Special techniques of stimulation isolate each dorsal clitoral nerve and may be more sensitive for identifying pathology [90]. Using unilateral dorsal penile nerve blocks, the existence of two unilateral bulbocavernosus reflex arcs has been demonstrated [107,108]. Thus, by detection from the left and right bulbospongiosus (and probably also the EAS) muscles, separate testing of right and left reflex arcs can be performed. In cases of unilateral (sacral plexopathy, pudendal neuropathy) or asymmetrical lesions (cauda equina), a healthy reflex arc may obscure a pathological one.

Sacral reflex responses on stimulation of the clitoral nerve have been proposed as being valuable in patients with cauda equina and lower motor neuron lesions; however, a reflex with a normal latency does not exclude the possibility of an axonal lesion in its reflex arc. Although most reports deal with abnormally prolonged sacral reflex latencies, it was suggested that a very short reflex latency may indicate the possibility of a tethered cord [109], the shorter latency being attributed particularly to the low location of conus. Shorter latencies of sacral reflexes in patients with suprasacral cord lesions were also reported. Continuous intraoperative recording of sacral reflex responses on clitoris stimulation is feasible if double pulses [110] or a train of stimuli are used and has become established in some neurosurgical centers focusing on lower spine surgery [84].

Sacral Reflex on Mechanical Stimulation

Mechanical stimulation has been used to elicit the bulbocavernosus reflex in both sexes [111], but there is as yet little experience with female patients. Either a standard commercially available reflex hammer or a customized electromechanical hammer can be used [97]. Such stimulation is painless and can be used in children or patients with pacemakers in whom electrical stimulation is contraindicated.

Diagnostic Usefulness of Sacral Reflex Testing

Sacral reflex testing should be a part of the "diagnostic battery," of which concentric needle EMG exploration of the pelvic floor muscles is the most important part [21]. Measurement of sacral reflexes is established and carried out in laboratories worldwide and is—apart from EMG—the most time-honored uroneurophysiological diagnostic procedure.

In those subjects, in whom the penilo-cavernosus/clitoro-cavernosus reflex is difficult to elicit, double electrical stimuli should be used. A complete reflex arc lesion should not be inferred by absence of a response if only single pulse is used for stimulation [35].

Penilo-cavernosus/clitoro-cavernosus reflex testing is suggested as a complementary test to CNEEMG examination of pelvic floor muscles in patients with suspected peripheral nervous lesions [112].

However, the expectation of some authors that, with measurement of sacral reflexes, a single, easily learned test could distinguish between neurogenic and nonneurogenic sacral dysfunction was unrealistic. Although testing reflex responses is a valid and useful method to assess integrity of reflex arcs, and electrophysiological assessment of sacral reflexes is a more quantitative, sensitive, and reproducible way of assessing the S2–S4 reflex arcs than any of the clinical methods, uncritical interpretation of results should be discouraged.

AUTONOMIC NERVOUS SYSTEM

The uroneurophysiological methods discussed so far assess only the myelinated fibers, whereas it is the autonomic nervous system, and the parasympathetic component in particular, that is most relevant for sacral organ function. It has been argued that local involvement of the sacral nervous system (such as trauma, compression, etc.) will usually involve somatic and autonomic fibers simultaneously. However, as there are some local pathological conditions (such as mesorectal excision of carcinoma or radical hysterectomy) that can cause a pure autonomic lesion, methods by which the parasympathetic and sympathetic nervous systems innervating the pelvic viscera could be assessed directly would be very helpful. Information on parasympathetic bladder innervation can, to some extent, be obtained by cystometry, but direct electrophysiological testing would be desirable. In cases where a general involvement of thin fibers is expected, an indirect way to examine autonomic fibers is to assess thin sensory fiber function. As unmyelinated afferent fibers transmit temperature sensation and pain, unmyelinated fiber neuropathy can be identified by testing thermal sensitivity. Thin (visceral sensory) fibers are tested by stimulating the proximal urethra or bladder and recording sacral reflex responses or cerebral SEPs.

Sympathetic Skin Response

The sympathetic nervous system mediates sweat gland activity in the skin, and changes in this activity lead to changes in skin resistance. On "stressful stimulation," a potential shift can be recorded with surface electrodes from the skin of the palms and soles and has been reported to be a useful parameter in the assessment of neuropathy involving unmyelinated nerve fibers [113]. The response (sympathetic skin response [SSR]) can also be recorded from perineal skin [114]. The SSR is a reflex that consists of myelinated sensory fibers, a complex central integrative mechanism, and a sympathetic efferent limb (with postganglionic nonmyelinated C-fibers).

The stimulus used in clinical practice is usually an electric pulse delivered to the upper or lower limb (to mixed nerves), but the genital organs can also be stimulated [114]. The responses are easily habituated and depend on a number of endogenous and exogenous factors including skin temperature, which should be at least above 28°C. The latencies of SSR on the penis following stimulation of a median nerve at the wrist could be obtained in all normal subjects [114]. No equivalent control data exist in women as yet.

Limited literature exists regarding the relationship between SSR results and bladder dysfunction. One study reports that diabetic cystopathy was associated with autonomic neuropathy as detected by SSR [115]. A correlation has been shown between the absence of the SSR response in foot and bladder neck dyssynergia following spinal cord injury [116]. Recording from the perineal region increases the diagnostic sensitivity for assessing sympathetic nerve function within the thoracolumbar cord [117].

The test is not sensitive for partial lesions as only complete absence of response has been regarded as abnormal. Its utility in evaluating bladder and urethral dysfunction is not yet established.

CONCLUSIONS

In routine diagnostics, uroneurophysiological testing is becoming established in patients with (suspected) peripheral nervous system lesions, where particularly (quantitative) concentric needle EMG and recording the clitoro-cavernosus (bulbocavernosus) reflex is recommended as standard (and standardized) procedure in selected patients, particularly if they are candidates for invasive therapeutic procedures [21,112]. It has been demonstrated that both techniques are indeed complementary and have —performed in the same patient—a higher sensitivity than each test on its own (i.e., 96%) [118].

Uroneurophysiological techniques continue to be useful in research and may become more relevant in the future for intraoperative identification and monitoring of nervous structures.

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37 Imaging of the Upper and Lower Urinary Tract: Radiology and Ultrasound

Andrea Tubaro, Kirsten Kluivers, Federica Puccini, and Antonio Carbone

INTRODUCTION

This chapter will review indications, techniques, and results of radiological (x-ray) and ultrasound (US) imaging of the upper urinary tract (UUT) and lower urinary tract (LUT) in women with LUT dysfunction (LUTD). Although some of the techniques may be considered based on their historical contribution, a knowledge of radiological imaging and the information obtained from these images remains an important part of the development of our understanding of pelvic anatomy and function. The crux of clinical research and ultimately clinical practice concerned with imaging in urinary incontinence (UI) and POP is to establish that there is a clinical benefit to the measurements that are obtained. Imaging is a method to evaluate anatomy of the individual patient and to diagnose conditions depending on the morphological or functional modifications of individual organs or structures. Imaging can confirm or augment the findings of physical examination and may provide information that is otherwise unattainable. The identification of the clinical scenarios in which this additional information is beneficial to the management of the patient is the ultimate measure of the utility of the study. Although we may postulate that intraobserver and interobserver variability of physical examination is higher when compared to imaging, this may not necessarily always be true, as well as the assumption that a correlate always exists between the two modalities.

Research into diagnostic accuracy is regulated by the standards for reporting of diagnostic accuracy initiative [1] although the recommendations are rarely adhered to in the (peer-reviewed) literature. The Oxford Centre for Evidence-Based Medicine introduced, in 2011, new criteria to grade the levels of evidence in manuscripts reporting studies on diagnostic tests [2]. The highest level of evidence according to the Oxford criteria is based on “systematic reviews of cross sectional studies with consistently applied reference standard and blinding” [2]. This is a paradigm change from the previous documents in which studies of diagnostic tests were not considered and proper evaluation of the available evidence is now possible.

The analysis of the literature related to the utility of imaging demonstrates that the evaluation of diagnostic accuracy is often performed properly and the available data include sensitivity and specificity as well as test–retest (intraobserver) and interobserver variability. Of note, a common problem is in the choice of a gold standard that most commonly is another imaging technique, physical examination or findings during surgical operation.

The problem in the comparison of imaging to physical examination is that whatever the outcome of the index test is, nobody can tell us whether the truth lies in what we can just speak about the concordance.

As long as imaging is considered an addition to physical examination, the goal may not be to show that there is a high level of agreement between the two, but rather to prove that adding imaging on top of physical examination results in a significant improvement in patient management and treatment outcome. Although it is easy to blame the investigators for a faulty study design, the reality is that designing a study on the clinical benefit of a new imaging technique in patients undergoing diagnostic studies or surgery is a very difficult problem because investigators deal with two different variables: the test under evaluation (e.g., US imaging of the pelvic floor) and the surgical procedure (e.g., surgery for anterior vaginal wall prolapse). In addition, large studies may be needed to evaluate the potential beneficial effects of imaging in certain subgroups of patients. Whenever the outcome of surgery is the primary outcome parameter, large multicenter studies are preferable, but when examining the literature in this area, most studies are relatively small and come from single institutions and the variability in patient selection, surgical technique, and outcome assessment must be taken into consideration.

Furthermore, a single positive study is rarely compelling enough to change standard practice and confirmatory studies are required. Moving from the identification of the gold standard to defining the best practice is a very long process but it remains the ultimate goal of studies on new imaging techniques.

Imaging of the pelvic floor in patients with UI and POP is limited by our lack of complete understanding of the physiopathology of these conditions. A classic historical example is the case of patients with stress UI (SUI). For decades, imaging techniques relied on x-ray imaging (e.g., voiding cystograms). This was based upon the assumption that quantification of the bladder neck mobility and the Green classification were of importance [3]. Further understanding of the anatomic relationships suggested alternative explanations and demonstrated the limitations of this technique [4–10]. Although the images confirmed the observations made during clinical examination and simplified evaluation of the patient in the standing position, specialists in the field demonstrated a diminished interest in the fluoroscopic imaging of SUI when selecting treatment alternatives, in part due to advances in surgical techniques. When new imaging modalities became available and techniques such as US imaging and MRI were introduced, research in the area of anatomy and anatomic relationships flourished again since not only the margins of the pelvic floor viscera but also images of the organs themselves together with the surrounding structures (muscles and fascias) could be obtained in x-ray imaging.

In recent years, US imaging of the pelvic floor rapidly replaced x-ray imaging because of technological improvements, availability in the office, low cost, lack of radiation hazard, and user-friendliness. Research in this area dates back to 1980 when US was first applied in patients with SUI [11]. Several papers investigated the relation between x-ray and US imaging [12–19], and the correlation between the two was found to be good [16], while US proved superior, particularly in obese women [19].

Although these data are certainly reassuring, they only suggest that US imaging can replace x-ray techniques but they do not establish any additional clinical utility. In contrast to CT scan and MRI, US imaging is not a “no-touch” technique. Interference between the exploring probe and the target tissue is unavoidable [20,21], although it can certainly be minimized. This is the reason why endocavitary imaging (transvaginal or transrectal) has been largely replaced by abdominal and perineal techniques. Since bony structures reflect the beam and affect the US images, but are required as reference points, abdominal imaging has been gradually replaced by perineal approach. Two-dimensional (2-D) cine loops or 3-D volumes may be acquired during imaging and can be reviewed offline at a later stage. Similar to CT or MRI techniques, nowadays, 3-D US images may be obtained through any plane. The depth of the perineal volumes in the cranial direction is, however, smaller in US compared with MRI, which may hamper imaging of the central compartment of the pelvic floor in US imaging [20]. The availability of high-speed computing made real-time or dynamic 3-D US imaging possible and is currently known as 4-D imaging. This technique has proved particularly interesting in the functional imaging of SUI and POP.

The lack of standardization in US imaging and MRI is impairing research in this area. Of note, there is no consensus regarding the ideal patient position (supine or standing) [22], picture orientation in US (caudal part on top [23] bottom, or right side of the picture [24]), reference lines in MRI [25], and degree of bladder filling (empty vs. full [26,27]). Furthermore, experience has demonstrated how difficult it is to standardize cough and Valsalva maneuvers, which is similarly a problem in all POP assessment tools [28,29].

In general, the challenge remains that our understanding of the physiopathology of UI and POP is still incomplete and the treatment methods currently applied for correction of the clinical conditions may not be significantly improved, in either selection or performance, by the information obtained by current imaging techniques or the research methods designed to demonstrate their utility.

IMAGING OF THE UPPER URINARY TRACT

The rationale for imaging the UUT in female patients with LUTD is twofold: to identify UUT malformations that may be associated with LUTD and to monitor the effect of LUTD on the UUT when necessary. Imaging of the UUT is always indicated in neurogenic UI, but in nonneurogenic LUTD, the imaging is rarely justified. In extraurethral UI, imaging of the renal moiety, which is sometimes dysplastic or ectopic, is of importance to plan adequate management and surgery. In myelodysplasia, elevated storage pressures in the urinary bladder can cause deterioration of the UUT with hydronephrosis and renal failure, and the kidney morphology and function must be monitored over time [30]. Severe POP may results in hydronephrosis because of angulation of the pelvic ureters by the uterine arteries (Figure 37.1) [31].

With the exception of these three conditions, there is no indication for UUT imaging in the nonneurogenic patient.

Imaging Techniques

Different imaging techniques can be used to picture the UUT: ultrasonography, x-rays, CT, MRI, and isotope scanning. In the absence of comparative data on their accuracy and clinical benefit in the management of patients with LUTD, the choice of the technique also depends on availability, expertise, and local policies. In general, the least expensive and hazardous techniques are recommended. Because of the low level of evidence available in the peer-reviewed literature on this subject, recommendations are generally based on expert opinion unless otherwise stated.

Ultrasonography

US is the standard technique for imaging the UUT because of its availability, low cost, and lack of x-ray exposure. Diagnosis of hydronephrosis is straightforward as the collecting system is normally hardly visible on US and imaging is more qualitative (hydronephrosis yes/no) rather than quantitative as there is no relation between the amount of UUT dilatation and the degree of obstruction, although there is a relation between the degree of dilatation and cortical damage [32]. Doppler analysis of interlobar and arciform arteries has been proposed to diagnose obstruction of the UUT although the technique never gained popularity [33]. In the presence of hydronephrosis, additional imaging is usually required to identify the cause and site of the obstruction. US imaging is ideal in the follow-up of patients with LUTD when UUT imaging must be repeated over time.

Intravenous Urography

This technique has been the cornerstone of UUT imaging for decades as it provides information on both renal anatomy and function. Indications are limited by the need of normal renal function (creatinine < 2.0 ng/dL) and no contraindications for the use of iodinated contrast agents [34]. Intravenous urography (IVU) is the first-line imaging modality for extraurethral incontinence although the renal unit associated with an ectopic ureter is, however, often small, poorly functioning, and ectopic and can sometimes be difficult to image unless delayed films and tomography are used (Figure 37.2) [35–37]. When the renal moiety cannot be imaged on IVU and CT, MRI or isotope scanning is recommended [38–40]. IVU is still recommended in case of ureterovaginal fistula although uro-CT and uro-MR can be also used, and dilatation of the UUT is observed in 84%–92% of fistula cases [41,42].

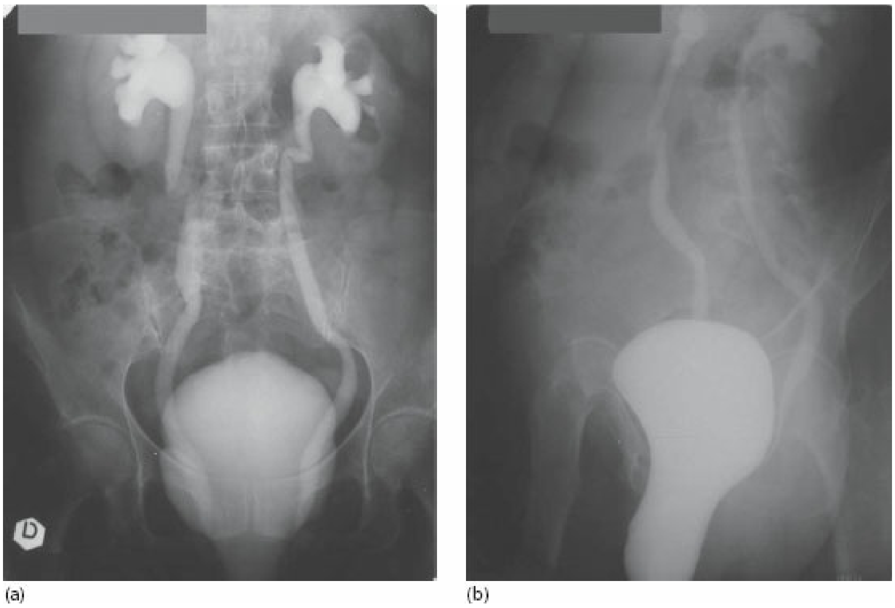


Figure 37.1 Intravenous pyelography. Bilateral hydronephrosis in a 54-year-old patient with grade IV genital prolapse: anteroposterior (a), oblique (b). (Courtesy of Prof. G. Tomiselli.)

CT and MRI

Both techniques have been recommended for the management of patients with a suspected ectopic ureter because of their ability to image small, poorly functioning renal moieties as well as the collecting system [43–46]. Both CT and MRI require normal renal function whenever contrast medium is used, and although MR contrast agents were considered safe, they may cause adverse effects [47–49].

Isotopes Scanning

Isotope scanning is mainly used to quantify function of the individual renal moieties and to locate ectopic or poorly functioning kidneys. Whenever renal function impairment is suspected and separate renal function must be quantified, isotope scanning is the technique of choice. The interpretation of isotope scanning is not always straightforward as there are various physiological factors and technical pitfalls that can influence the results. These include the choice of radionucleotide, timing of diuretic injection, state of hydration and diuresis, fullness or back pressure from the bladder, variable renal function, and compliance of the collecting system [50,51]. When an ectopic ureter is suspected, renal scintigraphy may be successful in imaging hypoplastic kidneys when other techniques have failed [52].

X-RAY IMAGING OF THE LOWER URINARY TRACT

For many years, x-ray imaging of the LUT has been performed in female patients with UI and POP whenever surgery was planned. The quantification of bladder neck mobility and pelvic organ descend was considered of importance for proper patient management, but a more strict evaluation of the available evidence failed to confirm any clinical benefit for most patients. X-ray imaging can sometimes help to identify coexisting conditions of the LUT such as bladder diverticula, urethral diverticulum, or comorbidities such as bladder stones, tumors, and foreign bodies (Figures 37.3 through 37.6). X-ray imaging in LUTD mainly consists of voiding cystourethrogram (VCUG) for the quantification of bladder neck mobility (Figures 37.7 and 37.8) or bladder prolapse (Figure 37.9); the opacification of the vagina and rectum has been proposed to achieve a more complete visualization of the pelvic organs (Figures 37.10 and 37.11) [53]. In the pediatric population, retrograde cystography and VCUG have been used to diagnose vesicoureteral reflux [54]. When a urethral diverticulum is suspected, positive-pressure urethrography has been shown to be more sensitive than VCUG [55–57], but x-ray imaging has been largely replaced by US imaging and particularly MRI that is now considered the gold standard for proper delineation of the diverticulum anatomy and the relation with the surrounding structures [58–60].

Quantification of Bladder Neck Mobility

VCUG was pioneered by Mikulicz-Radecki in 1931 [61]. The technique was further developed by Stevens and Smith with the introduction of a metallic bead to identify the urethra and by Ardran et al. who proposed the use of cinematographic technique with the opacification of the vagina and rectum [62,63]. The combined use of imaging and pressure–flow recordings was proposed in the 1960s and 1970s and rapidly gained acceptance in the urological community [64,65]. The description of VCUG methodology goes beyond the scope of this chapter but the interested reader can find details about the technique’s history and methodology in a review by Olesen [57]. A number of different parameters of VCUG have been proposed and assessed for reliability over the years. The posterior urethrovesical (PUV) angle is defined by two lines passing along the posterior urethra and the trigone [8]; cutoff values of 115° or more were proposed [3,9]. The degree of urethral inclination is calculated as an angle between the proximal urethral axis and the vertical plane; unfortunately, the angle also varies with pelvic inclination, although cutoff values of <45° or >45° have been described [3]. The angle between a line through the middle of the internal urethral orifice and the urethral knee and a line through the posterior surface of the symphysis and the lowermost part of the obturator foramen closest to the film is defined as the urethropelvic angle (values of 95° are measured in controls and a cutoff value of 70° has been proposed to diagnose bladder descent) [61]. The symphysis orifice (SO) distance is measured at rest as the distance on a horizontal line from the symphysis to the internal urethral orifice (normal values are 31 mm and values <20 mm are the cutoff points for descent and were used to diagnose anterior bladder suspension defects or bladder base insufficiency) [61,66]. In continent women, the urethral axis at rest (UAR) was found to be related to age ($R^2 = 0.28$); patients with UI had a mean UAR of 25° and a mean urethral angle at straining (UAS) of 43°. Showalter et al. measured UAR and UAS before and after surgery showing that both angles returned to near normal after surgery suggesting a correlation between the correction of the defective bladder support and cure [67]. The funneling of the proximal urethra, the flatness of the bladder base, and the most dependent portion of the bladder base are important qualitative parameters estimated on straining films [9].

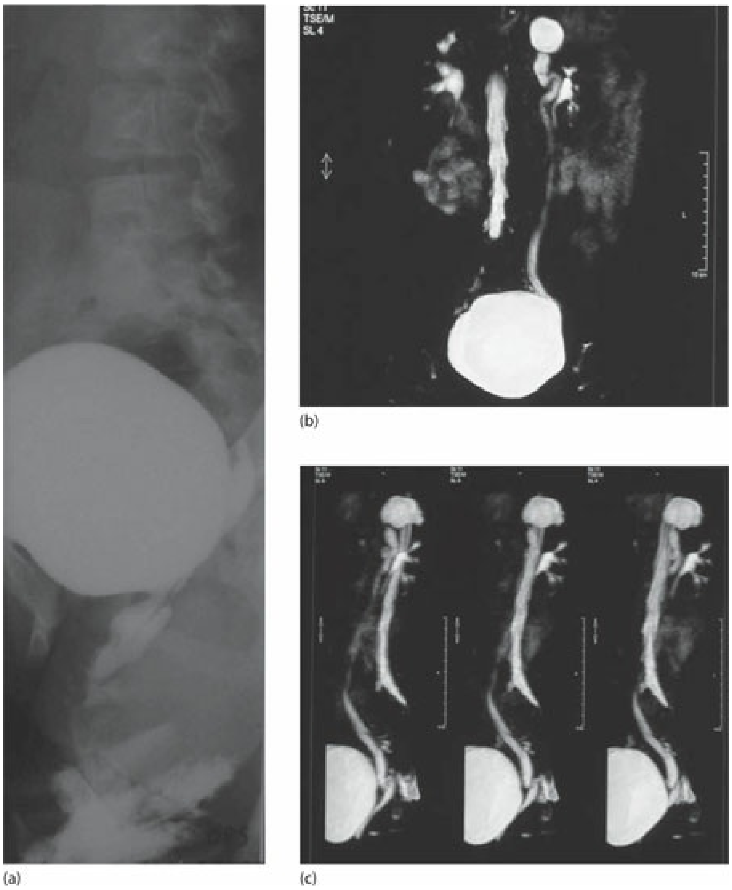


Figure 37.2 Intravenous pyelography in a 16-year-old patient with urinary incontinence. The intravenous pyelogram shows a complete duplex system on the left side. On a lateral projection, the ureter of the upper renal moiety travels below the bladder base, reaching the most distal part of the urethra (a); the anatomic condition is confirmed on uro-MR (b and c). (Courtesy of Prof. G. Tomiselli.)

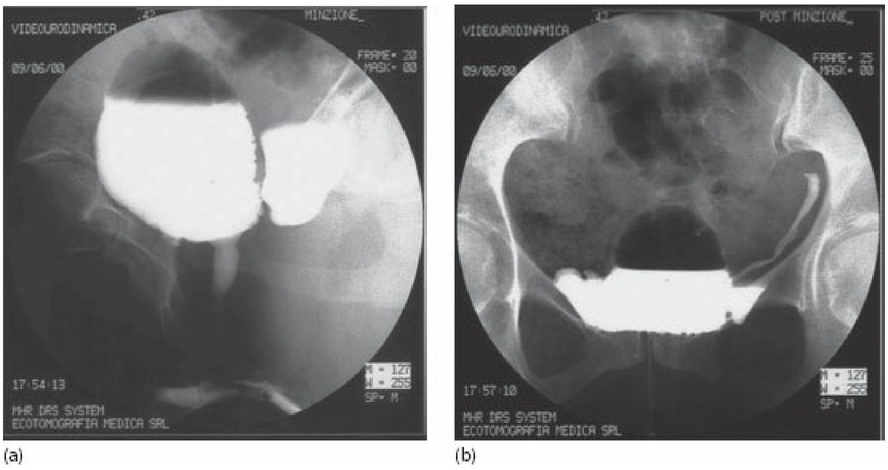
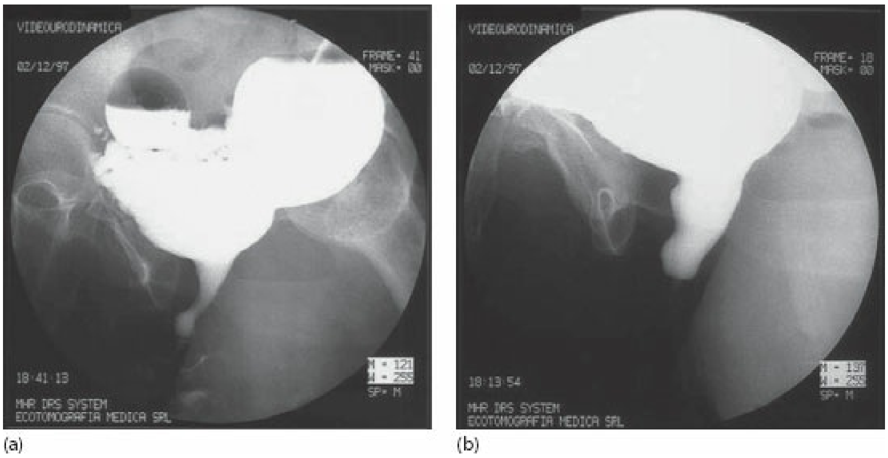


Figure 37.3 Digital fluoroscopy picture obtained during videourodynamics in a 63-year-old female with voiding dysfunction. The dilation of the proximal urethra and a bladder diverticulum is evident on a voiding picture (a); vesicoureteral reflux is apparent on the postvoiding image (b). (Courtesy of Prof. G. Tomiselli and Prof. A. Carbone.)



(a) (b)

Figure 37.4 Digital fluoroscopy in a 72-year-old patient with voiding dysfunction. A decompensated bladder is observed during voiding (a) and severe dilation of proximal urethra is seen during videourodynamics (b). (Courtesy of Prof. G. Tomiselli and Prof. A. Carbone.)

The analysis of the peer-reviewed literature suggests VCUG is not discriminant between continence and incontinence although promising data have been also published [3,5,10,67,68]. Interobserver and intraobserver agreement values of 43%–79% and 53%–99%, respectively, have been reported for VCUG parameters [9,69–71]. Overall, specificity and sensitivity values of 44%–76% and 53%–100%, respectively, were published [10,72]. The type and degree of suspension defects were not related to the degree of SUI [6,69,70], with positive and negative predictive values of 0.70 and 0.52, respectively, on voiding colpocystourethrography [4,66]. Comparison of VCUG and US imaging suggested a good degree of correlation between the two techniques, particularly with regard to bladder neck position and mobility, PUV, urethral inclination, SO distance, and rotation angle [6,72–74]. Similar values of specificity, sensitivity, and interobserver agreement were also found. The availability and user-friendliness of the US technique favor its use in most urogynecology practices. VCUG was also compared to MRI and comparable data for bladder neck position and cystocele descent were found [75,76]. Although the difference in the patient position between VCUG (standing) and MRI (lying) is of concern, comparison of standing and lying colpocystourethrography did not show any significant difference [76].

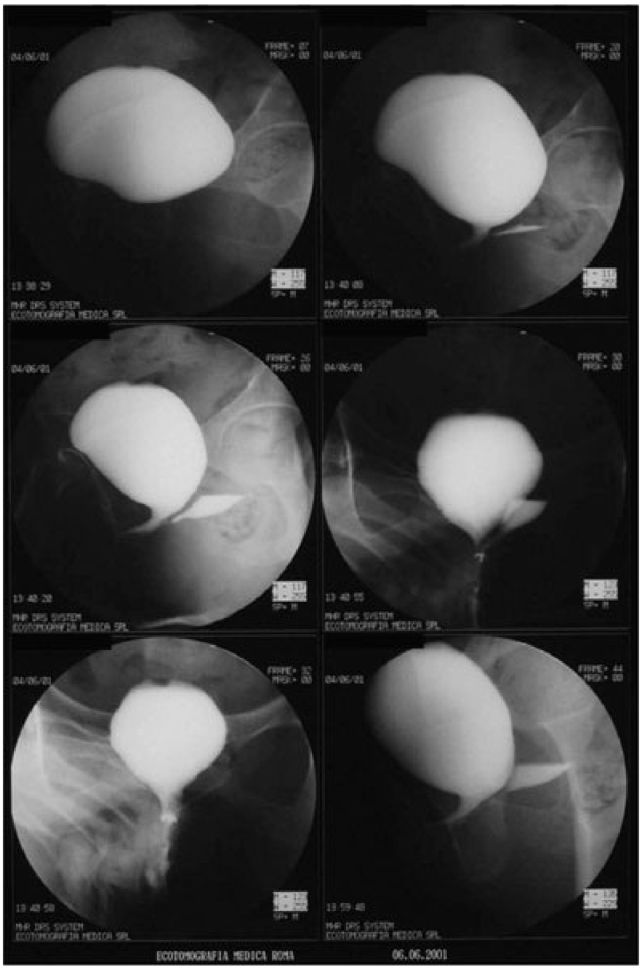


Figure 37.5 Voiding cystourethrogram in a 29-year-old patient with urinary incontinence. During the voiding phase, reflux of contrast medium into an ectopic ureter draining the upper moiety of a complete duplicated left renal system can be seen. In the last phase of the voiding study, the refluxing medium drains into the urethra. (Courtesy of Prof. G. Tomiselli.)

Overall, VCUG studies of women with and without UI failed to provide evidence of clinical utility. Several published studies showed significant overlap in the degree of bladder neck mobility and restoration of normal bladder neck mobility following surgery was not necessarily associated with the cure of UI. These data, together with the introduction of US imaging and MRI of the pelvic floor, obviated the need for VCUG in the management of the standard patient with UI or POP. Although both US imaging and MRI opened a series of new perspective in the imaging of patients with UI, the measurement of bladder neck mobility failed to be of any clinical utility whatever technique was used.

Videourodynamics

The technique is sometimes considered the "gold standard" in the evaluation of LUTD [69]. Actually, there is no evidence that the combination of retrograde and voiding cystourethrography plus cystometry is superior to the two examinations performed separately; however, videourodynamics (VUDN) is frequently performed for convenience in the neurogenic population with LUTD [77–80] and in the pediatric population when indicated (e.g., suspicion of vesicoureteral reflux) [81,82]. The use of VUDN in female patients with UI is not recommended although it may play a role in selected cases. One study compared VCUG with VUDN in women with LUTD and found that in 7.5% out of 200 patients, a correct diagnosis could only be made on VUDN [69]. Although these data are certainly appealing, the small x-ray hazard should also be considered [53,63,83–85].

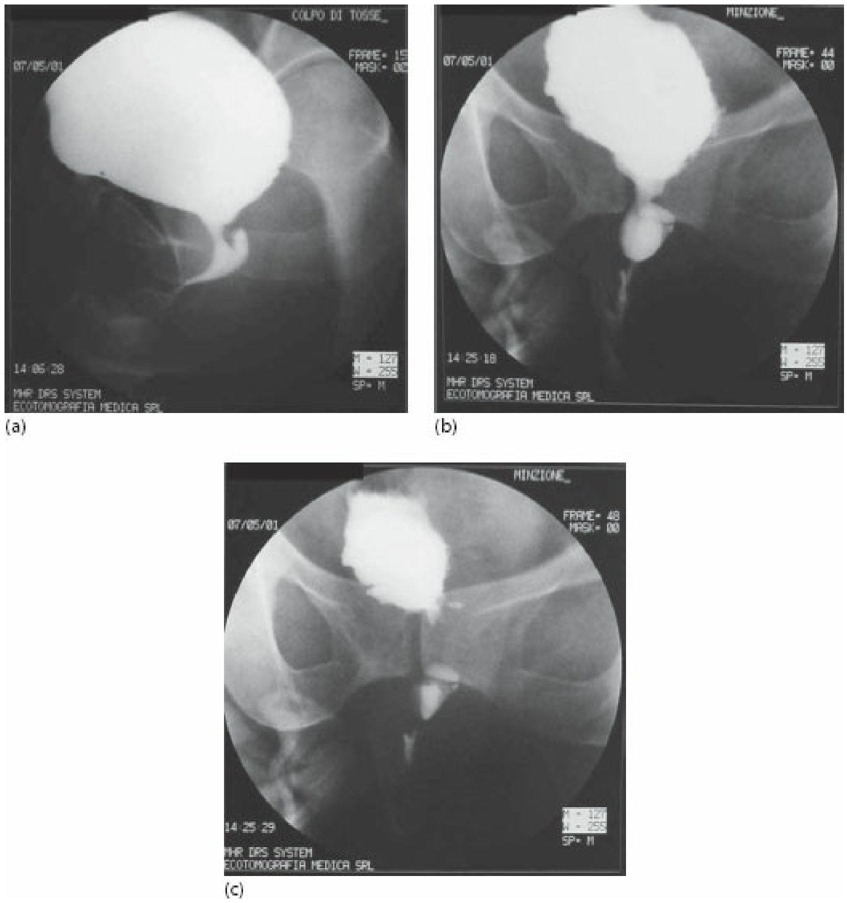


Figure 37.6 Urethral diverticulum of the posterior urethral wall is evident on voiding cystourethrogram in oblique (a) and in anteroposterior projections (b, c). (Courtesy of Prof. G. Tomiselli.)

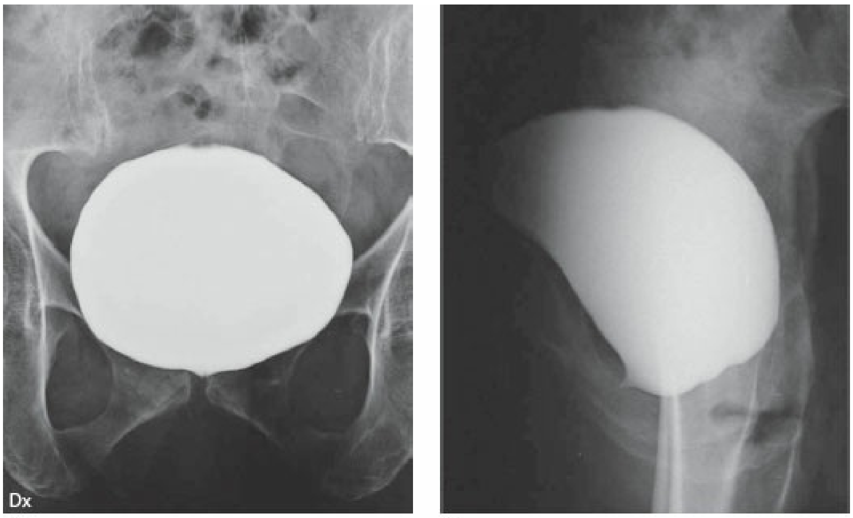


Figure 37.7 Cystourethrography in a 68-year-old patient without urinary incontinence. A symmetrically distended bladder is evident on the anteroposterior image (a), with the bladder base above the lower margin of the symphysis pubis; in the true lateral projection (b), the anterior and posterior urethrovesical angles are easily observed in the picture taken just before micturition. (Courtesy of Prof. G. Tomiselli.)

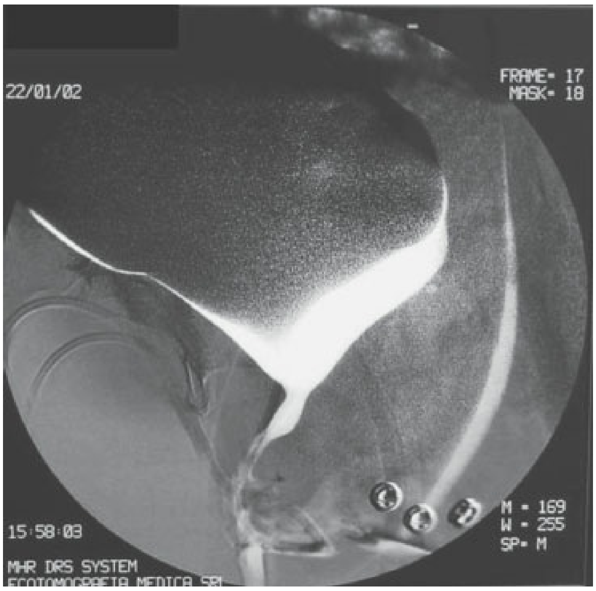


Figure 37.8 Voiding cystourethrogram with digital subtraction. There is normal funneling of the bladder neck with mild downward displacement during micturition. (Courtesy of Prof. G. Tomiselli and Prof. A. Carbone.)

CONCLUSIONS

The use of x-ray imaging in female patients with UI and POP is limited. IVU, CT, and MRI of the UUT maintain a diagnostic role when evaluation of the renal moiety is needed in patients with ectopic ureters and the condition of the UUT needs to be monitored. X-ray imaging of the LUT is not recommended in the standard female patients with UI or POP. Notwithstanding a large body of evidence is available in the peer-reviewed literature concerning diagnostic accuracy, intra- and interobserver variability, and comparison with other imaging techniques, VCUG cannot be recommended in the evaluation of the standard patient with UI or POP. VCUG is not recommended for the diagnosis or classification of UI. The technique may still have a role in the evaluation of complex patients and in patients with recurrent UI or POP.

ULTRASOUND OF THE LOWER URINARY TRACT IN URINARY INCONTINENCE

In clinical practice, imaging of the female urethra is usually performed whenever the presence of a diverticulum is suspected.

Although diverticula can easily be shown on US, better anatomical definition is achieved with MRI that is thus considered the “gold standard” technique. Proper knowledge of the imaging characteristics of the normal female urethra is of importance for adequate interpretation of findings. Transurethral, perineal, transvaginal, and transrectal imaging can be used. The echogenic characteristics of fibrous and muscular structures depend on the angle between the exploring beam and orientation of the muscle fibers. When the normal female urethra is imaged from a perineal approach, the US beam is parallel to the structures and the internal sphincter appears hypoechogenic; when the US beam is orthogonal to the structures such as in transvaginal/transrectal imaging, smooth muscle fibers appear hyperechogenic. Thus, it is difficult to evaluate possible changes to urethral tissues (e.g., fibrosis) on US since the echogenic pattern of it also depends on how the imaging is performed. Furthermore, the echogenic pattern of the female urethra may change during dynamic imaging because of the rotation of the structure on Valsalva and the relative change of incidence between the US beam and the internal sphincter.

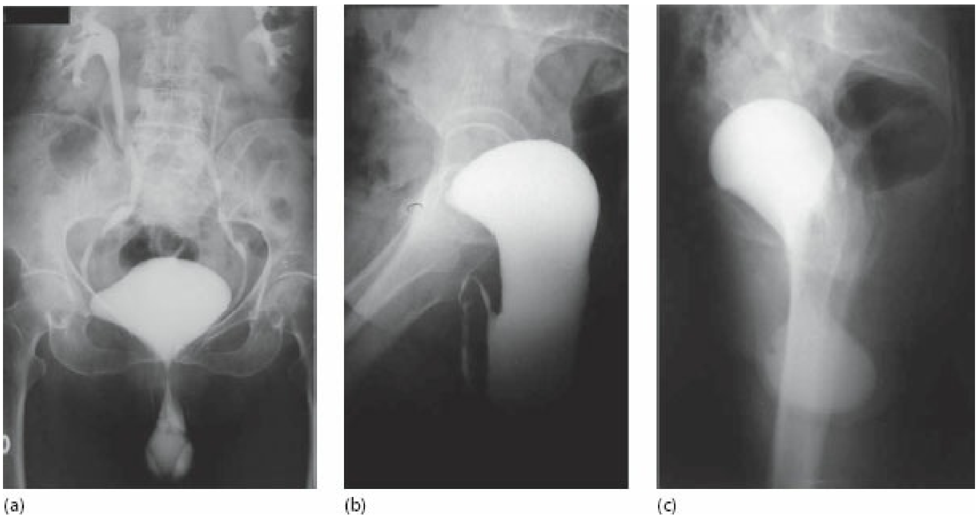


Figure 37.9 Grade IV genital prolapse can be observed in a 63-year-old patient during intravenous pyelography in anteroposterior (a) and true lateral projection (b); the relationship between pubic bone, bladder trigone, and urethra is best appreciated during voiding cystourethrogram in a true lateral projection (c). (Courtesy of Prof. G. Tomiselli.)

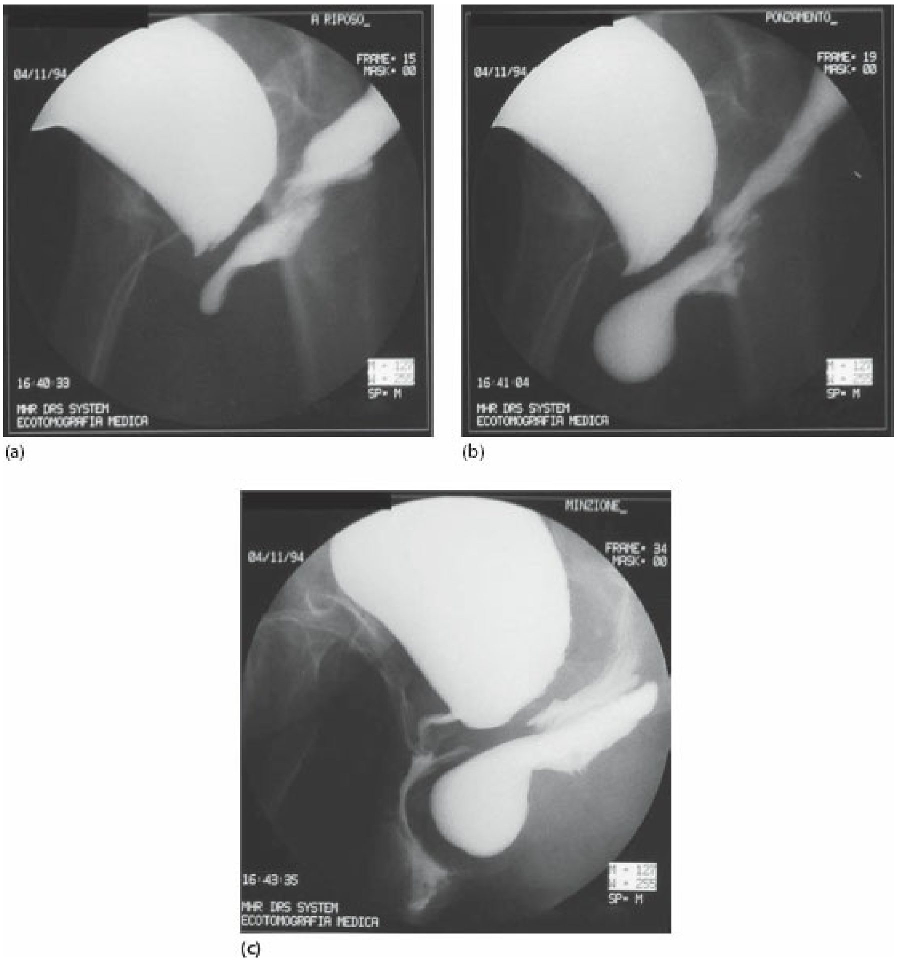


Figure 37.10 Voiding cystourethrogram in a patient with contrast medium both in the bladder and in the rectum. Pictures taken at rest (a), during Valsalva (b), and during voiding (c) show a gradual distension of the rectocele pouch. (Courtesy of Prof. G. Tomiselli and Prof. A. Carbone.)

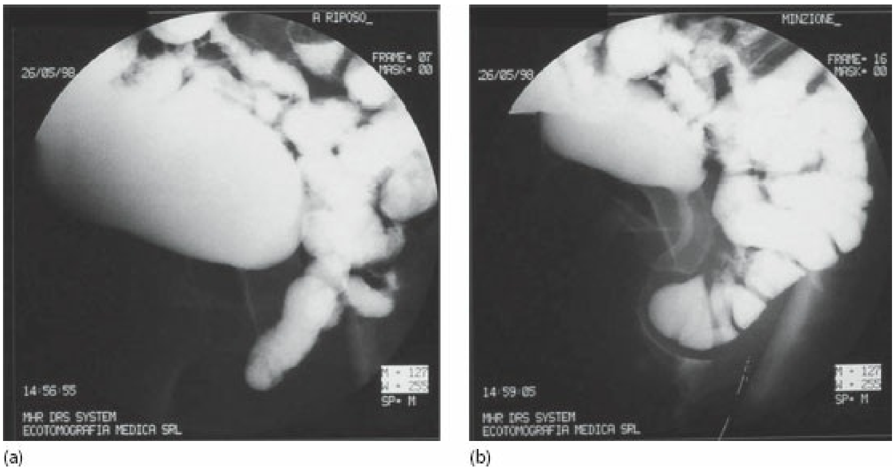


Figure 37.11 Cystourethrography with simultaneous administration of small bowel contrast allows the diagnosis of enterocele in a 61-year-old patient suffering from vaginal vault prolapse. Small bowel protruding down to the perineum level can be observed both at rest (a) and during voiding cystourethrogram (b), with a significant increase of the enterocele mass when abdominal pressure increases. (Courtesy of Prof. G. Tomiselli.)

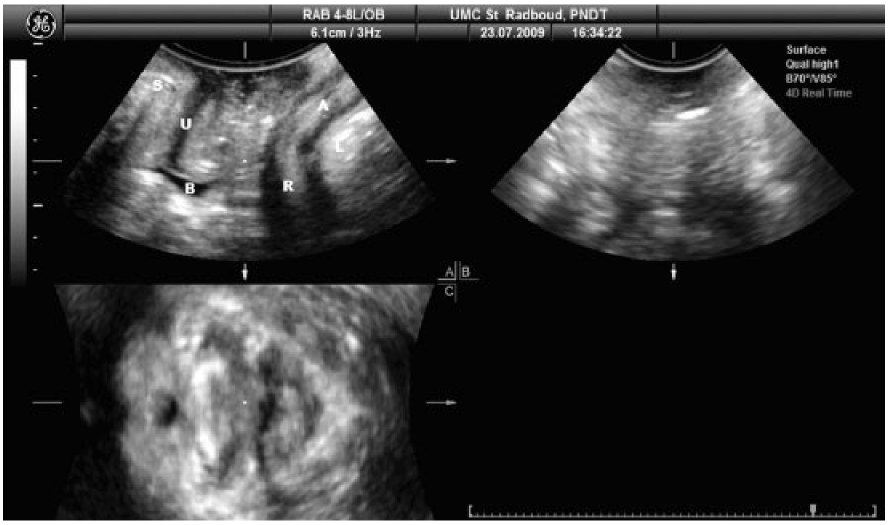


Figure 37.12 Perineal ultrasound imaging in a woman with normal pelvic anatomy. Midsagittal (left upper), coronal (right upper), and axial (left lower) two-dimensional view. *Abbreviations*: S, symphysis pubis; U, urethra; B, bladder; R, rectum; A, anus; L, levator ani muscle.

The external sphincter is known to be hyperechogenic on US (Figure 37.12) and is more difficult to visualize. The rationale of assessment of the thickness and volume of the female urethra in SUI relies on the hypothesis that these measurements and the strength are related, so that measurement of sphincter volume could be a proxy for the parameters of the urethral pressure profile (UPP). The measurement of the urethral sphincter has been shown to be reproducible [86–88]. Urethral volumes as assessed with a formula using 2-D measurements and 3-D volume measurements differed significantly [88]. The measurement of the striated sphincter volume seemed to be of importance as this was found to be related to symptoms and signs of SUI [86,87] and with UPP [89–92]. Urethral sphincter volume was associated with the outcome of surgery for SUI [93].

Right or wrong, pelvic floor imaging in SUI patients aims mainly at the quantification of bladder neck mobility. The bladder outlet is easily visible on US, independently from the degree of filling. The position of bladder neck with respect to the lower margin of the pubic bones is measured at rest and during provocative maneuvers (coughing, Valsalva maneuver), thus reproducing the conditions under which SUI occurs in a particular patient. Bladder neck displacement can also be measured during squeezing [94]. During Valsalva, the bladder neck and urethra are considered to rotate posteriorly and inferiorly (caudally and dorsally), and the displacement can be measured in different ways [95–99] with reasonable clinical reproducibility [100,101]. The large variability of urethral mobility in continent nulliparous women (1–40 mm) [102–105] makes the provision of normative data impossible. Parous women are known to have a larger degree of bladder neck mobility than nulliparous [92,94,106–109] and hypermobility is considered to be associated with SUI [24,106]. The sensitivity and specificity of US imaging of bladder neck mobility for the diagnosis of SUI vary between 92% and 96% [109] and 83% and 68% [110], respectively. Analysis of urethrovesical movement patterns on dynamic perineal US imaging in continent and incontinent women did not result in any characteristic movement pattern being associated with SUI [111]. Notwithstanding a huge research effort, US imaging of the bladder neck failed to provide a significant advantage in the management of patients with SUI [112,113]. The comparison of interobserver variability of different methods to quantify urethral mobility, such as Q-tip test, Sensor-Q^{TM} test, and US, showed a lower interobserver reliability for the US imaging technique [114].

POSTVOID RESIDUAL URINE

Measuring postvoid residual (PVR) in patients with UI and POP is considered part of the safety assessment before and after surgery. PVR is not uncommon in women with LUTD and is considered to be associated with an increased risk of urinary tract infection. The condition may develop de novo following surgery for SUI and POP. Since US imaging was first used in the evaluation of PVR, it has been regarded as the gold standard compared to catheterization [115–118]. To correct for deviations of the bladder shape from a sphere, various formulae have been proposed with different correction factors. In a study comparing 12 formulae, the formula “π × height × width × depth in centimeters/6” showed the best agreement between US volume and catheterized volume [119]. In daily clinical practice, the residual volume is probably best approximated by height × width × depth in centimeters × 0.5. Automated US systems are widely used as they have been shown to be accurate and usable by nursing staff [120]. Data from asymptomatic peri- and postmenopausal women suggest a median PVR of 19 mL with 95% of subjects having a PVR < 100 mL [116]. In another study, women with LUT symptoms showed an average PVR < 30 mL in 81% of cases; larger volumes were associated with increasing age, higher grades of POP, and increased prevalence of recurrent urinary tract infections [121].

BLADDER WALL THICKNESS MEASUREMENT FOR THE DIAGNOSIS OF DETRUSOR OVERACTIVITY

In 1994, Khullar et al. showed a significant difference in the bladder wall thickness (BWT) of female patients with detrusor overactivity (DO) and controls (6.7 ± 0.6 mm vs. 3.5 ± 0.6 mm, respectively). In 1996, US evaluation of BWT was proposed as a diagnostic tool to identify patients with DO, since 94% of women with a urodynamic diagnosis of DO had a BWT > 5 mm. Confirmatory data were published in 2002 and 2003. The lack of standardization in the US measurement of BWT hampered a more widespread adoption in daily practice. Promising results on automated measurement of BWT were published and confirmatory data are eagerly awaited [122,123]. Although several papers confirmed the diagnostic value of BWT measurement for the diagnosis of DO, a retrospective analysis of a patient cohort undergoing perineal US for pelvic floor evaluation showed only a low diagnostic accuracy of BWT measurement [124]. Automated systems for the measurement of BWT and US estimated bladder weight did not provided yet the expected improvement in the measurement accuracy and standardization of the technique.

IMAGING OF PELVIC FLOOR MUSCLES

Different groups have investigated pelvic floor anatomy [204] and biomechanics [125–130,205] and much progress has been made in recent years. Computer models have shown that the pelvic floor muscles need to stretch 3.3 times their normal muscle length [130]. Avulsion traumas of the levator ani muscle (LAM) from the pubic bone have been shown to be associated with POP in the anterior and central compartment [131,132], even if not every LAM defect described on US correlates with increased hiatal distention or bladder neck descent [206,207,210]. Recently, the moment of inertia of the pelvic floor muscle (PFM) has been evaluated as a new parameter of pelvic floor damage involved in the pathogenesis of POP [209]. From a clinical standpoint, however, research on imaging still needs to provide an answer to the hypothesis that information on pelvic muscles morphology can predict the outcome of physical and surgical intervention for UI and POP. US and MRI seem interchangeable when evaluating pelvic floor anatomy at rest [211].

The evaluation of pelvic floor function may be considered as an integral part of the physical examination in patients with UI or POP, and US is increasingly used for this purpose. US imaging of pelvic floor muscles during exercise has been used as a strong biofeedback for the patients undergoing pelvic floor rehabilitation [133,134]. The importance of good pelvic floor function is proven by the significant therapeutic effect of pelvic floor rehabilitation in UI. Significant changes in imaging parameters were found following exercise, including bladder neck resting position [135], PFM thickness [136], and levator hiatus area [212,213]. Parameters like the cranial lift of the urethra in relation to the pubic bones during squeezing, the dimension of the genital hiatus, and the posterior anorectal angle were measured on US, but the sensitivity of US parameters may not be enough to assess the state of PFM function, and even correlation with data obtained from palpation and perineometry is still under debate [27,137–140,214].

Measurements of pelvic muscle thickness and volume may be performed with 3-D US (Figure 37.13) and MRI [22,141–144], but only low test–retest and interobserver variability have been observed [22,145,146]. Normative data in healthy controls and athletes have been published [102,136,147]. As one could expect, pelvic floor muscles were found to be thinner in women with POP [24,148–150] or UI [148,151] and their genital hiatus was larger [152]. Women who undergo regular exercise had thicker muscles compared to controls [147] and Chinese women had thinner muscles than Caucasians [144]. Pelvic floor function depends on the integrity of its different muscles (Figure 37.14). The levator ani, or in more detail the sling of the puborectal muscle, may suffer avulsion from the pubic bones in vaginally parous women who have delivered vaginally [215], and the risk of trauma increases with maternal age at first delivery [153]. Levator trauma has been observed at the time of labor but no effective therapeutic measures have been identified [154,155]. Muscle detachment is best visualized when the muscle contracts as this maneuver increases the gap with the pubic bone. On an axial plane, the loss of the characteristic H shape of the vagina is an indirect sign of levator ani detachment [112,156], and it is considered to correspond to what was previously described as paravaginal defects [157–160]. Methods for quantification of muscle defects on MRI [161] and US imaging [143] have been proposed; levator–urethra gap, levator–symphysis gap, and puborectalis attachment width may be diagnosed reliably by both techniques [216]. MRI is attractive and promising but still may fail in detecting LAM defects [217]; thus, new techniques have been explored and diffusion tensor imaging with fiber tractography seems to allow a good 3-D visualization of pelvic floor [218].

Levator ani detachment (Figure 37.15) observed on US and MRI is associated with a two- to sixfold increase in the risk of POP irrespective of hiatal area enlargement [154,216,219–222] in the anterior and central compartments [131,162] and of fecal incontinence (FI) [220,223,224]. Avulsion of the muscle did not seem to be associated with an increased risk of SUI [163], and overall, LUTS are less frequent in women with POP and major LAM injuries rather than in women with minor LAM defects [225]. Muscle detachment from the pubic bone is associated with decreased muscle strength on physical examination [157], with a more caudal position of perineal structures and larger hiatus at rest or during physical exercise, irrespective of POP [226,227]. LAM defects as described on MRI correlate well with outcome of POP surgery, the major defects being associated with worse vaginal support after surgery. The correlation between detection of avulsion on 3-D US imaging and palpation is poor [164] mainly due to high interobserver variability in the physical examination of muscle defects unless adequate training and expertise are available [165,228,258]. The measurement of the genital hiatus on US (Figure 37.16) is a reproducible measurement [22,156,220], and data at rest correlate well with MRI data, although a lower degree of correlation was found during Valsalva [142,145]. Values of >30, >35, and >40 cm^2 were described as mild, moderate, and severe ballooning of the genital hiatus [166]. In nulliparous women, areas of 6–36 cm^2 have been measured [147,152]. Vaginal delivery was associated with an enlargement of the levator hiatus [167,230,231]. Hiatal dimensions at rest, at contraction, and in some cases at Valsalva were further correlated with the severity of POP [129,143,149,208,229]. A recent study has shown that virtual reality measurements of the levator ani hiatus volume are comparable to those obtained with conventional 3-D ultrasonography [232]. On MRI of the dimensions of the bony pelvis at the level of the muscular pelvic support, no differences in these dimensions could be found between women with and without POP [161,233].

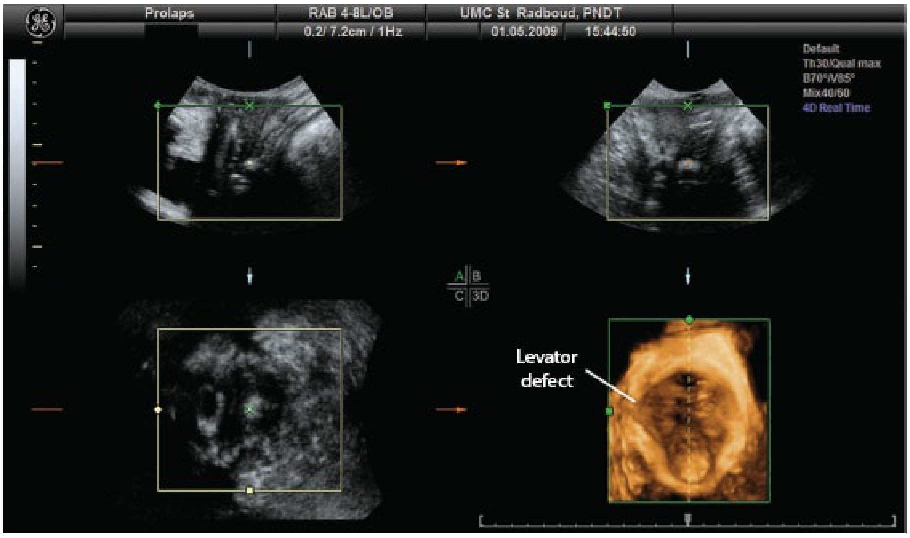


Figure 37.13 Perineal midsagittal (left upper), coronal (right upper), and axial (left lower) two-dimensional view and three-dimensional rendered image (right lower). The rendered image suggests a right-sided levator defect, which needs to be confirmed in the tomographic ultrasound imaging.

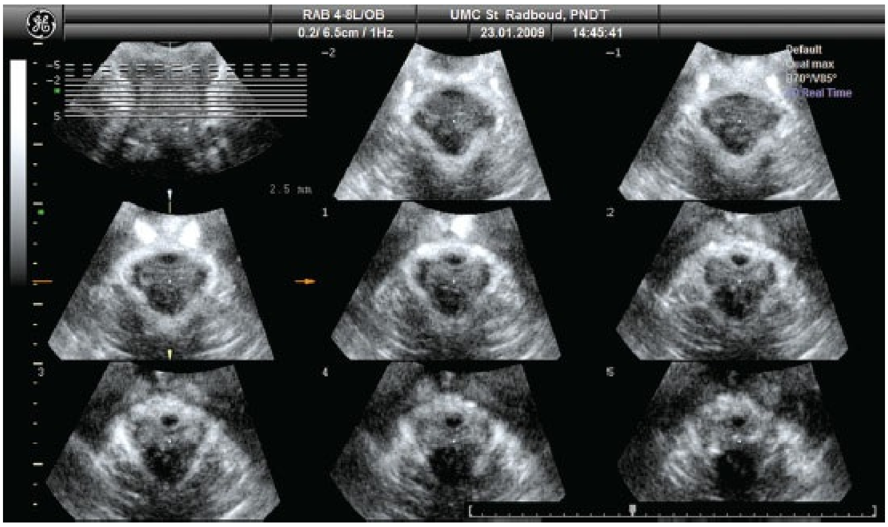


Figure 37.14 Tomographic ultrasound imaging in oblique axial plane. Normal attachments of the levator ani muscle.

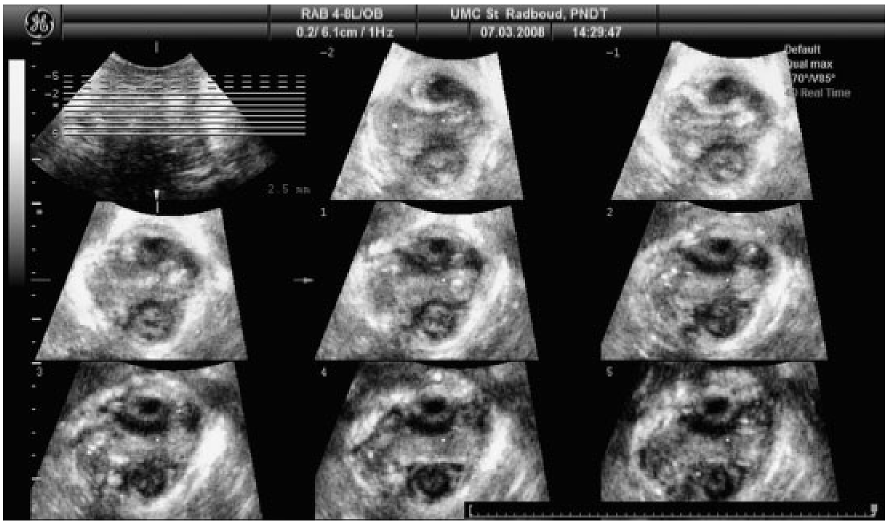


Figure 37.15 Tomographic ultrasound imaging in oblique axial plane. Right-sided avulsion of the levator ani muscle from the symphysis pubis (levator defect).

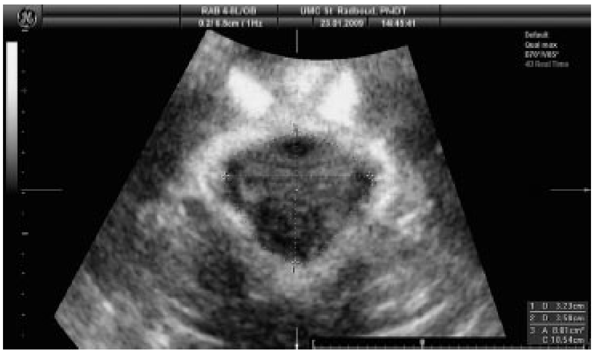


Figure 37.16 Perineal two-dimensional image in oblique axial plane. Measurement of hiatal dimensions.

US imaging and MRI are both appropriate methods in the investigation of the integrity of sphincter ani muscle. On US, the internal anal sphincter can easily be visualized, whereas for the external sphincter, more expertise may be needed [168]. A recent study has shown that thickening of the internal sphincter occurred with increasing age, whereas only thinning of the external sphincter correlated with fecal incontinence but not with aging [169]. Together with EAS injuries during delivery, levator ani major defects seem to contribute to the development of FI [223].

IMAGING OF PELVIC ORGAN PROLAPSE

There is a large natural variability in the degree of pelvic organ descent for all three compartments in nulliparous and parous women, with at least 15% of nulliparas showing functional abnormality of the LAM [234]. After delivery, an increase of pelvic organ mobility was found in all compartments [170]. A correlation was also found between increase of organ mobility, length of the second stage of labor, and mode of delivery. Operative vaginal delivery was associated with the highest rate of increase in pelvic organ mobility. Generally speaking, the effect of vaginal delivery on pelvic organ descent is more evident in the anterior and central compartment than in the posterior one [171,172]. The first delivery has a larger impact on bladder neck descent than the subsequent ones [89]. Interestingly, pelvic organ mobility is not merely a negative factor as US imaging performed during pregnancy showed that a larger bladder neck mobility and a larger and more distensible genital hiatus were associated with normal vaginal delivery [172,173]. On the other hand, women with anterior POP have a 67% more compliant support system compared to women without POP, and levator ani deficiency severity is associated with grade of POP [235,236]. Unfortunately, greater bladder neck descent is also associated with a higher risk of UI [28].

The sensation or visualization of a bulge in the vagina has shown to be the only symptom that correlated with the degree of POP [174,208]. This finding was irrespective of the method used for the quantification of the degree of POP: POP quantification (POP-Q), dynamic MRI, or US imaging [175,237]. There is one study where POPQ predicted prolapse symptoms better than US [176] and another where levator hiatal area as measured by 3-D US is strongly associated with signs and symptoms of POP [131]. A cutoff of more than 6 cm for genital hiatus (gh) plus perineal body (pb) that is equivalent to hiatal area on US seems to show optimal sensitivity and specificity in predicting objective and subjective prolapse, as well as prolapse recurrence after surgery when gh + pb is equal or more than 8.5 cm [149,238–240]. Moreover, recent findings recommend sustained Valsalva maneuver for at least 6 seconds or two to three times to best assess hiatal distention and POP by transperineal US, and this might further ameliorate imaging techniques specificity, if properly performed [241,242,259,260]. In MRI, various reference lines for quantification of POP have been studied, and the pubococcygeal line had shown minor superiority [25,177]; thus, for the sake of standardization, the use of this line has been advocated, but more recently, the MPL has been employed with success [243,244], and the LASV, the volume bounded inferolaterally by the levator ani muscle, has shown good correlation with clinical findings [245]. Of note, MRI allows the dynamic study of the pelvic floor with at least two different pulse sequences—true FISP and HASTE—which may contribute to a better patient assessment than other techniques [246]. In US, the lack of a reference line through two bony points is an obvious limitation. A horizontal line passing through the lower margin of the symphysis pubis has been used [178], whereas a line through the anal canal is used as a reference point to quantify the severity of rectocele (Figure 37.17) [178]. A cutoff value of 15 mm for descent below the line through the symphysis and of 20 mm for the depth of a rectocele has been proposed as a threshold for symptomatic prolapse [179]. Good reproducibility and correlation have been shown for the anterior compartment as assessed on MRI and US imaging [20,178,180] and physical examination. The assessments may thus be interchangeable and the additional value of imaging techniques seems limited in this compartment, as well as in the central one [20, p. 176,247]. Imaging of the posterior compartment has also been explored in several studies [179,181,184]. Poor, moderate, and good interobserver variability in US imaging and MRI has been described [100,177,182,185]. Comparison of x-ray imaging and US showed similar rates of detection for enteroceles (71%) [184]. Although US and clinical staging or intraoperative findings correlated well [24,181,183], one-third of patients with clinical enterocele (Figure 37.18) were negative on US. Furthermore, no clinical benefit has been identified from US imaging of enteroceles, while MRI seems more accurate [247]. The posterior anorectal angle can be measured on US with a good degree of correlation with defecography [179,184,186]. The clinical meaning of perineal descent and the best assessment method has not been fully unraveled. MRI is able to identify high rates of posterior prolapse, especially when the MPL line is employed, even those without clinical significance [20,244,248,249]. In four studies, which have assessed the correlation between POP symptoms and perineal descent on US imaging, MRI, and defecography, a statistically significant correlation was observed in all studies [174,175,184,187,250]. Although imaging of POP is captivating, the question whether imaging is superior to clinical examination remains open.

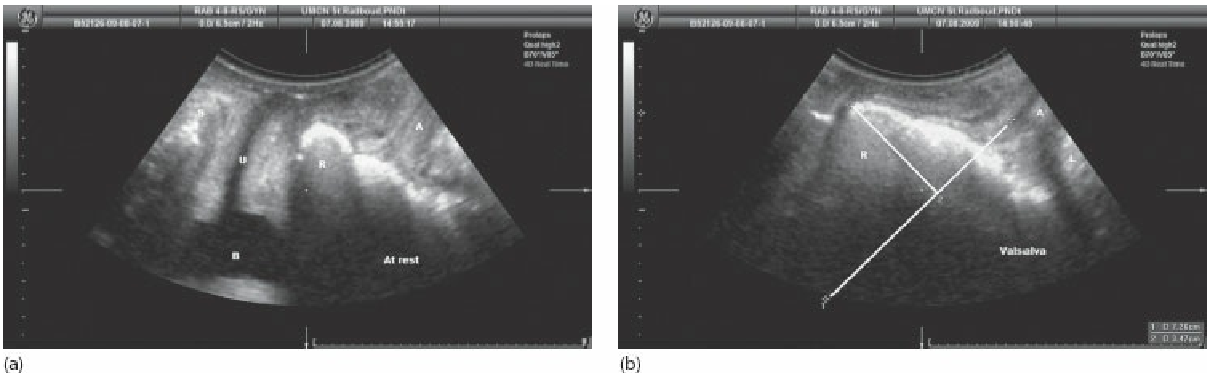


Figure 37.17 Perineal midsagittal two-dimensional view at rest (a) and on Valsalva (b) in a woman with rectocele. The measurement of the depth of the rectocele is performed perpendicular to a straight line through

the anterior border of the anal sphincter complex (3.47 cm). *Abbreviations*: S, symphysis pubis; U, urethra; B, bladder; R, rectum; A, anus; L, levator ani muscle.

ULTRASOUND IMAGING AND SURGERY FOR URINARY INCONTINENCE AND PELVIC ORGAN PROLAPSE

The role of US imaging during and after incontinence surgery has been investigated. Researchers have tried to standardize the amount of bladder neck suspension during the Burch procedure and to correlate the relative position of urethral slings and the urethra with the outcome of surgery. Actually, no definitive conclusions can be drawn on the relation of sling position, resolution of POP rather than UI, or postoperative complications [172,188–196,251]. In some studies, tension-free vaginal tapes were found to be positioned more cranially compared to transobturator tapes and caused more urethral kinking during straining; nevertheless, comparable cure rates were achieved [197,198]. US imaging is clearly superior as compared to other imaging techniques regarding the visualization of polypropylene mesh materials (Figure 37.19) as used in POP and UI surgery, and it had been also successfully employed to correlate vaginal anatomical and functional changes following colpocleisis surgery [252]. US also demonstrated a change in levator hiatal biometry following POP repair, revealing a reduction in hiatal area but no changes in hiatal distensibility [253]. Various studies have recently explored the causes of POP relapse, such as mesh dislodgment or preoperative LAM avulsion, but no conclusive data have been obtained yet [199–201,254]. In this field, MRI has been evaluated as a promising technique [255,256]. The use of MRI has proven to be of certain value in evaluating the outcome of surgery, but only as regards the apical compartment, no correlation among MRI imaging, POP-Q, and symptoms was observed [257]. US imaging of bulking agents injected for SUI (Figure 37.20) showed a good correlation between the height and volumes of the injected collagen bulges and clinical outcome, with a collagen volume of 2.8 mL considered to be ideal [202,203].

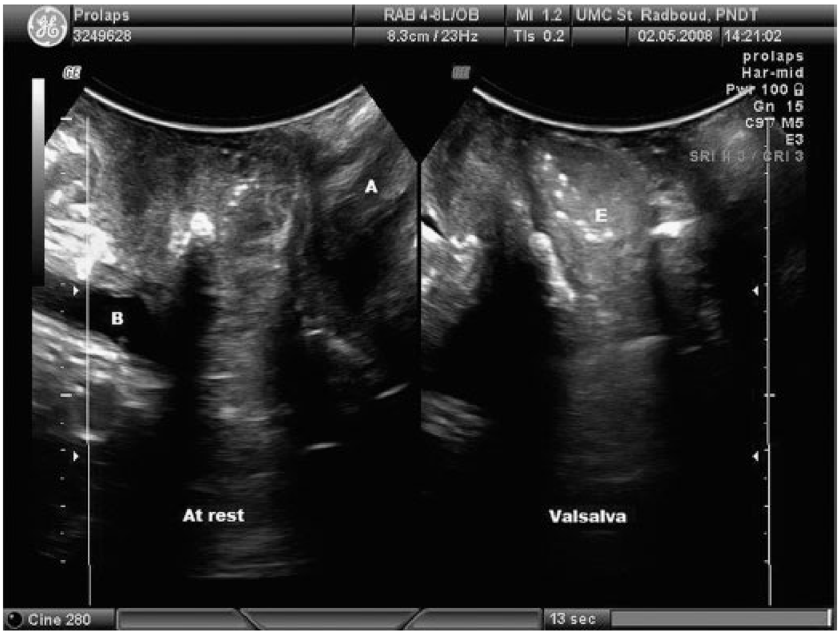


Figure 37.18 Perineal midsagittal two-dimensional view at rest and on Valsalva in a woman with enterocele. *Abbreviations*: B, bladder; E, enterocele; A, anus.

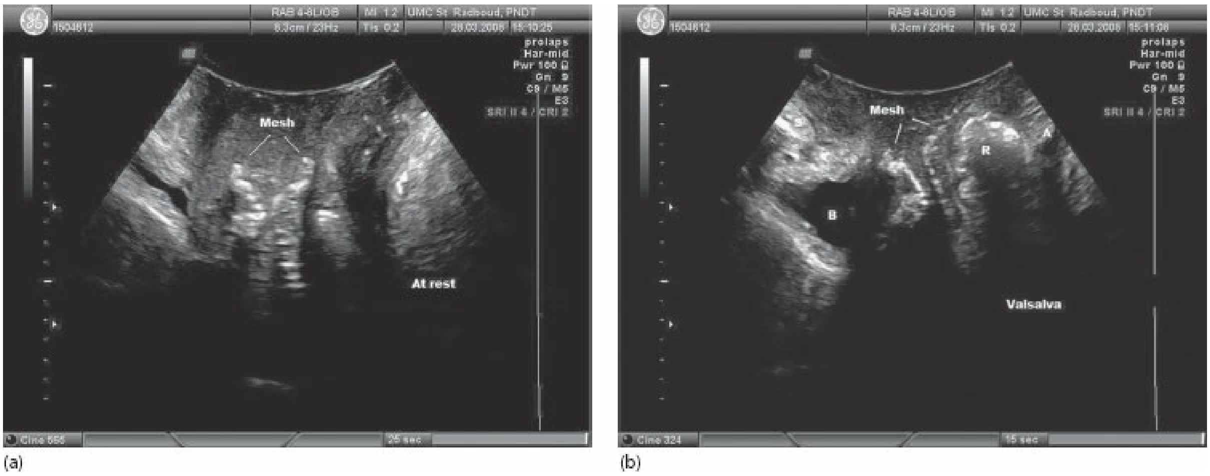


Figure 37.19 Perineal midsagittal two-dimensional view at rest (a) and on Valsalva (b) in a woman with polypropylene mesh (prolift anterior and posterior). *Abbreviations*: S, symphysis pubis; B, bladder; R, rectum; A, anus.

CONCLUSIONS

Research into US imaging of the pelvic floor in UI and POP continues to be active and the quality of the published data was increased significantly over the last decade. Imaging is a powerful tool for research into UI and POP pathophysiology. Both US and MRI proved to be comparable to physical examination and sometimes superior although this rarely translates into a real clinical benefit. Research in this area has proved to be inventive, innovative, and prolific thanks to a widespread use of US systems in urological and urogynecological offices. The evidence currently available should be carefully scrutinized to identify areas of consensus and areas that still need further verification and confirmation. The lack of proven clinical utility should not reduce our research efforts and imaging is a powerful approach to improve our understanding of LUTDs.

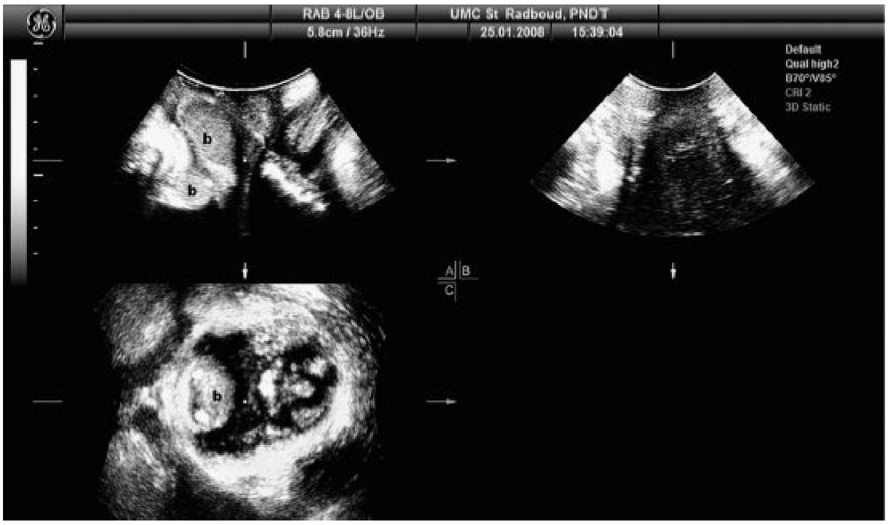


Figure 37.20 Perineal ultrasound imaging in a woman following periurethral bulking agents for stress urinary incontinence. Midsagittal (left upper), coronal (right upper), and axial (left lower) two-dimensional view. *Abbreviation*: b, periurethral bulking agent.

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38 Magnetic Resonance Imaging in Urogynecology

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INTRODUCTION

True insight into the mechanisms underlying pelvic organ prolapse (POP), urinary incontinence, and fecal incontinence requires an appreciation of the pelvic anatomy, including the muscular and ligamentous mechanisms. These relationships in the asymptomatic population, and the deficiencies seen in symptomatic women, require an approach able to assess the anatomical relationships both in a static situation and also when undergoing physical stress. Cross-sectional imaging is able to achieve this and gives valuable insights from which our current knowledge-base can be developed. In addition, for individual patients, MRI scanning can offer supplementary information as needed for diagnostic understanding with a view to treatment. MRI has shown rapid technical development in recent years, and it is now able to offer detailed insights using a range of protocols and modalities, in combination with physical manipulations of the scan subject. Such progress is invaluable for understanding female pelvic floor anatomy for populations and individuals, understanding the changes evident in symptomatic situations, identifying women potentially at risk of future problems, and understanding impact of past events, such as childbirth or surgery.

MRIs map 3-D anatomy, which is generally displayed in standard orientations (coronal sections, sagittal sections, or transverse sections). With MRI, it is possible to see the individual lower urinary tract and genital structures, the individual muscles of the pelvic floor, and the bony structures. Furthermore, additional post-imaging processing can focus on specific aspects of interest and potentially display the anatomy in three dimensions. Comparisons between MRI and formal anatomical dissection in cadaveric specimens [1] have served as a validation supporting the conclusions of MRI findings.

MRI was generally used statically in specific situations, such as investigation of urethral diverticula. This is now augmented with dynamic imaging, in which a series of scans are obtained at rest and during movement or function (e.g., squeezing, straining, or defecation). This is especially contributory for preoperative assessment of patients with multicompartment POP defects and failed surgical POP repairs. Not only is MRI an indispensable tool for clinical decision making, but it also has tremendous potential as a research tool in trying to understand the pathophysiology of these complex disorders [2].

MRI Methodology

MRI scanning uses strong magnetic fields and radio waves, without the involvement of ionizing radiation. A strong magnetic field is placed around the subject, and the scanner detects a radiofrequency signal emitted by excited hydrogen atoms. The strength of the magnetic field is measured in tesla units, with most MRI systems currently operating at 1.5 T. Increased magnetic strengths are commercially available, and the technological development means magnetic field strength is likely to evolve foreseeably. Stronger magnets currently require superconduction in very cold temperatures (liquid helium). Permanent magnets can also be used to generate weaker fields, and these have the potential to create a non-enclosed MRI scanner.

Contrast between different structures is ascertained from the rate at which excited atoms return to the equilibrium state. The nature of return to the equilibrium state involves two independent processes of T1 (spin–lattice) and T2 (spin–spin) relaxation. T1 is basically representative of the different amounts of magnetization recovery, which is achieved by changing the repetition time. T2 is the difference in magnetization decay and is achieved by changing the echo time. Distinguishing T1 and T2 gives different imaging displays that may enhance detection of specific aspects, and both approaches are typically used in scanning protocols. For example, T2 is good for detecting edema and for assessing zonal anatomy, such as in the uterus. Contrast agent, comprising gadolinium and a chelating agent, can also be administered intravenously.

Static sequences are obtained mainly using T2-weighted axial and sagittal planes. Dynamic sequences use single-slice ultrafast acquisitions during the tested activity, in coronal and axial planes (Figures 38.1 and 38.2). The T2-weighted sagittal sequences are useful to show the bladder neck and the cervix. Sagittal acquisitions help to adjust coronal images by identifying the midline of the pubic symphysis and the anatomical landmarks. Coronal planes explore dynamic physiology of the levator muscles. Measurement of the urogenital hiatus and detection of levator ani injuries can be performed in axial plane images [3].

Imaging Protocols

There are many protocols for MRI scanning. A specific approach has been described for female pelvic MRI acquisition [4,5]. Before scanning, the patient is asked to empty her bladder and she should have clear explanation of what to expect, including instructions in any dynamic maneuvers that may be required, e.g., straining. A multicoil array is placed in position, reaching sufficiently inferior that any POP is fully captured. A standard axial fast spin echo sequence is taken to achieve high-resolution axial images of the pelvic organs, muscles, and supporting connective tissues.

For dynamic imaging, a midline slice should include the symphysis, bladder neck, vagina, rectum, and coccyx. If necessary, two contiguous locations may be specified where it is not possible to fit all structures into a single imaging slice. The patient is then asked to strain at maximum effort. T2-weighted imaging of the sagittal midline images is then obtained with image acquisition aiming to take less than 3 seconds. Dynamic MRI is generally done with the patient supine and with her thighs flexed. Dynamic MRIs with opened antennas are now available to realize the acquisitions in a standing or a sitting position (e.g., with defecation). Nonetheless, it is not certain that imaging in a standing position improves its relevance [3].

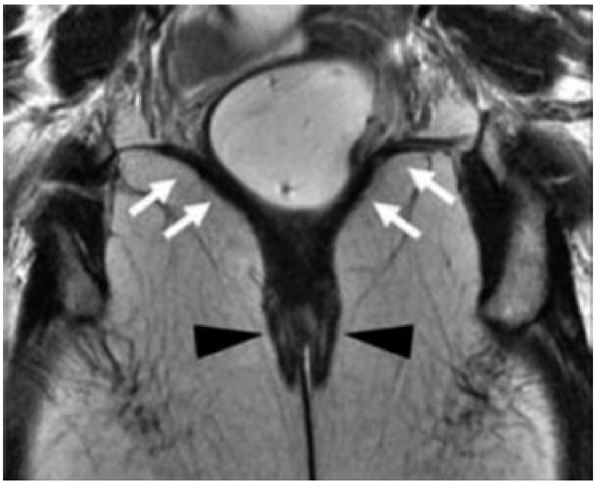

Figure 38.1 MRI of normal female pelvic anatomy in the coronal plane. There is normal thickness and symmetry of levator ani, iliococcygeus, and pubococcygeus muscles (white arrows), which align with puborectal muscle fibers of the anal sphincter (black arrowheads).

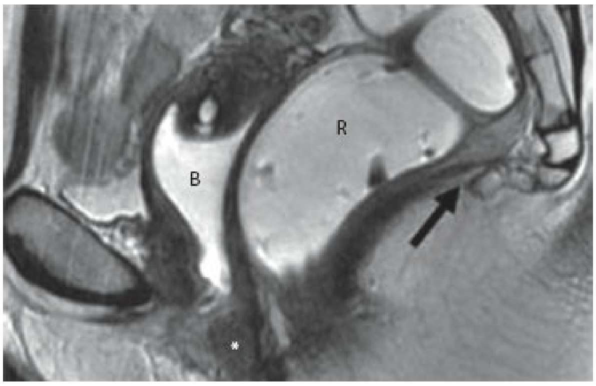

Figure 38.2 MRI of normal female pelvic anatomy in the axial plane. The puborectalis muscle forms a sling around the rectum. Posteriorly, the fibers fuse anterior to the coccyx to form a midline structure, the levator plate (arrow). *, perineal body; B, bladder; R, rectum.

Imaging Artifacts

MRI scan images are captured in a sequence of “slices,” taken in parallel along a line related to the scanned subject. The relationship to the subject can be varied, but there is a risk of errors in linear and angular measurements, termed “slice angle errors.” Accordingly, accurately ascertaining linear measurements on 2-D images requires a standardized and consistent approach between subjects, or conversion to a 3-D image from which to take measurements.

“Chemical shift” artifact is a separate problem that can cause apparent discrepancy in size for equivalent structures on opposite sides of an axis. As a consequence, within subject comparisons of dimensions for different sides may be unreliable, and between-subject comparisons invalid, unless the scanning parameters are set up appropriately and maintained consistently throughout the entirety of data acquisition.

Safety

The strength of magnetic field means that MRI is contraindicated in the presence of cardiac pacemakers, cochlear implants, and some other surgical implants. The presence of any internal metal fragments, body-worn metal (jewelry), or stray metal objects in reach of the magnetic field also have to be excluded for the safety of the patient and the scanner.

The patient undergoing scanning is placed in a confined environment, and this is problematic for patients prone to claustrophobia. Careful support for such patients and use of suitable medications according to hospital practice may be warranted. Permanent magnets have the potential to create an open (non-enclosed) MRI scanner that might be helpful in situations where a patient cannot tolerate a confined space.

Gadolinium side effects may include headache, nausea, and temporary dizziness in 1%–5%. A feeling of coldness may occur at the injection site. Anaphylactic reactions occur in about 1 in 10,000 people. Gadolinium contrast medium should be avoided in patients with kidney disease (chronic or acute). Case reports of nephrogenic systemic fibrosis, leading to skin contractures and organ failure, have been described with gadolinium contrast in a minority of patients with preexisting severe renal dysfunction.

For women in the first trimester of pregnancy, safety is uncertain, but it may be preferable to alternative options [6,7].

MRI CHANGES IN SYMPTOMATIC WOMEN

Alterations in the vaginal shape can clearly be demonstrated in women with POP using MRI [8]. T1 signal intensity can identify muscle atrophy in women with stress urinary incontinence (SUI) [9]. The likelihood of a role for levator weakness can be appreciated in women with SUI, and such laxity and thinning of the levator ani muscle in SUI have been reported [10]. However, it is likely that there is degree of overlap between symptomatic women and asymptomatic nulliparous women [11]. In women with SUI, the bladder neck lies close to the pubic symphysis, the lumen of the vagina has a widened H-shape, and the urethropelvic ligaments are near horizontal. The urethropelvic ligaments were reported to attach to the lateral aspect of the urethra to the medial aspect of the levator sling [12].

For some symptomatic women, bony changes may be evident: the transverse inlet can be wider, the intertuberous and interspinous diameters can be increased, the sacral length can be increased with a deeper curve, and the anteroposterior outlet can be narrowed [13]. The technology for 3-D imaging continues to develop, and progress in understanding clinical anatomy of the levator ani and bladder neck [4] will continue. For example, 3-D reconstruction has been undertaken to compare asymptomatic women with women found to have urodynamic stress incontinence or symptomatic POP [5]. The latter study reported the levator–symphysis gap as a marker for disruption of the attachment of the anterior puborectalis attachment.

The urethra can be imaged effectively using MRI. For example, urethral diverticula can be visualized clearly (Figure 38.3a through d). In addition, placement of an MRI coil vaginally can demonstrate the periurethral and perivaginal connective tissues [14] and the location of the striated urethral sphincter [15].

Puborectalis is uniformly intact in nulliparous women [16] (Figure 38.4a). In primiparous women, around 20% have some degree of structural defect or deviation (Figure 38.4b and c). If a disruption is present at the attachment to the superior pubic ramus, there is a high prevalence of SUI [16]. Such disruptions correspond with a reduction in maximum urethral closure pressures (MUCPs), associated with reduction in the voluntary increment in MUCP during pelvic floor muscle contractions [17]. Taken together, these findings would suggest that vaginal childbirth may weaken the urethral closure mechanism, thereby disposing the patient to urinary incontinence.

MRI in asymptomatic nulliparous women shows some structural differences between African-American and Caucasian-American women, which may be relevant to potential for subsequent development of pelvic floor problems. Nulliparous African-Americans have significantly thicker levator ani muscles [18] and a higher urethral volume [19]. Functionally, they have higher resting and squeezing MUCPs in comparison to the Caucasian women.

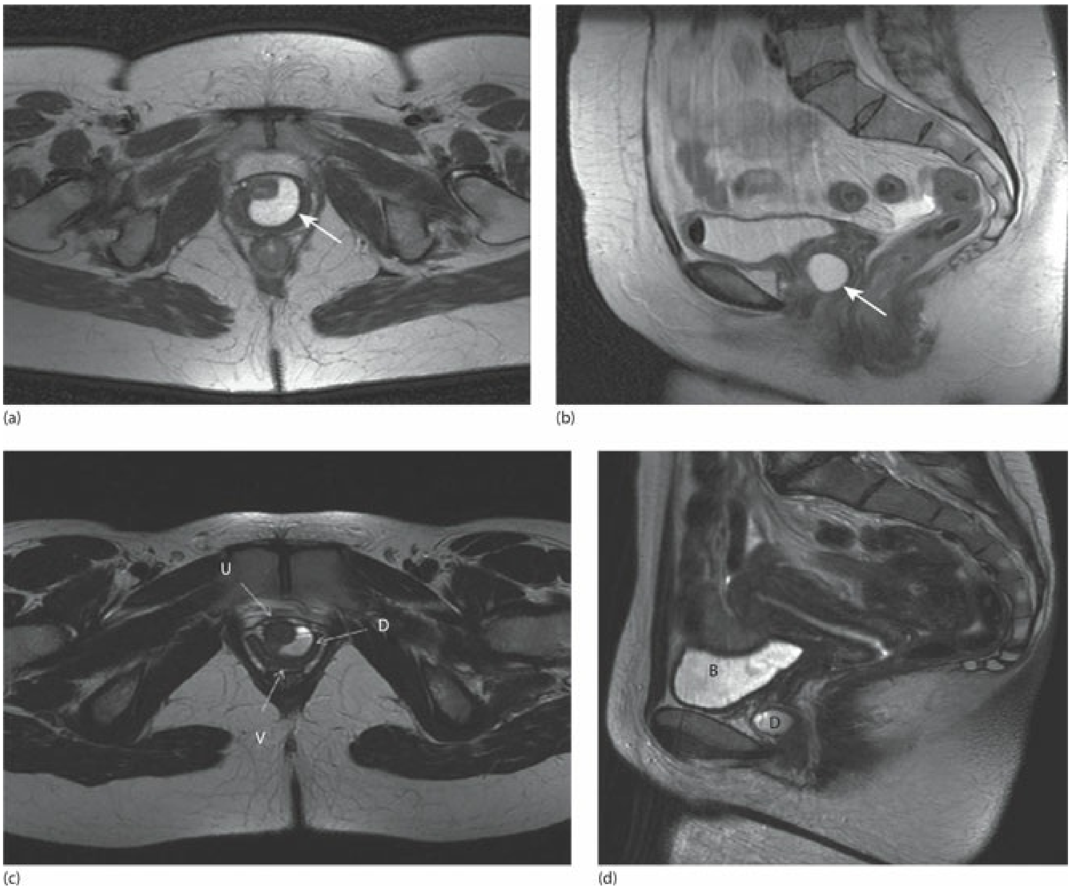

Figure 38.3 MRI in female patients with urethral diverticula. (a, b) Case 1: (a) the diverticulum (arrow) in the

transverse plane; (b) same case in the sagittal plane. (c, d) Case 2: (c) the diverticulum in the transverse plane; (d) same case in the sagittal plane. B, bladder; U, urethra; D, diverticulum; V, vagina.

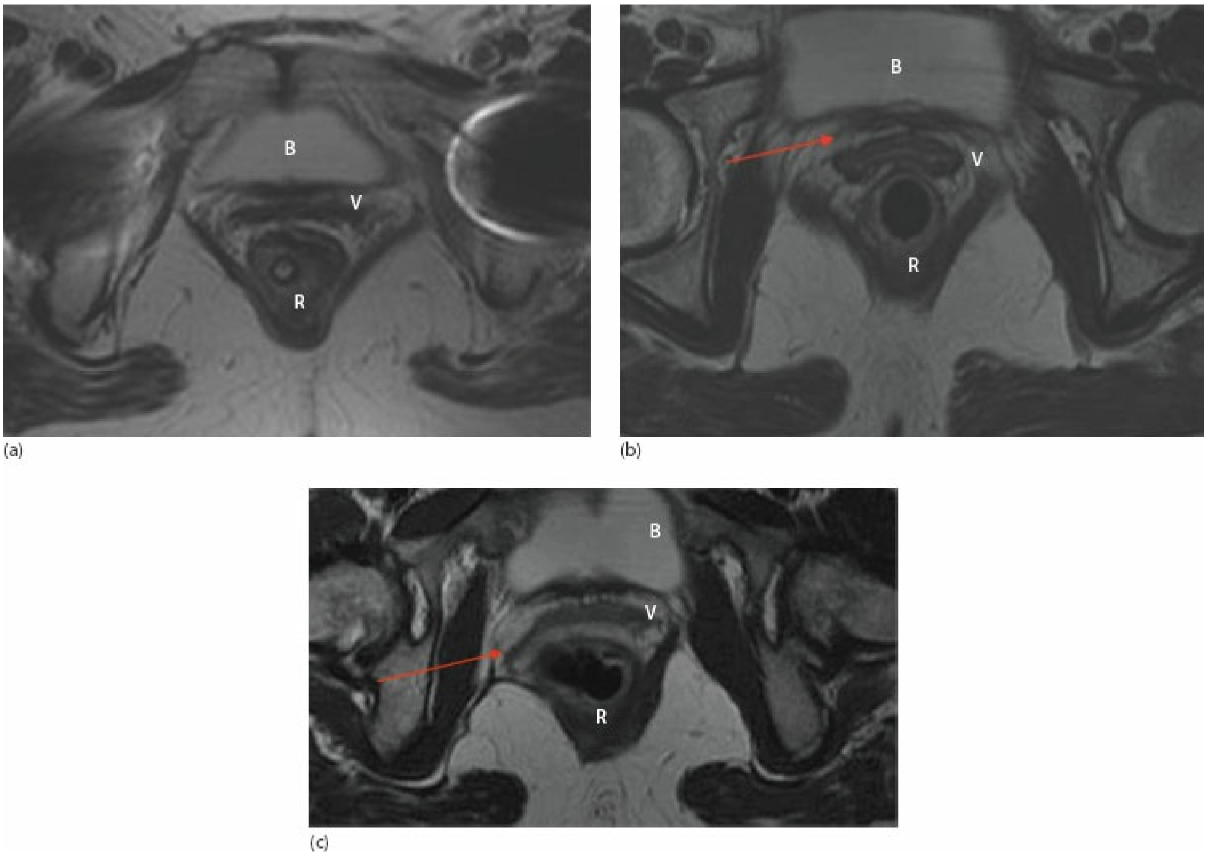

Figure 38.4 MRI images of vaginal anatomy. B, bladder; V, vagina; R, rectum. (a) Normal vaginal anatomy. (b) Mild fascia lateral defect (red arrow). (c) More severe fascia lateral defect (red arrow), with deviation of the posterior vaginal fornix.

Dynamic MRI has enhanced the understanding of pelvic floor anatomy and dysfunction. It has the advantage of detailed anatomical views of all three compartments at rest and during Valsalva. Several attempts to standardize MRI measurements have been made. Five midsagittal pelvic reference lines have been employed to quantify prolapse using MRI and used to measure the extent of prolapse [20]. The pubococcygeal line (PCL) (Figure 38.5), which is thought to approximate the plane of the levator plate, is the most widely used reference line for assessing POP, with an excellent intra- and interobserver reliability. It is a straight line between the inferior border of the pubic symphysis and the last coccygeal joint. The distance from the PCL to the bladder neck, cervix, and anorectal junction should be measured on images obtained when the patient is at rest and during maximal pelvic strain. MRIs allow us to obtain a contemporary visualization of different compartment defects [21] (Figures 38.6). In healthy volunteers, there is minimal movement of the pelvic organs with respect to the PCL, even during maximal strain [2]. Other parameters are the H-line, from the inferior border of the symphysis to the posterior wall of the rectum at the level of the anorectal junction, and the M-line, which goes perpendicularly from the PCL to the most posterior aspect of the H-line (Figure 38.5). The H- and M-lines tend to elongate with pelvic floor relaxation. With these landmarks, it is possible to standardize and to grade the prolapse severity. However, the concordance of measurements made with MRI with those made using clinical examination seems poor [22]. Hypotheses for this variability are the differences in the patient's position (dorsal lithotomy during MRI versus gynecological position during clinical examination), a different coactivation of the levator ani between MRI and clinical examination, and the use of a speculum in gynecological examination.

Betschart and colleagues have proposed a new standardized approach called the pelvic inclination correction system (PICS) [20]. Based on bony structures and the body axis, the PICS corrects for variation in pelvic inclination, at rest or straining, and allows for the standardized measurement of organ displacement in the direction of prolapse. It is widely recognized that the angle of pelvic inclination can change during specific maneuvers such as the Valsalva and Kegel maneuvers. This angle can also be affected by the way that an individual lies in the scanner (e.g., with knees supported versus legs extended). The optimal pelvic reference system should allow the investigator to compensate for these variations.

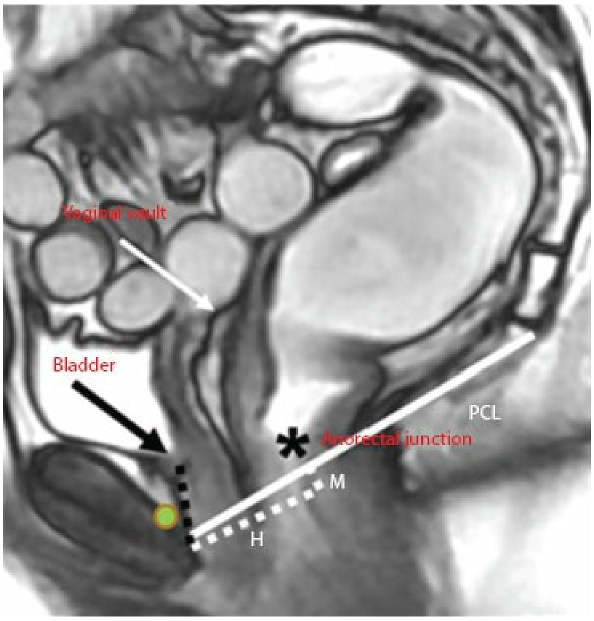

Figure 38.5 The most commonly used reference lines in female pelvic MRI. The *pubococcygeal line* (PCL), from the inferior border of the pubic symphysis to the last coccygeal joint. All the distances from PCL (bladder neck, cervix, and anorectal junction) are measured at rest and during maximal pelvic strain. The*H-line*, from the inferior border of the symphysis to the posterior wall of the rectum at the level of the anorectal junction. The*M-line*, perpendicularly from the PCL to the most posterior aspect of the H-line. The *green circle* denotes the urethral axis, which is vertical during straining and defection.

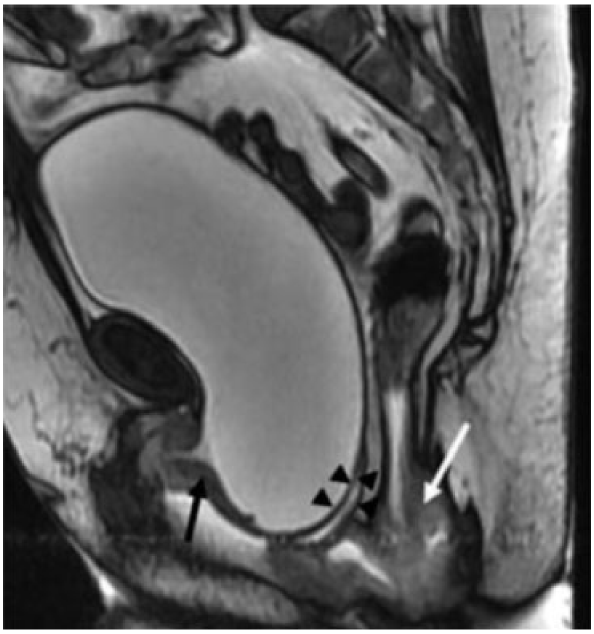

Figure 38.6 Large cystocele with urethral kinking (black arrow), which contributes to inefficient bladder emptying. The vagina is filled with sonographic gel (arrowheads); intra-anal full-thickness rectal invagination

(white arrow) at the level of the anal canal, thus impeding stool passage.

ADDITIONAL POSSIBILITIES WITH MRI

Magnetic Resonance Defecography

Defecatory dysfunction and fecal incontinence may result in the presence of impaired support due to rectocele or a deficient perineal body, or physical impedance as a consequence of POP. When the patient does abdominal straining, the additional pressure and altered organ positions may worsen the symptomatic issues. Intrinsic bowel issues, such as rectal prolapse or intussusception, are another substantial factor. MR defecography is a method for elaborating underlying issues of this type [23]. Contrast in a suitable medium is placed into the relevant body cavities, images at rest are obtained, and the patient is then instructed to undertake relevant physical activities to highlight the anatomical features during high speed scanning, ideally in the upright position.

MR defecography has an important role in the definition of particular situations involving the posterior compartment. Sagittal images during defecation can be used to recognize and differentiate an anterior or posterior rectocele (Figure 38.7a and b). The difference between rectal mucosal intussusception and rectal full-thickness intussusception can only be inferred at conventional defecography (Figure 38.8a and b), and it is relevant, as the treatment for the two conditions is different. Furthermore, in the case of enterocele, MRI can identify the content of the peritoneal cul-de-sac (Figure 38.9a and b), which may be fat or bowel loops. Using MRI, it is also possible to recognize particular situations that may be difficult to diagnose only by clinical examination (Figure 38.10).

MRI in Postoperative Evaluation

Another application of MRI is the evaluation of complications or recurrence after POP repair. Dynamic MRI can verify the effectiveness of support of anterior and posterior pelvic floor structures, for example, after placement of polypropylene mesh implants. Postoperative dynamic MRI might also be helpful to understand the development of recurrent POP and to support its early detection. Siegmann and colleagues [24] demonstrated that dynamic MRI could detect clinically occult cases of POP 3 months after pelvic floor repair in 73% of the cases. These postoperatively detected pelvic floor dysfunctions are probably caused by preexisting multicompartment defects that were not detected in the preoperative clinical evaluation. POP due to defect in one compartment may suppress the symptomatic detection of a defect of another pelvic floor compartment. Hence, symptoms from another POP may be detectable once the leading pelvic floor compartment has been repaired. However, these occult recurrences did not correspond to clinical symptoms on short-term follow-up (3 months), so their diagnostic relevance has yet to be established. Notwithstanding, it is possible that dynamic MRI can reliably identify POP after pelvic floor repair before the onset of symptoms [24].

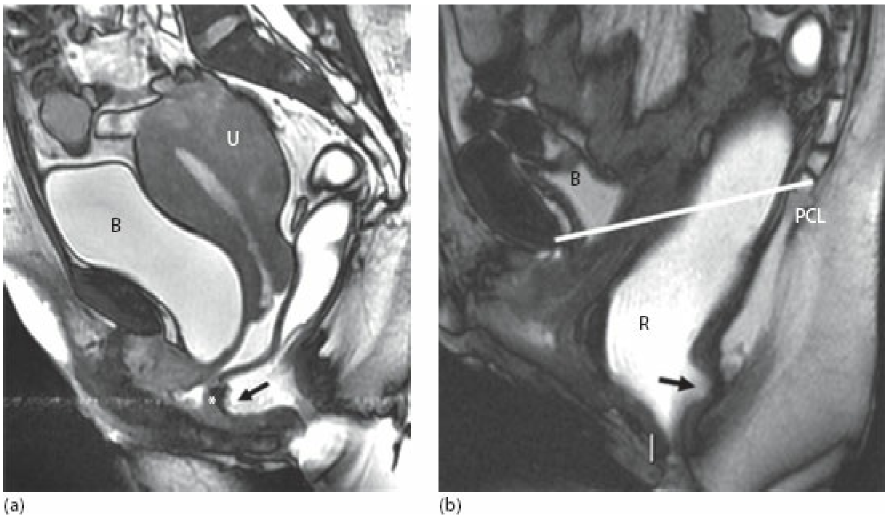

Figure 38.7 Posterior compartment. (a) Sagittal images during defecation. B, bladder; U, uterus; R, rectum; PCL, pubococcygeal line. Anterior rectocele is evident as an outpouching of the anterior rectal wall (arrow),

with stretching of the perineal body (*) and protrusion of the rectum into the vaginal lumen. (b) Severe perineal descent, incomplete opening of the anal canal and appearance of a small posterior rectocele (arrow).

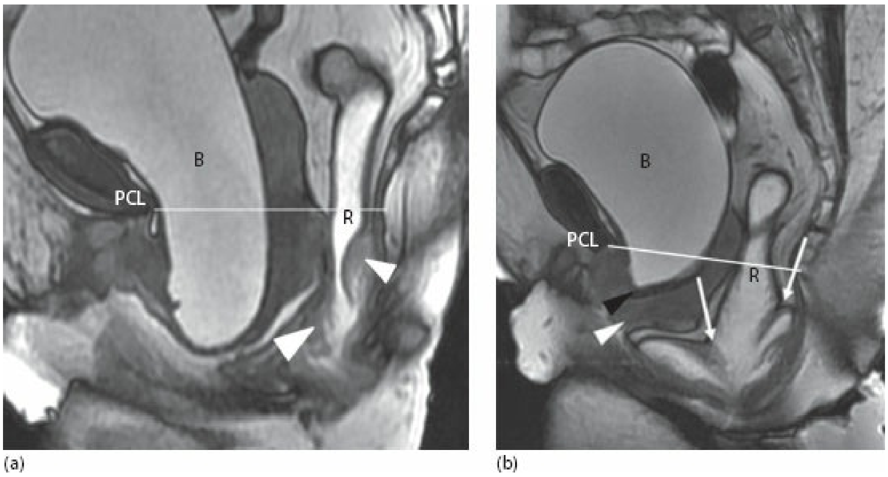

Figure 38.8 (a) Rectal mucosal intussusception. During defection, abnormal thickening and redundant infolding of the mucosal layer in the posterior and anterior rectal wall (arrowheads). Mucosal infolding occupies the rectal lumen and obstructs normal passage of stools. There is associated anterior and middle compartment prolapse. B, bladder; R, rectum; PCL, pubococcygeal line. (b) Intrarectal invagination (arrows). The invagination obstructs the rectal lumen causing intrarectal residue after defecation. Cystocele (black arrowhead) and cervical prolapse (white arrowhead) are associated. B, bladder; R, rectum; PCL, pubococcygeal line.

Several studies used dynamic MRI to investigate prolapse correction after sacrocolpopexy. MRI can be used not only to investigate clinical outcome but also to investigate postoperative pain or recurrent symptoms of prolapse by assessing suspected mesh infection, lumbosacral osteomyelitis, and integrity of mesh attachment [25].

Dynamic pelvic MRI is particularly useful to evaluate bowel dysfunction, as well as urinary stress incontinence, urgency, or retention. For example, when the posterior mesh is too short or is fixed with too much tension, the patient may complain of dyschezia or anal pain [26].

3-D Female Pelvic Floor Reconstruction

Computed integration of the image stacks can be used to extrapolate 3-D reconstructions of the subject anatomy. For female pelvic floor image reconstruction, specified structures (e.g., the component lower urinary tract or genital tract organs) are separately identified, which requires a combination of manual and semiautomated processing. Their surfaces are then rendered, i.e., the “gaps” between the respective organs in the successive slices are filled. Color-coding can be used to distinguish between specific structures. Variations in the color can also be used to portray additional facets, such as the altering thickness of muscle [27] or the bladder wall thickening in the presence of bladder tumors [28].

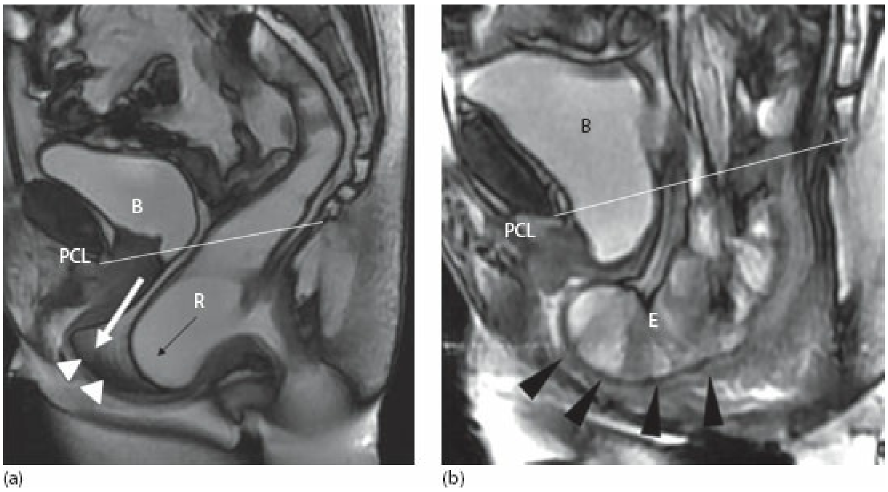

Figure 38.9 Enterocele MRI image. (a) Large anterior rectocele (black arrow). A peritoneal cul-de-sac (white arrows) herniating into the rectovaginal space, with a large fat-containing enterocele. B, bladder; R, rectum; PCL, pubococcygeal line. (b) In this case, at late defecation the rectovaginal space is occupied by a large enterocele (arrowheads). Rectocele and cystocele are contemporary present. B, bladder; E, enterocele; PCL, pubococcygeal line.

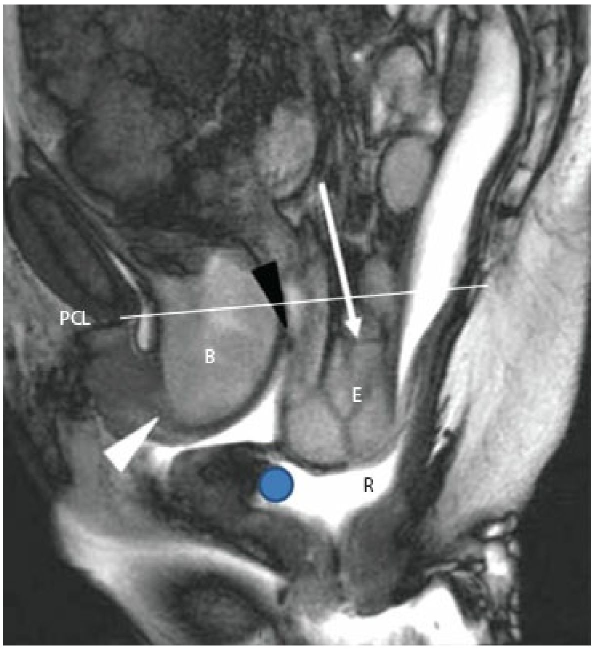

Figure 38.10 Cystocele (white arrowhead) and vaginal vault prolapse (black arrowhead) are present and associated with a large enterocele (E) that closes the rectal lumen causing obstructed defecation and incomplete emptying of the anterior rectocele (blue circle). B, bladder; R, rectum; PCL, pubococcygeal line.

Correspondence of data taken from a 3-D reconstructed structure with functional data measured in the same patient provides some validation of the processing. For example, volume data measured from 3-D image reconstructions of the external anal sphincter in nulliparous women correlate with the length of the high-pressure zone at squeeze in anorectal manometry [29]. The 3-D reconstructions can be used for planning surgical interventions, facilitating the surgeons' mental assimilation of the surgical anatomy in a quicker and more intuitive way than "scrolling" back and forth through the image stack.

A progression of the method is to simulate what might occur in particular events. For example, a simulation of childbirth using MRI of the bony pelvis and levator ani, and simulated passage of a fetal head shows the likely extent and location of stresses in the muscle [30] and that the strength of levator ani attachment could influence the extent of muscle stretch [31].

It is important to recognize that the reconstructions do not offer additional imaged information since the only patient-derived data come from the image stack; the 3-D reconstruction comes from assumptions delivered by computed algorithms that rely on the successive images in the stack being sufficiently close together to give adequate representation.

CONCLUSIONS

MRI gives a considerable amount of anatomical information, with some ability to observe pathological processes such as edema and inflammation. Techniques to generate new approaches to displaying the output have given extra opportunities to improve application of imaging in real-life contexts. Further technological developments offer new opportunities to understand how physical stresses affect structure and potentially relate to function.

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39 Endoscopy

Musaab Sarmad Yassin, John Michael Henderson, and Francis Xavier Keeley

INTRODUCTION

Endoscopy refers to the use of a telescope to directly visualize an internal structure or organ. It may be used in the evaluation of a patient with urological symptoms and demonstrate abnormalities such as malignancy, calculi, diverticula, or fistulae. Urethroscopy, cystoscopy, ureteroscopy, and renoscopy refer to endoscopy of the urethra, bladder, ureter, and kidney, respectively.

Endoscopy requires a light source, irrigating fluid, and endoscope (Figure 39.1). A camera is usually applied to the endoscope head to allow ergonomic use of the equipment. The irrigant fluid allows distension of the bladder and removal of blood or debris to allow a clear view. The most common fluid used is warmed 0.9% saline or sterile water. If electrocautery is planned, a nonconducting solution such as 1.5% glycine is required. Light is delivered to the tip of the endoscope via noncoherent fiber bundles demonstrating total internal reflection. The light source used is usually xenon, which is more expensive and a neutral tone, or halogen, which is cheaper, is a more yellow tone, and requires a white balance.

HISTORY

Urological diseases have been prevalent throughout the ages. Historical treatments for these diseases were often crude and delivered without asepsis or anesthesia. The lithotrite was an instrument inserted blindly into the male urethra to attempt to crush bladder calculi.

Developments in lens and light technology led to significant improvements such as the Nitze–Leiter cystoscope in 1879 [1].

A further revolution in design was achieved by Harold Hopkins, Professor of Physics at the University of Reading. His “rod-lens” system was a tube of glass with thin air lenses that replaced the traditional air tube with glass lenses. Karl Storz developed a system of transmitting cold light from an external source through noncoherent fibers to provide illumination. Their collaboration in 1966 produced a dramatically improved instrument of smaller diameter with a better image.

TYPES OF ENDOSCOPE

Urological endoscopes can broadly be divided into rigid, semirigid, and flexible scopes. Rigid telescopes employ the Hopkins rod-lens system by which light is transmitted to illuminate the target and the image is returned to the eyepiece. Various angles of telescope allow optimal visualization of parts of the urological tract. Zero-degree telescopes are ideal for urethroscopy, whereas cystoscopy requires a 12° or 30° scope. A 70° telescope allows the bladder neck to be thoroughly inspected. An offset eyepiece, as employed with nephroscopes, allows the introduction of straight instruments, e.g., ultrasonic or pneumatic lithotripsy. A semirigid endoscope allows a small degree of flexibility but is rigid enough to retain the advantages of a rigid endoscope.

Cystoscope sizes are expressed in French (Fr) that refers to the external circumference in millimeters. Rigid cystoscopes are available in a number of different sizes (e.g., 22F or 26F) that allow passage of instruments to resect bladder tumors (resectoscope) or crush bladder calculi (lithoclast). The larger caliber of the irrigation channels in a bigger endoscope improves flow and vision when blood or debris is present in the bladder.

Flexible endoscopes have two bundles of optic fibers, which facilitate illumination (noncoherent) and image (coherent) transmission. Two control wires deflect the tip 270° each way (Figure 39.2) making complete maneuverability possible [2]. These flexible materials do not resist temperatures in an autoclave, so decontamination, rather than sterilization, is used to clean them. The slower flow through this narrower caliber instrument may make clear visualization more difficult than in a rigid instrument. An instrument channel is present to allow passage of guidewires, needles, and forceps. The use of this channel may further hinder irrigant flow.

INDICATIONS

Specific situations where cystoscopy should be considered include the presence of hematuria or significant past medical history. Cystourethroscopy is not routinely indicated in the assessment of a patient with lower urinary tract symptoms alone. Blood in the urine (hematuria) may be divided into visible (macroscopic or *frank* hematuria) or nonvisible (microscopic or using dipstick urinalysis) and is an indication for cystourethroscopy to diagnose an underlying condition, such as bladder cancer. However, if there is only a trace of blood on dipstick, it may be discounted without undertaking endoscopy [3]. The past medical history should be reviewed; for example, a woman with new-onset storage urinary symptoms, leukocyturia, and a past history of a difficult placement of a midurethral tape may need cystoscopy to exclude tape exposure.

Certain urological symptoms are strong indicators of specific pathology. The passage of air (pneumaturia) or feces (fecaluria) in the urine strongly suggests a colovesical fistula, and cystoscopy may reveal inflamed urothelium around the site of the fistula. Continuous incontinence may result from a vesicovaginal fistula or ectopic ureter bypassing the urinary sphincter. Postvoid dribbling in the female can indicate a urethral diverticulum (UD), the opening of which may be visible at urethroscopy.

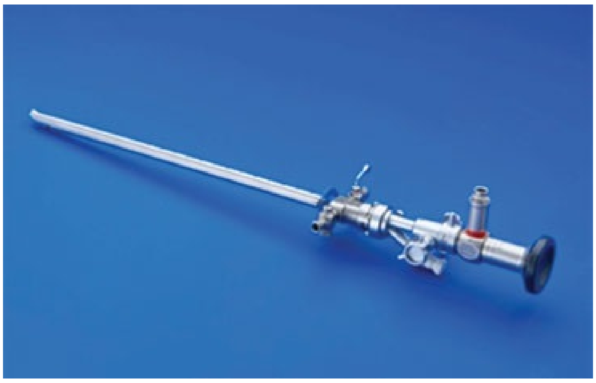


Figure 39.1 Rigid cystoscope. (Courtesy of Karl Storz Endoscopy, Culver City, CA.)

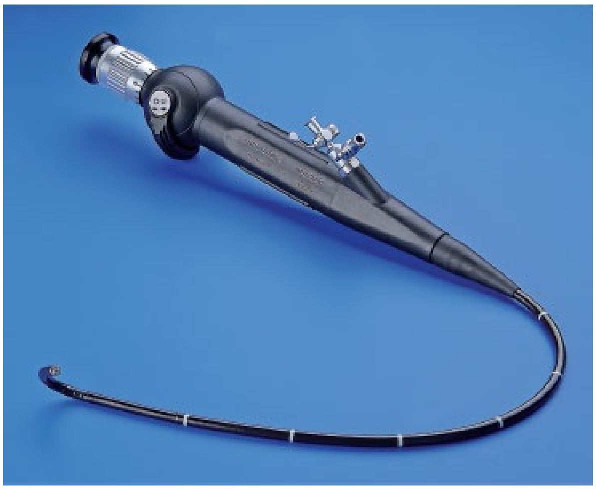


Figure 39.2 A flexible endoscope. (Courtesy of Karl Storz Endoscopy, Culver City, CA.)

Cystourethroscopy is indicated after mesh insertion to ensure that the bladder or urethra has not been inadvertently perforated (Figure 39.3).

CYSTOURETHROSCOPY

Informed consent should be obtained and appropriate antimicrobial prophylaxis administered according to local practice. The cystoscope should be assembled correctly and connected to sterile irrigant fluid at approximately 90 cm above the patient's pubic symphysis. If a halogen light source is used, a white balance should be performed. Lubrication of the urethral meatus with an anesthetic gel is followed by gentle passage of the cystoscope, following the lumen of the urethra.

A thorough and systematic inspection of the urethra and bladder is always required. Identification of the ureteric orifices at the apex of the trigone is followed by careful inspection of the lateral, posterior, anterior walls, and bladder neck (for which a 70° or flexible endoscope is required). The bladder may have muscular ridges (trabeculations) or outpouchings (diverticula) that suggest outflow obstruction (Figure 39.4).

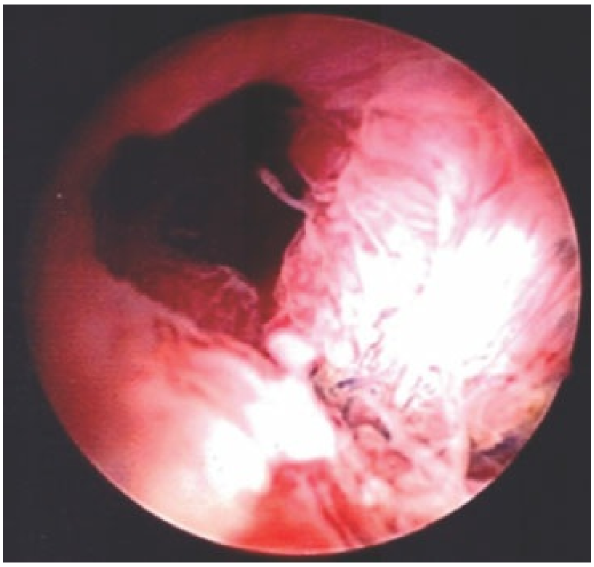


Figure 39.3 Mesh seen in urethra following treatment for stress incontinence.

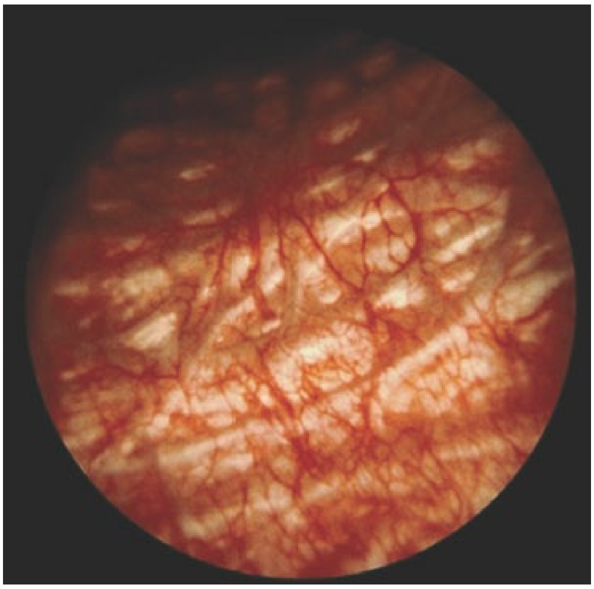


Figure 39.4 Bladder trabeculation; thickened ridges on the inner surface of the bladder.

Mucosal abnormalities should be documented as to their location, size, multiplicity, and appearance and ideally should be photographed. One crucial appearance that must be identified is the transitional cell carcinoma (TCC), the commonest form of bladder cancer (Figure 39.5). Smaller areas may be biopsied and the base coagulated. Larger areas may require formal resection.

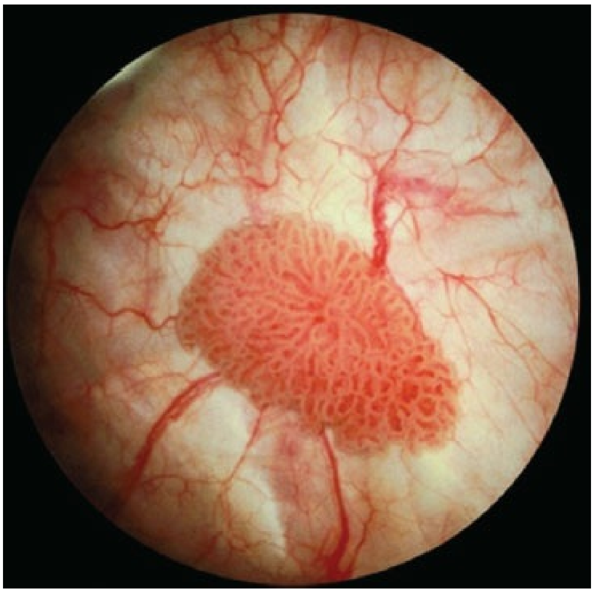


Figure 39.5 A small transitional cell cancer (TCC) of the bladder. The regular fronding of the lesion and normal-appearing nearby urothelium suggests it is probably a well-differentiated TCC.

Distension of the bladder may be used to help in the diagnosis of bladder pain syndrome (BPS). This is a symptom complex of bladder pain associated with at least one other urinary symptom in the absence of another diagnosis. Cystodistension allows the classification of BPS according to the International Society for the Study of Interstitial Cystitis classification, depending on the cystoscopic findings of glomerulations (Figure 39.6) or Hunner's ulcer, in addition to certain histological findings on biopsy.

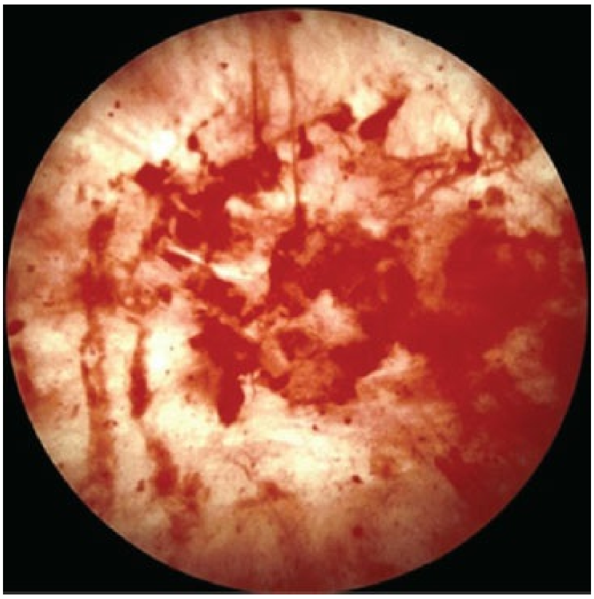


Figure 39.6 Bladder glomerulations after distension in a patient with bladder pain syndrome.

UPPER TRACT PROCEDURES

Once access to the bladder has been obtained, the upper tracts may be accessed via the ureteric orifices. Retrograde injection of contrast under radiographic screening allows definition of the upper tract anatomy, including filling defects caused by tumors or calculi. These abnormalities may be treated with laser lithotripsy. Self-retaining double-pigtail stents (Figure 39.7) can be inserted into the ureter. This may be done prophylactically to aid in identification of the ureter intraoperatively or to relieve obstruction or treat ureteric injury.

NEW DEVELOPMENTS IN ENDOSCOPY

The technological developments in the field of endoscopy have led to improved image quality with smaller, more maneuverable instruments. Refinements in optical technology have facilitated improvements in identification of abnormal tissue. Narrowband imaging refers to the use of light in the blue (415 nm) and green (540 nm) spectrum that are strongly absorbed by hemoglobin. This enhances the contrast between normal urothelium and hypervascular malignant tissue. The surface capillaries appear brown and the deeper veins cyan.

Fluorescence cystoscopy involves the administration of a photoactive porphyrin, e.g., hexaminolevulinate (HAL) or 5-aminolevulinic acid (ALA) 1 hour before cystoscopy. These porphyrins preferentially accumulate in malignant tissue and appear red under blue light (of wavelength 380–450 nm). There is some evidence that the use of fluorescence cystoscopy improves cancer detection rates and reduces recurrence [4].

The limitation on image quality of a normal cystoscope is the interface between the eyepiece and the camera. Digital endoscopes (Figure 39.8) rely on a charge-coupled device on the tip of the endoscope (“chip-on-the-tip”). The projection of the image onto the capacitor results in the accumulation of an electrical charge proportional to the light intensity at that location. These charges are processed into a high-quality image on the monitor. An LED illumination source is incorporated into the instrument, reducing the bulk and weight overall.

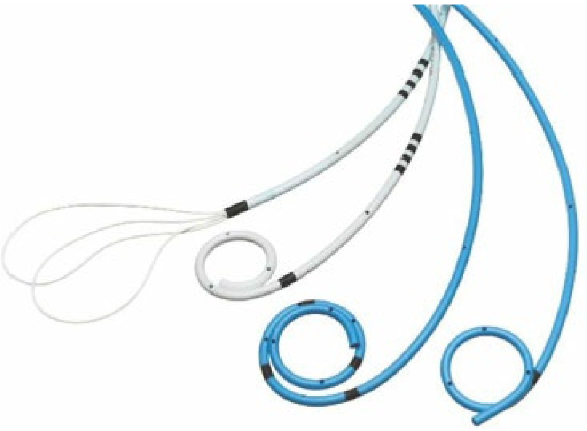


Figure 39.7 Self-retaining double-pigtail stents. (Courtesy of Boston Scientific, Marlborough, MA.)

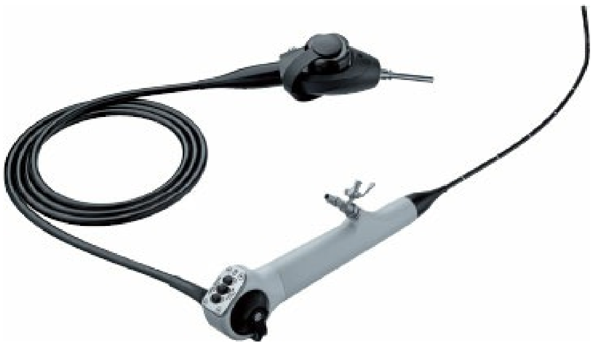


Figure 39.8 A digital flexible endoscope. (Courtesy of Karl Storz Endoscopy, Culver City, CA.)

OPERATIVE TECHNIQUE (STEP BY STEP) [5]

Patient positioning varies according to the instrument used. The lithotomy position is used for rigid cystoscopy, while the supine position is standard for flexible cystoscopy. Skin cleaning and disinfection is required followed by administration of a lubricating local anesthetic gel.

Rigid Cystoscopy

Instrument Insertion

The comparative shortness of the female urethra allows investigation using a rigid endoscope.

Gently introduce the sheath without mucosal injury to avoid possible urethral strictures. Avoid using pressure or force.

Blind insertion with the closed instrument (sheath and obturator) is possible.

Inspect the urethra to rule out urethral tumors, diverticula, and fistulae.

Inspection of the Bladder

Start inspection with the 30° telescope, and use different telescope (i.e., 70°) to inspect all areas of the bladder (i.e., dome, bladder neck).

Start with inspection of the trigone and then systematically evaluate the base, lateral walls, and posterior wall.

Inspect the dome of the bladder by turning the cystoscope 180°. Sometimes manual pressure on the lower abdomen helps bring the dome into view.

Use irrigation fluid inflow and outflow as necessary.

Look for the following:

- Ureteral orifices (position and form)
- Tumors
- Trabecula
- Lesions of the mucosa
- Diverticula and fistulas
    - Stones and foreign bodies

Additional Investigations: Consider Additional Investigations as Indicated

- Bladder washing
- Vaginal and/or rectal palpation
- Vaginal inspection
- Stress test and Marshall–Marchetti test

Flexible Cystoscopy

The patient should empty the bladder prior to performing a flexible cystoscopy. Preparation and local anesthesia are discussed earlier.

Instrument Insertion

Use lubricating gel.

Slowly pass the cystoscope through the urethra with continuous-flow irrigation.

A systematic inspection of the bladder is mandatory as described earlier.

By deflecting the instrument more than 180°, it is possible to inspect the bladder neck in a retrograde fashion.

Consider repeating the cystoscopy if the vision is impaired due to debris, blood clots, or active bleeding.

Normal Findings

- Healthy bladder mucosa appears yellow to pink with small vascular branches.
- Ureteral orifices.
    - ◦ Located within the trigonal rim.
    - ◦ Slit-like or a flat indentation.
    - ◦ Refluxive orifices are commonly lateralized and/or horseshoe-like in shape.

Procedure Report

A report should be written at the end of every cystoscopy, if possible with schematic drawings or video documentation of pathologic findings.

***Practical Tips* [5]**

- Dynamic cystoscopy: Examination of the bladder under variable filling may also be helpful to inspect all areas.
- Chromocystoscopy: If ureteral orifices are not identifiable, use indigo-carmine-blue dye intravenously.
- ALA-induced fluorescence cystoscopy for the detection of lower urinary tract tumors.

***Common Complications* [5]**

- Pain and dysuria (occasionally)
- Bleeding or transient gross hematuria
- Traumatic lesion of the urethra (occasionally)
- Perforation of the bladder (very rarely), possible in pronounced bladder tumors and impaired vision or contracted bladder
- Traumatic urethral strictures due to mucosal lesions (uncommon)
- False passage especially in blind insertion of the instrument (Figures 39.9 and 39.10; see also Figures 39.11 through 39.13)

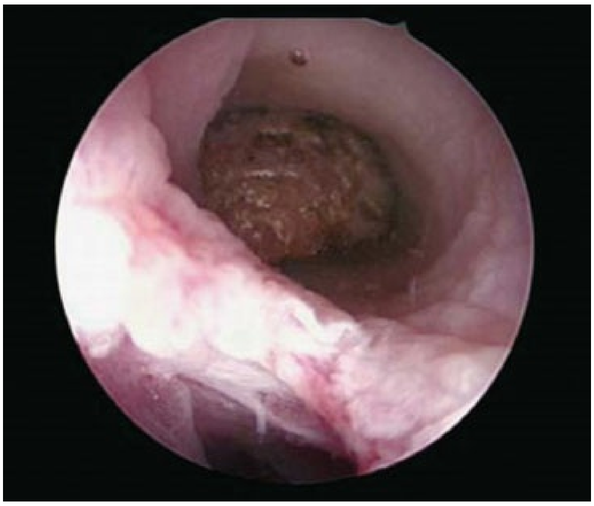


Figure 39.9 Urethral calculus with false passage. (With kind permission from Springer Science+Business Media: *Manual Endourology: Training for Residents*, 2005, Hohenfellner R and Stolzenburg J-U.)

***Limitations and Risks* [5]**

- Cystoscopy during untreated urinary tract infection (UTI) should be avoided because of a possible exacerbation of sepsis.
- Culture specimens are required to prove sterility of the urinary tract prior to endoscopy for patients with pyuria.
- Endoscopy should be performed after specific antibiotic therapy.
- Acute and heavy bleeding may lead to insufficient endoscopic evaluation.

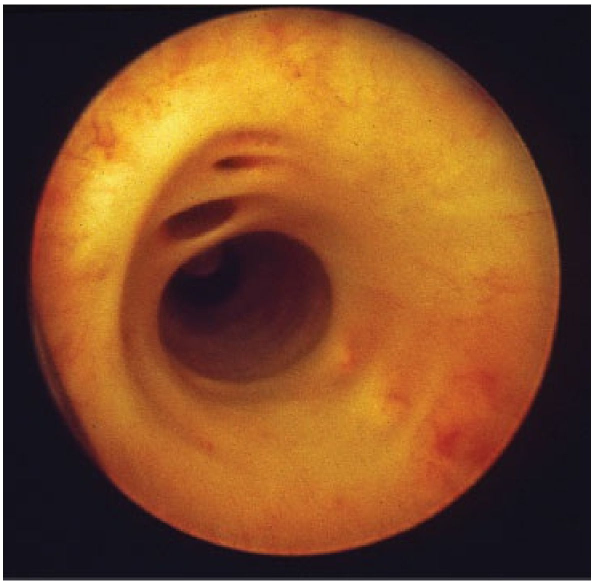


Figure 39.10 False passage urethra. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

Contraindications [5]

- Acute urethritis, acute prostatitis, and acute epididymitis
- UTI
- Strong coagulopathy

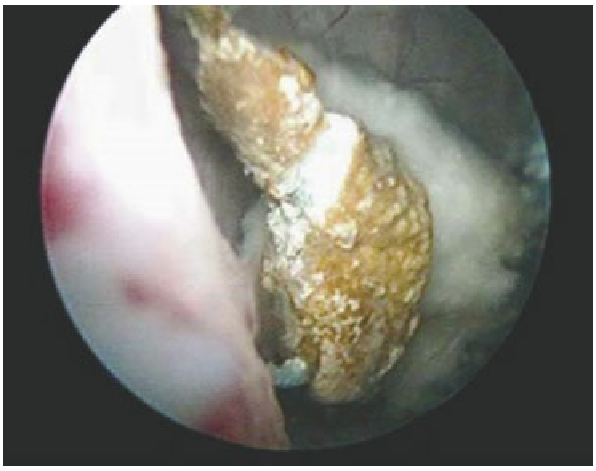


Figure 39.11 Suture and incrustation after incontinence surgery. (With kind permission from Springer Science+Business Media: *Manual Endourology: Training for Residents*, 2005, Hohenfellner R and Stolzenburg J-U.)

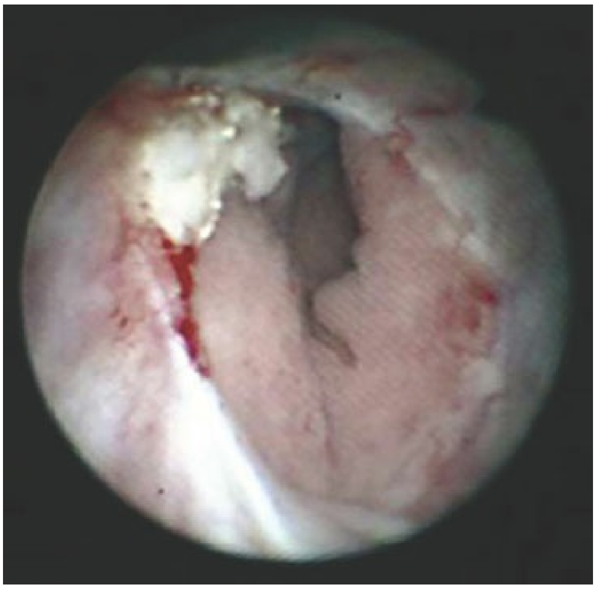


Figure 39.12 Endoscopic view from the distal part of an ileoureteral substitute. (With kind permission from Springer Science+Business Media: *Manual Endourology: Training for Residents*, 2005, Hohenfellner R and Stolzenburg J-U.)

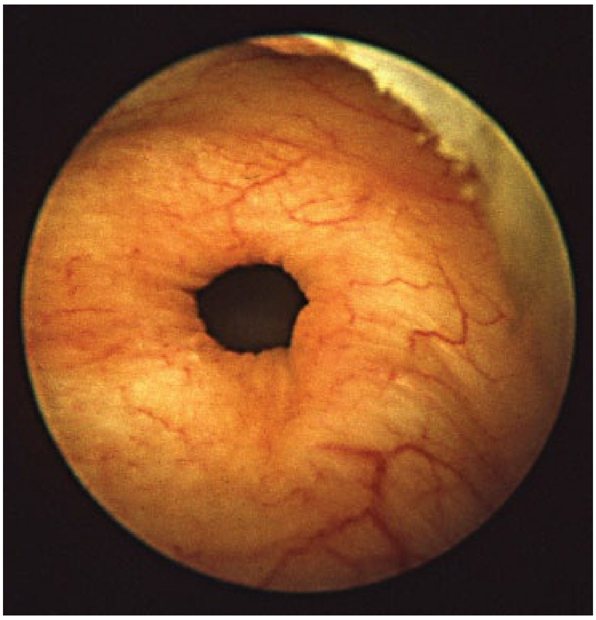


Figure 39.13 Refluxing ureter running into a ureterocele. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

NORMAL ENDOSCOPIC FINDINGS

Normally, the urethral mucosa is pink and smooth with a posterior longitudinal ridge, called the urethral crest (Figure 39.14). The ureterovesical junction (UVJ) is typically round or an inverted horseshoe shape and is completely coapted until the irrigating fluid opens the lumen. The UVJ normally closes briskly and has minimal mobility on Valsalva maneuver.

The bladder mucosa has a smooth surface with a pale pink to glistening white shade. The translucent mucosa affords easy visualization of the branched submucosal vasculature. The mucosa of the dome thickens and develops a granular texture as it gives way to the trigone. The trigone is triangular in shape, with the inferior apex directed toward the UVJ and the ureteral orifices forming the superior apices. As the cystoscope is advanced past the UVJ, the trigone is apparent at the bottom of the field.

The interureteric ridge is a visible elevation that forms the superior boundary of the trigone, running between the ureteral orifices. The intramural portion of the ureters can often be seen as they course from the lateral aspect of the bladder toward the trigone and ureteral orifices (Figure 39.15).

Although there is marked variation in the ureteral orifices, they are generally circular or slit-like openings at the apex of a small mound (Figure 39.16). With efflux of urine, the slit opens and the mound retracts in the direction of the intramural ureter.

The bladder is roughly spherical in shape when distended, but numerous folds of mucosa are evident in the empty or partially filled bladder. The uterus and cervix can be seen indenting the posterior wall of the bladder, which creates posterolateral pouches where the bladder drapes over the uterus into the paravaginal spaces. At times, visualization of the anterior bladder dome requires manual pressure on the lower abdomen.

URETHRAL FINDINGS

While congenital urethral anomalies are quite uncommon, urethral duplication has been reported, and typically the most anterior lumen drains the true bladder. Due to the blind ending and the possibility of urine deposition and entrapment in the false urethra, resection of the duplicate urethra may be required. Urethral stones and strictures are other frequent findings (Figure 39.17a and b).

Urodynamic Stress Incontinence

The urethral hypermobility typical of urodynamic stress incontinence causes the UVJ to open and descend in response to cough and Valsalva maneuver, and the patient may not be able to close the UVJ to the *hold* and *squeeze* commands. Urethroscopic findings typical of the patient with intrinsic sphincter deficiency include a rigid, immobile urethra with poor coaptation (Figure 39.18). In severe cases, the UVJ is unresponsive to commands and the lumen is visualized in its entirety from meatus to UVJ. Detrusor overactivity should be suspected if there is uncontrollable urethral opening during filling.

Female Urethral Diverticulum

UDs occur in 1%–3% of women and can be generally described as a periurethral cystic structure adjacent to the urethra. UDs are often diagnosed in the evaluation of nonspecific lower urinary tract symptoms including dysuria, pelvic pain, vaginal mass, dyspareunia, and recurrent UTIs. Their clinical presentations vary from completely asymptomatic, incidentally noted lesions on physical examination or radiographs to very debilitating, painful vaginal masses associated with incontinence, stones, and/or tumors. Anatomical variations between patients and in the location, size, and complexity of these lesions ensure that each case is unique [7]. The vast majority of UDs, however, are likely to be acquired and are diagnosed in adult females. In two large series of UD, there were no patients reported who were younger than 10 years of age arguing against a congenital etiology for these lesions [7–9].

The female urethra is a musculofascial tube approximately 3–4 cm in length, extending from the bladder neck to the external urethral meatus, suspended to the pelvic sidewall and pelvic the majority of the glands draining into the distal one-third of the urethra. Skene glands are the largest and most distal of these glands. These glands drain outside the urethral lumen, lateral to the urethral meatus. Most acquired female UDs are thought to originate from pathologic processes involving the periurethral glands [7]. In over 90% of UD cases, the ostium is located posterolaterally in the mid or distal urethra, which corresponds to the anatomic location of the periurethral glands [7,10,11]. UDs have been attributed historically to recurrent infection of the periurethral glands, with obstruction, suburethral abscess formation, and subsequent rupture of these infected glands into the urethral lumen.

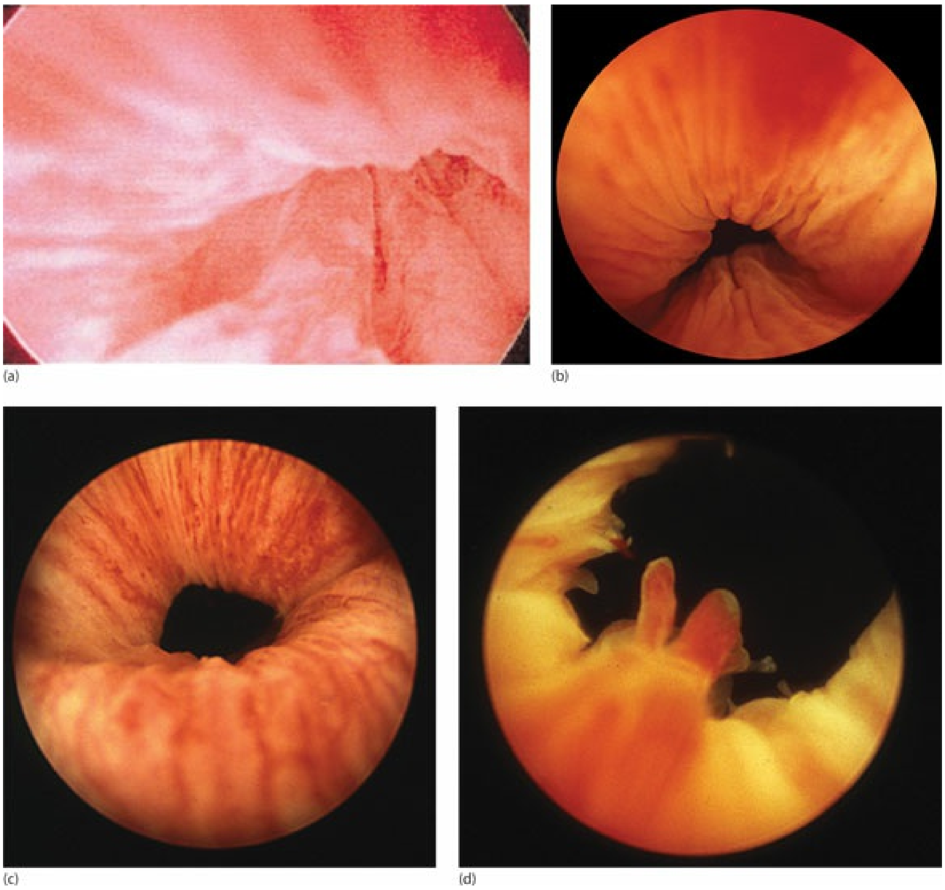


Figure 39.14 (a) Urethral lumen showing urethral crest and normal coaptation. (From Carr L and Cundiff GW, Endoscopy, in Cardozo L and Staskin D, eds., *Textbook of Female Urology and Urogynecology*, Informa, London, U.K., 2010. With permission.) (b) Normal female urethra. (c) Proximal urethral opening of normal female urethra. (d) Pseudopolyps close to the internal meatus—normal finding. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

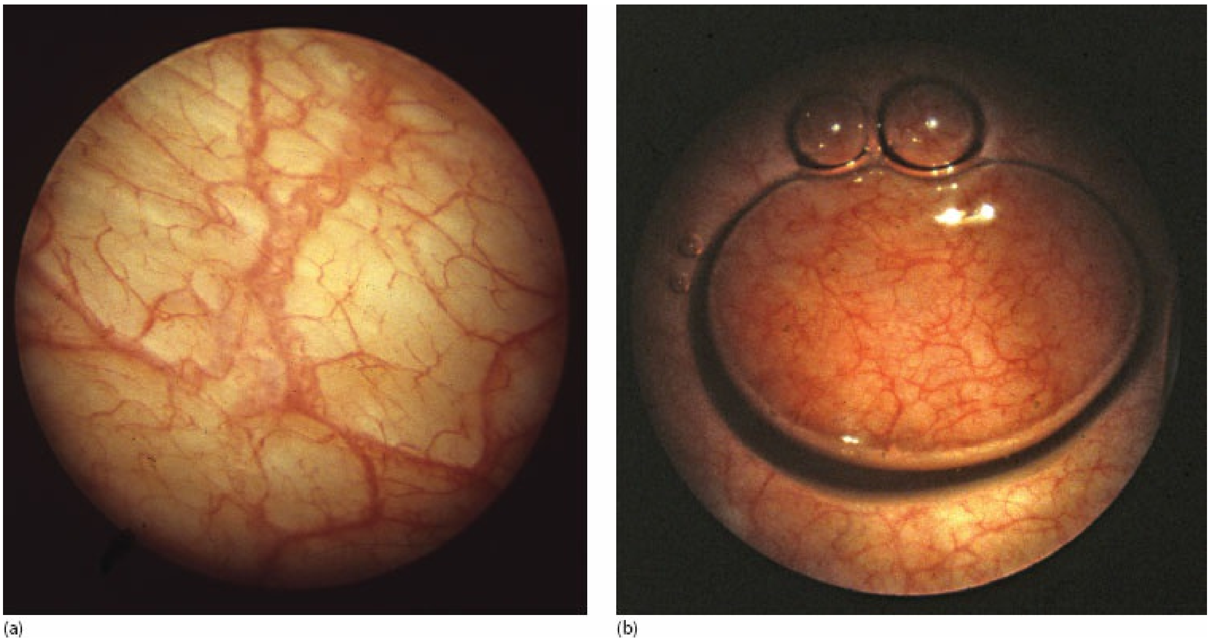


Figure 39.15 (a) Normal bladder. (b) Roof air bubble looking. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

As conceptualized by Young and colleagues (1996), UDs represent a cavity dissecting within the confines of the fascia of the urethropelvic ligament [7]. This defect is often an isolated cyst-like appendage with a single discreet connection to the urethral lumen termed the neck, or ostium. However, complicated anatomic patterns may exist, and in certain cases the UD may extend partially ("saddlebag" UD) around the urethra, anterior to the urethra [12], or circumferentially around the entire urethra [7,13].

The urethroscopic diagnosis is most accurate when the bladder is filled, and a finger in the vagina occludes the bladder neck or proximal urethra. A steady flow of fluid into the urethra is maintained as the scope is withdrawn and the urethra massaged by the finger pressing upward from below (Figure 39.19).

BLADDER FINDINGS

Nonmalignant Bladder Lesions

Epithelial Metaplasia (Figure 39.20)

Epithelial metaplasia is focal areas of transformed urothelium with normal nuclear and cellular architecture surrounded by normal urothelium usually located on the trigone and composed of squamous (squamous metaplasia) or glandular (glandular metaplasia) cells. Squamous metaplasia often has a knobby appearance and is covered by white, flaky, easily disrupted material lying on the trigone. Glandular metaplasia appears as clumps of raised red areas that appear inflammatory and are often confused for cancer. Approximately 40% of women and 5% of men have squamous metaplasia of the bladder, which is usually related to infection, trauma, and surgery [14]. Spinal cord injury is associated with squamous metaplasia most likely from catheter trauma and UTIs [7].

Cystitis Cystica and Glandularis (Figures 39.21 and 39.22)

Cystitis cystica and/or glandularis is a common finding in normal bladders, usually associated with inflammation or chronic obstruction [15]. Cystitis glandularis can be associated with pelvic lipomatosis and may occupy the majority of the bladder. Cystitis glandularis may develop into or coexist with intestinal metaplasia, which are benign tumors. There have been a few case reports of cystitis cystica or glandularis transforming into adenocarcinoma, and therefore regular endoscopic evaluation of patients with these entities is recommended [7,16].

Eosinophilic Cystitis (Figure 39.23a through d)

Eosinophilic cystitis may appear as a red–brown patch cystoscopically, and the diagnosis can only be made by histological evaluation.

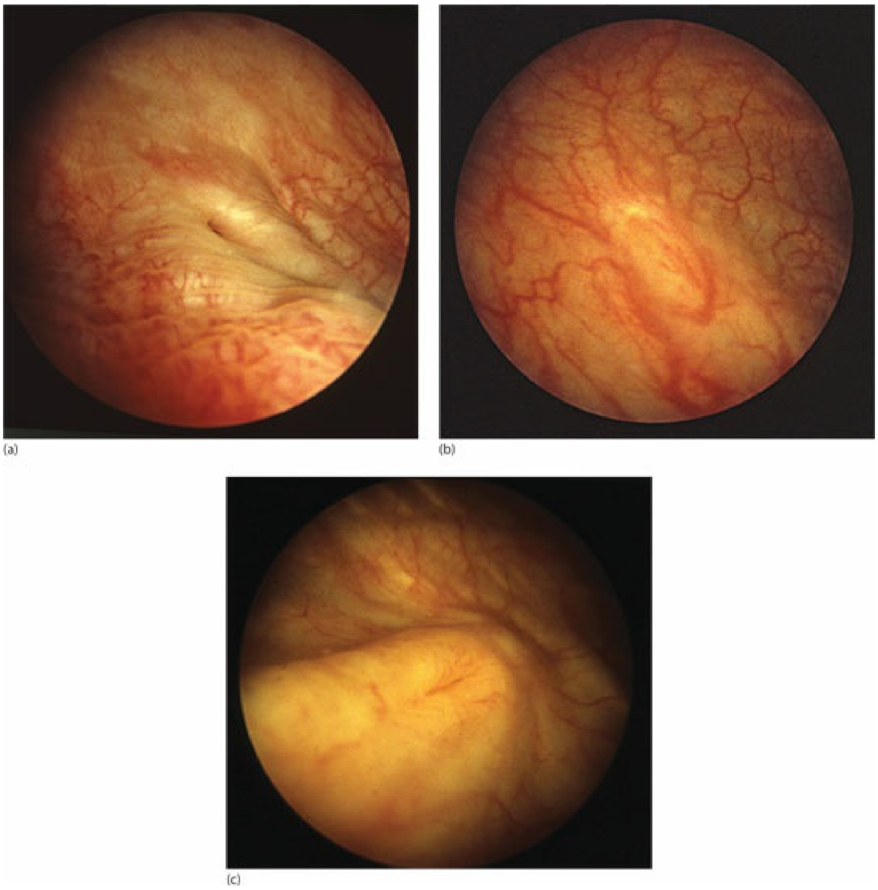


Figure 39.16 (a) Normal right ureteral orifice. (b) Ureteral orifice—difficult to discover. (c) Sleeping ureteral orifice. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

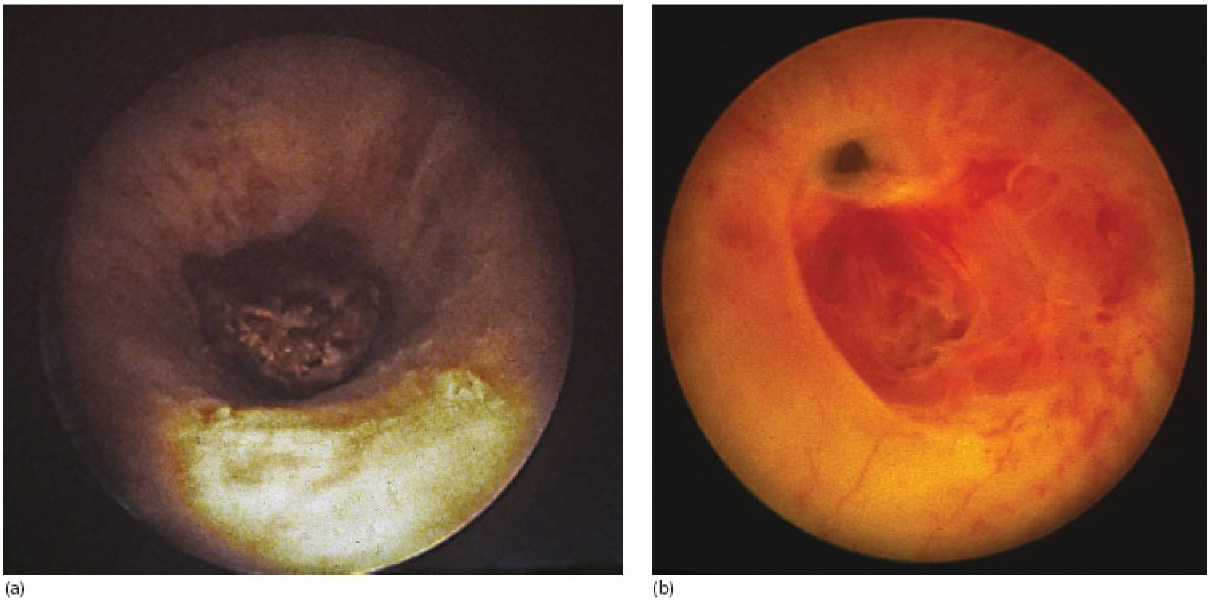


Figure 39.17 (a) Urethral stone stuck in the urethra. (b) Urethral stricture + false passage below. This false passage is the usual result of using force to catheterize patients with strictures and sometimes because of using the wrong technique in catheterizing a normal urethra! (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

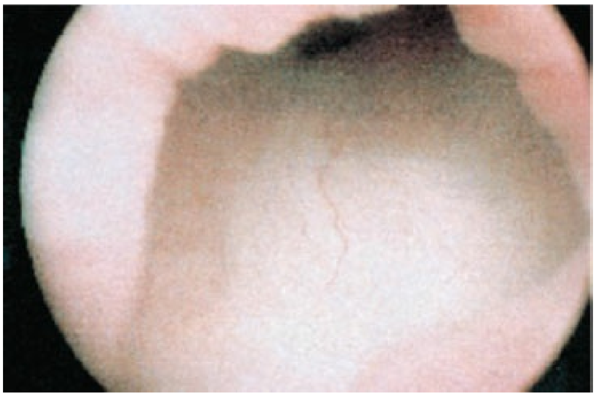


Figure 39.18 Intrinsic sphincteric deficiency. (From Carr L and Cundiff GW, Endoscopy, in Cardozo L and Staskin D, eds., *Textbook of Female Urology and Urogynecology*, Informa, London, U.K., 2010. With permission.)

Leukoplakia

Leukoplakia is similar to squamous metaplasia with the addition of keratin deposition that appears as a white flaky substance floating in the bladder. Leukoplakia occurs in other organs that are covered by squamous epithelium and is often premalignant. However, cytogenetic studies on bladder leukoplakia are consistent with a benign lesion, and no treatment is necessary [7].

Leiomyoma

Leiomyomas are the most common nonepithelial benign tumor of the bladder composed of benign smooth muscle. Leiomyomas appear as smooth indentations of the bladder and can be confused with a bladder tumor except for the normal urothelium overlying the tumor. These tumors occur most commonly in women of childbearing age and are histologically similar to leiomyomas of the uterus [7,17].

Bladder Trabeculations

Bladder trabeculations are most commonly associated with bladder outlet obstruction (Figure 39.24); nevertheless, this is a nonspecific finding. Grades of trabeculation have been proposed but none is universally accepted. As a general rule, more severe trabeculation has been associated with detrusor compromise. Histological analysis of trabeculations has demonstrated a mixture of smooth muscle bundles with an abundance of interfascicular collagen deposition.

Diverticula (Figure 39.25)

Diverticula are urothelial-lined pockets without smooth muscle backing that can either be congenital (i.e., Hutch diverticula located adjacent to a ureteral orifice) or acquired (commonly in the setting of outlet obstruction). They may have either a large or a narrow neck, and if poorly draining can be a source of recurrent infection.

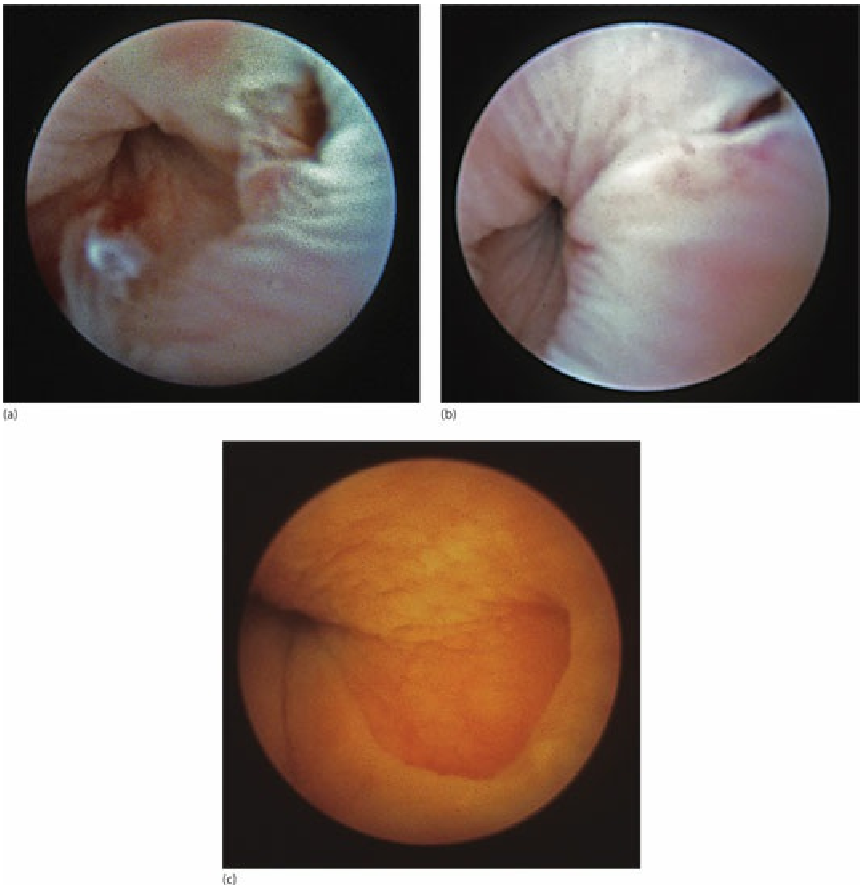


Figure 39.19 (a–c) Urethral diverticulum to the left. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

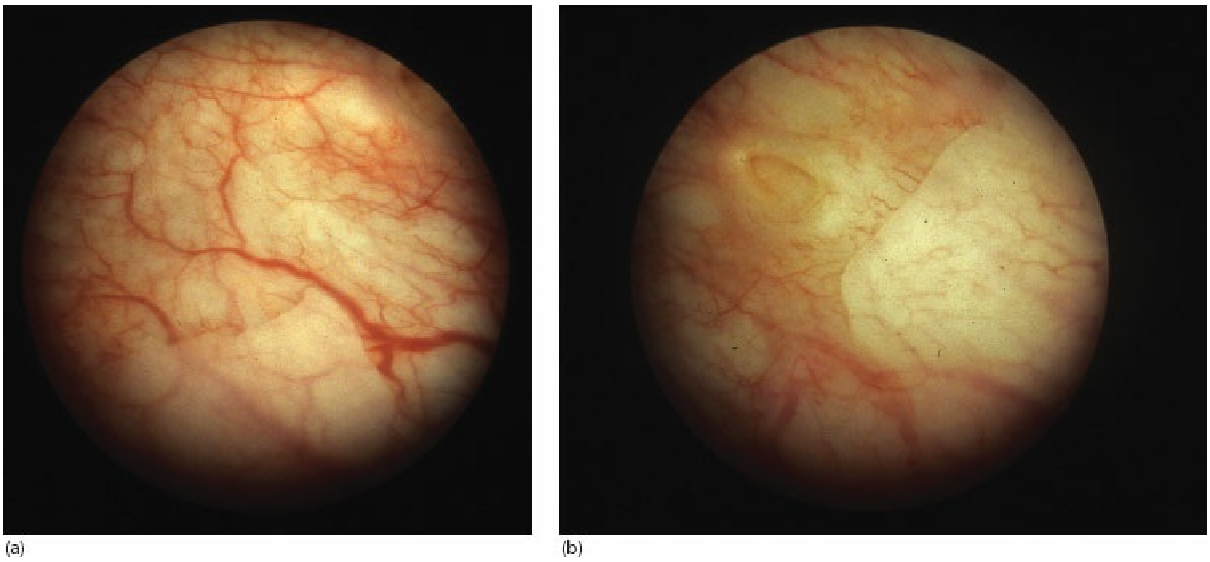


Figure 39.20 Normal bladder + epithelial metaplasia. (a) Bladder. (b) Trigone. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

Foreign Bodies

Intravesical foreign bodies may present with hematuria or as urge incontinence due to mucosal irritation. Bladder calculi may result from urinary stasis or the presence of a foreign body, or an inflammatory exudate may coalesce and serve as a nidus for stone formation (Figures 39.26 and 39.27).

Stones have an extremely variable cystoscopic appearance in terms of color, size, and shape but generally have an irregular surface. Foreign bodies and stones are usually accompanied by varying degrees of general or localized inflammatory reaction.

Urinary Tract Fistulae

Fistula represents an extra-anatomic communication between two or more epithelial or mesothelial-lined body cavities or the skin surface. The potential exists for fistula formation between a portion of the urinary tract (i.e., kidney, ureters, bladder, and urethra) and virtually any other body cavity [7].

Diagnosis is made in three steps after a fistula is suspected. The first step is to confirm that watery drainage is urine; Pyridium may be used for this aim. The next step is to exclude urinary incontinence occurring from the urethra by filling the bladder and observing for loss from the urethra or vagina. Finally, the source of the fistula needs to be identified. This commences with a speculum inspection, which may reveal a fistula site to the vagina. The double-contrast test is also useful, although cystoscopy and the flat tire test are the best ways to visualize the fistula site in the bladder.

Vesicovaginal Fistulae

Vesicovaginal fistulae (VVF) are the most common acquired fistula of the urinary tract [18]. VVF are thought to result most commonly from an incidental unrecognized iatrogenic cystotomy located along the anterior vaginal wall at the level of the vaginal cuff [7,19].

Cystoscopy should be done in patients with a suspicion of VVF. Immature fistulae may look as an area of localized bullous edema without distinct ostia, while mature fistulae may have smooth margins with ostia of different sizes. Sometimes, it might be difficult to identify the exact fistula tract in a small VVF. In these cases, a guidewire or ureteral catheter can be placed through the cystoscope into the fistula tract. Visualization of the wire in the vagina confirms the exact location of the VVF on both the bladder and genital sides [7].

Cystourethroscopy can confirm the presence of the fistula and assess the size of the tract and the presence of collateral fistulae in addition to the location of the ureteral orifices in relation to the fistula. Small fistulae, usually less than 3–4 mm in diameter, may be amenable to simple fulguration, which can be performed at the time of cystoscopy [19]. This is crucially important in the situation of a prior history of pelvic malignancy; a biopsy of the fistula is often done to evaluate for the possibility of a recurrent malignancy [7]. Fistulae located near or at the ureteral orifice may require ureteral reimplantation. This type of requirement would usually mitigate against a completely transvaginal attempt at repair [7].

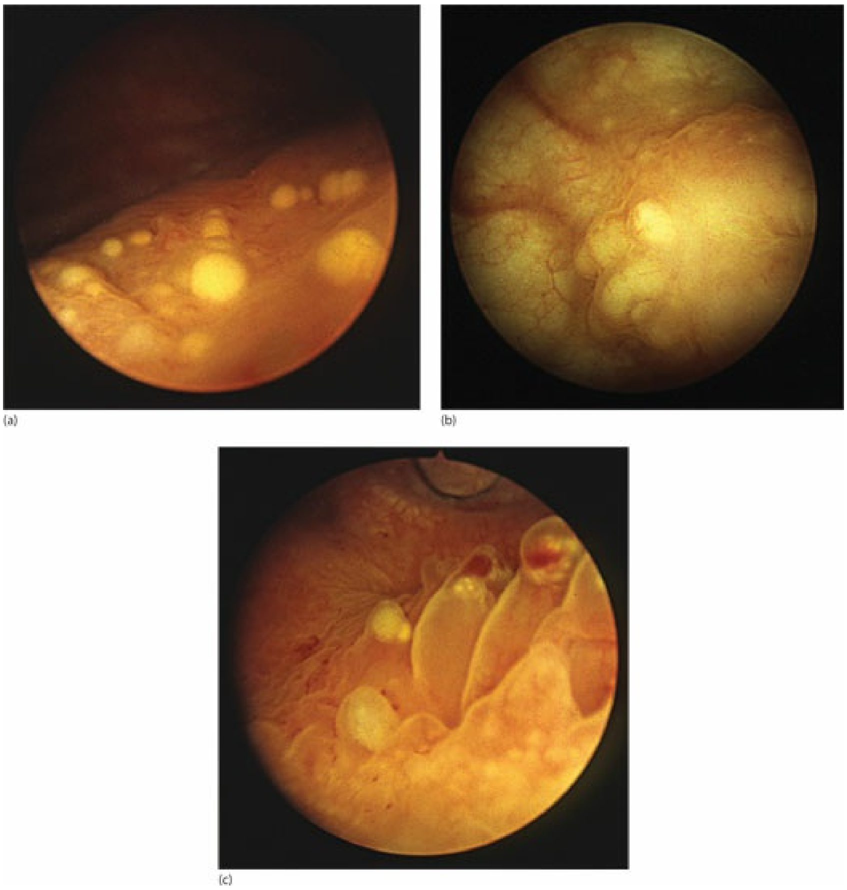


Figure 39.21 (a) Cystitis cystica; (b) cystitis cystica, multilocular; (c) cystitis glandularis. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

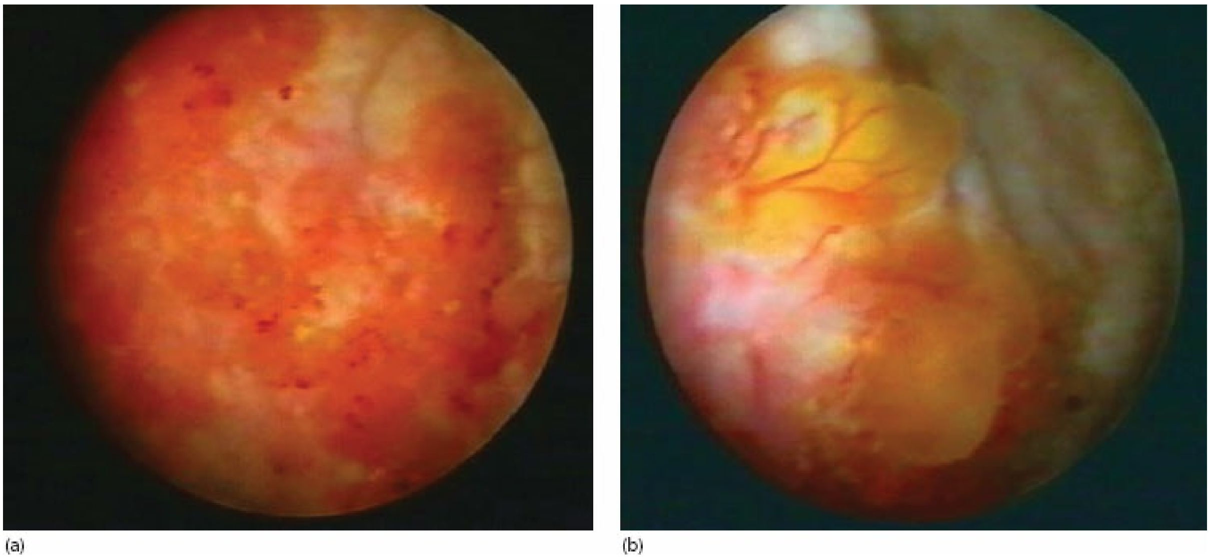


Figure 39.22 Endoscopic finding of a patient with cystitis glandularis showing (a) miliary multiple polypoid lesions and (b) a major polypoid lesion resembling a bladder tumor. (With kind permission from Springer Science+Business Media: *Manual Endourology: Training for Residents*, 2005, Hohenfellner R and Stolzenburg J-U.)

Bladder Pain Syndrome/Painful Bladder Syndrome/Interstitial Cystitis

Bladder pain syndrome/painful bladder syndrome/interstitial cystitis (BPS/PBS/IC) is defined with the triad of bladder pain, urinary frequency, and urgency. It is a distinct condition, and it is likely that the urgency experienced by these patients differs from that experienced by those with overactive bladder [20]. While BPS/PBS/IC remains largely a diagnosis made by symptom assessment, the inclusion of typical cystoscopic findings in the original National Institute of Arthritis, Diabetes, Digestive and Kidney Disease criteria [21] highlights the historical role of cystoscopy in the evaluation of patients with BPS/PBS/IC. More recent studies have downplayed the importance of cystoscopy for making the diagnosis [22].

Two different forms of IC/PBS have been described, and prognosis and treatment may vary depending upon the form detected. *Classical* disease is characterized by erythematous patches, termed Hunner's ulcers (or Hunner's patches), which occur in less than 10% of patients. Only cystoscopy can accurately determine if inflammatory disease is present, as only approximately 30% of these patients show abnormalities on urinalysis that would otherwise prompt a cystoscopic examination. *Nonclassical* disease is characterized by a normal examination on cystoscopy with typical symptoms and no evidence of any other pathology [23]. When Hunner's ulcers are seen on cystoscopy (Figure 39.28), biopsies should be taken from these lesions to exclude carcinoma in situ. No reports point to IC/PBS as a potential premalignant condition; however, it is important to rule out bladder cancer, especially the presence of carcinoma in situ in patients aged over 40 years with a smoking history. [23,24].

Hydrodistention under anesthesia is still considered by many urologists to be the "gold standard" to aid in the diagnosis of IC/PBS. Glomerulations, submucosal petechiae, are frequently seen after the irrigant pressure is released. The bladder capacity is measured at 80–100 cmH_2O (anesthetic bladder capacity) and is usually reduced in the IC/PBS patient (normal anesthetic bladder capacity, 800–1200 mL; in IC/PBS usually <800 mL). Distention is limited to short periods of time, typically 2–5 minutes at a pressure of 80–100 cmH_2O. Submucosal hemorrhage (glomerulations) is often seen after hydrodistention and typically resolves (Figure 39.29). In patients with Hunner's ulcer, a biopsy should be done to rule out the presence of malignancy and fulguration of ulcers should be performed. Hydrodistention should not be performed in these patients, to avoid profuse hemorrhage and possible bladder perforation. All biopsy sites, fulguration areas, and mucosal tear locations should be noted to avoid confusion of these lesions on future cystoscopic evaluation (Figure 39.30). Finally, instillation of 20–30 mL of a short-acting anesthetic agent, i.e., 1% lidocaine, may be helpful for patients undergoing hydrodistention to allow for faster recovery and decreased pain following the procedure [24].

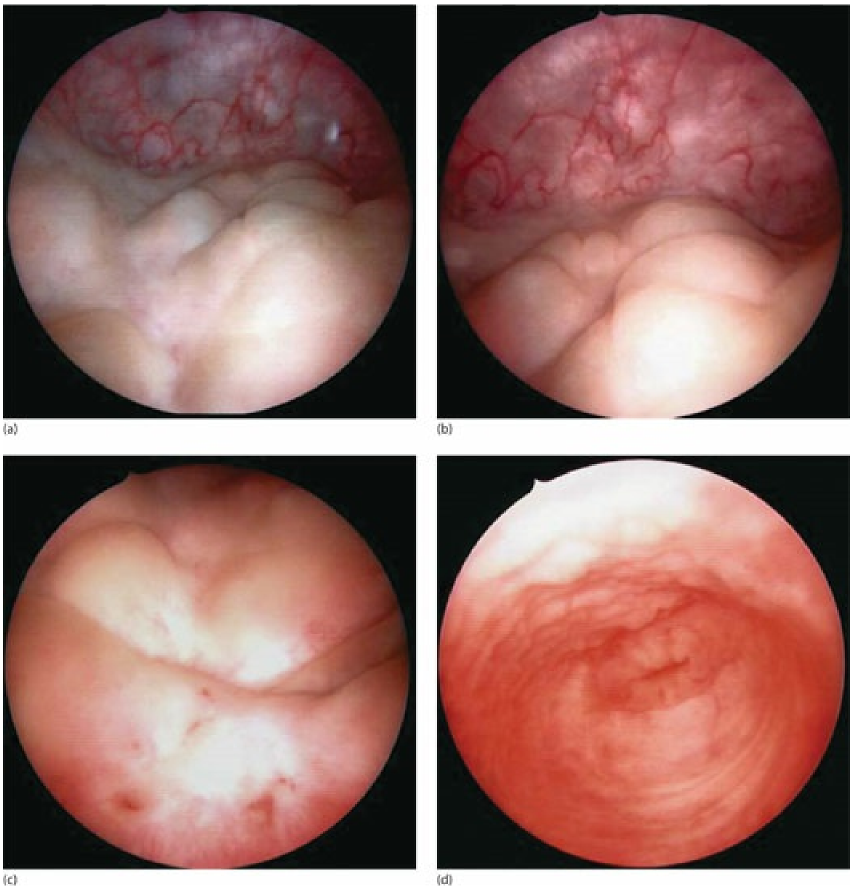


Figure 39.23 (a–d) Eosinophilic cystitis as a symptom of an idiopathic hypereosinophilia syndrome. (Courtesy of R. Nofal, Department of Urologie, Borromäus-Hospital, Leer, Germany.) (a) Tumorlike induration at the bottom of the bladder. (b) Tumorlike induration of the ureteral orifice, left side. (c) Induration of the ureteral groin. (d) Endoscopic view of the vagina. (With kind permission from Springer Science+Business Media: *Manual Endourology: Training for Residents*, 2005, Hohenfellner R and Stolzenburg J-U.)

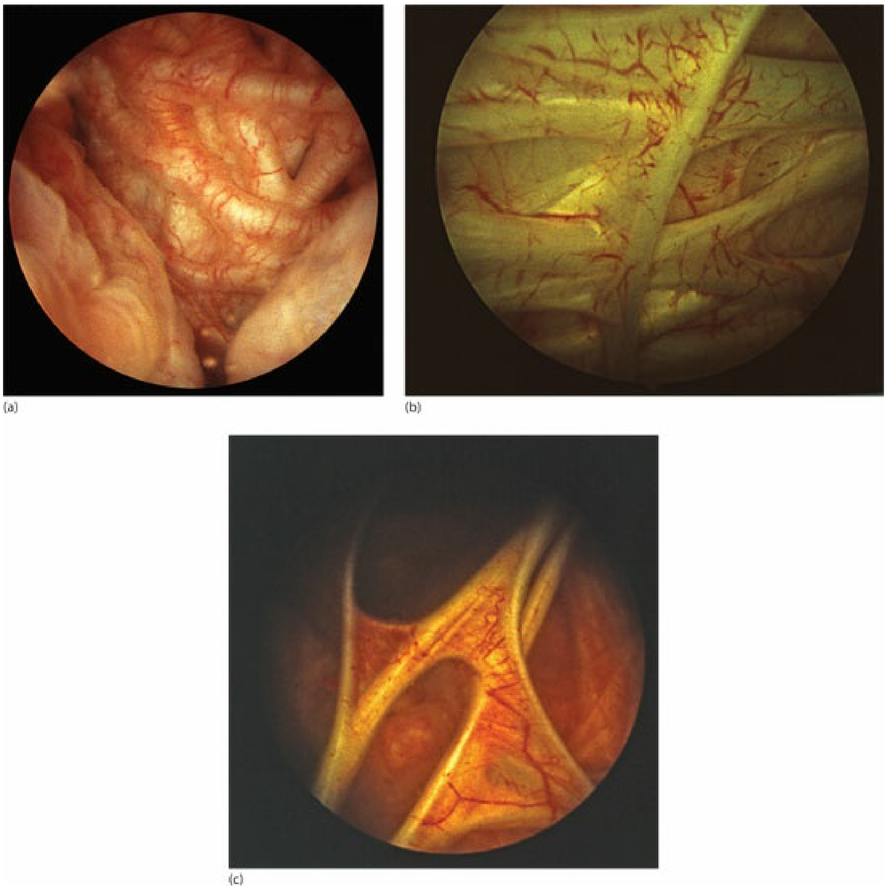


Figure 39.24 (a) Trabeculation, bladder half filled. (b) Maximally distended trabeculated bladder. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.) (c) Trabeculation in a thin-walled bladder—this picture is usually seen in old women. These patients will be at a high risk of bladder perforation especially during bladder biopsies. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

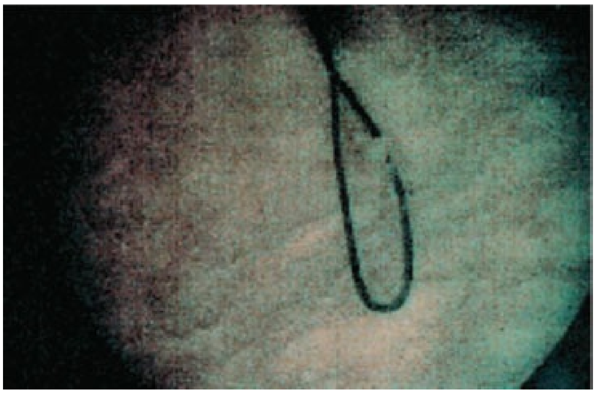


Figure 39.26 Intravesical suture with adherent calculi. (From Carr L and Cundiff GW, Endoscopy, in Cardozo L and Staskin D, eds., *Textbook of Female Urology and Urogynecology*, Informa, London, U.K., 2010. With permission.)

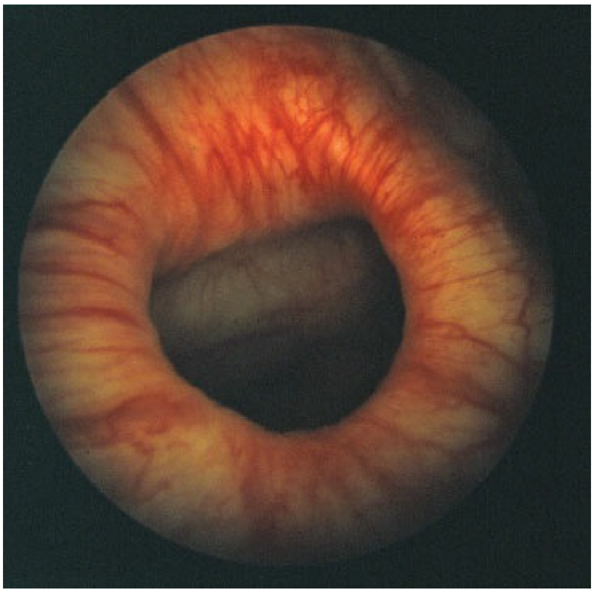


Figure 39.25 Bladder diverticulum. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

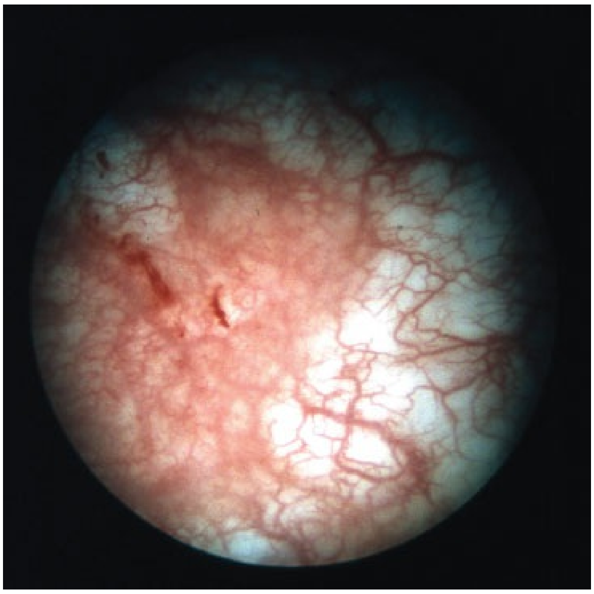


Figure 39.28 Hunner’s cystitis—hemorrhage and edema. These are almost always extratrigonal. They tend to bleed and tear easily with even small amounts of bladder filling. In this setting, hydrodistention would be unwise, as it would likely lead to bladder perforation. (From Smith AD, Preminger G, Badlani G: *Smith’s Textbook of Endourology*. 2011. Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.

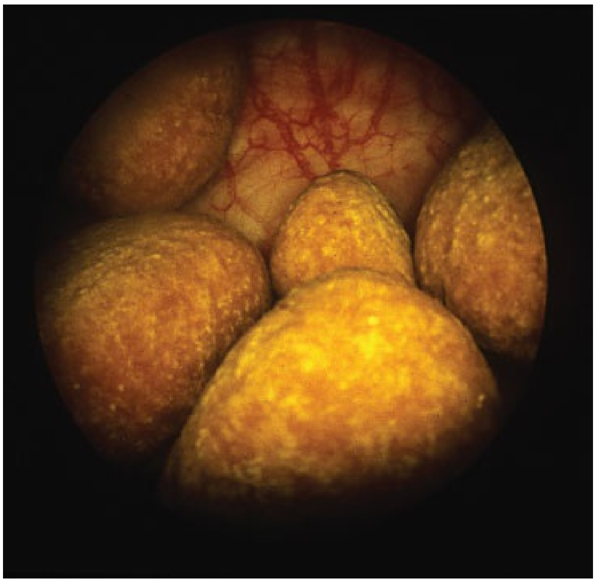


Figure 39.27 Marblelike bladder stones. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

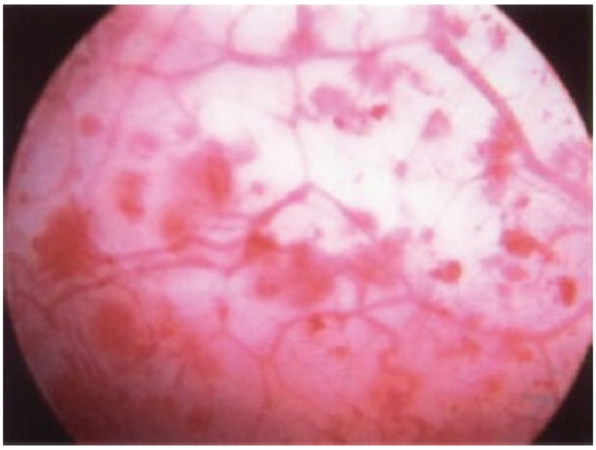


Figure 39.29 Glomerulations: submucosal hemorrhages typically seen in the interstitial cystitis/painful bladder syndrome patient after hydrodistention. (From Smith AD, Preminger G, Badlani G: *Smith's Textbook of Endourology*. 2011. Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.)

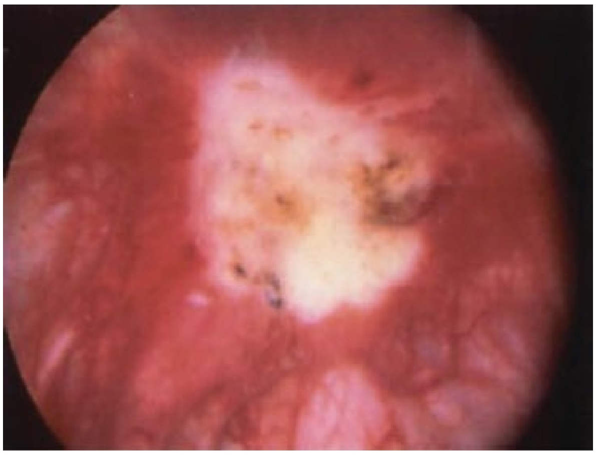


Figure 39.30 Hunner's ulcer after fulguration. Note the surrounding intense inflammatory reaction that develops rapidly after the applied energy. This is typically seen during the course of the ablative procedure.

(From Smith AD, Preminger G, Badlani G: *Smith's Textbook of Endourology*. 2011. Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.)

Reduction of symptoms ranges from 30% to 56% 26. However, the overall mechanism of symptom relief after hydrodistention is still unknown 26. The procedure is considered safe; however, complications such as hematuria, bladder perforation, and bladder necrosis have been reported. Bladder perforation can usually be managed conservatively with catheter drainage. Vesical necrosis is a rare but serious complication of hydrodistention [24–26].

Malignant Bladder Lesions

Bladder cancer is the second most common cancer of the genitourinary tract. It accounts for 7% of new cancer cases in men and 2% of new cancer cases in women [27]. Bladder lesions of uncertain etiology must be investigated under anesthesia because of the common need for cold-cup biopsies and fulguration to determine their malignant potential. Urinary cytologies and other urinary markers are helpful in determining if malignant cells are present in bladder washings but none sensitive enough to prevent the need for tissue diagnosis.

The diagnosis and initial staging of bladder cancer is made by cystoscopy and transurethral resection (Figure 39.31). Superficial, low-grade tumors usually appear as single or multiple papillary lesions. Higher-grade lesions are larger and sessile. Carcinoma in situ (CIS) may appear as flat areas of erythema and mucosal irregularity. Use of fluorescent cystoscopy with blue light can enhance the ability to detect lesions by as much as 20% [28]. In this procedure, hematoporphyrin derivatives that accumulate preferentially in cancer cells are instilled into the bladder and fluorescence incited using a blue light. Cancer cells with accumulated porphyrin such as 5-aminolevulenic acid or HAL are detected as glowing red under the fluorescent light [27,29].

The World Health Organization recognizes a papilloma as a papillary tumor with a fine fibrovascular stalk supporting an epithelial layer of transitional cells with normal thickness and cytology. Papillomas are a rare benign condition usually occurring in younger patients [27].

Approximately 90% of all bladder cancers are TCC (Figure 39.32). These tumors most commonly appear as papillary, exophytic lesions; less commonly, they may be sessile or ulcerated. Whereas the former group is usually superficial in nature, sessile growths are often invasive. Carcinoma in situ typically has a flat, red, velvety appearance that may be multifocal [27].

Adenocarcinoma—Adenocarcinomas account for <2% of all bladder cancers. It may be preceded by cystitis and metaplasia. Primary adenocarcinomas often arise along the floor of the bladder, while adenocarcinomas arising from the urachus occur at the dome. Both tumor types are often localized at the time of diagnosis, but muscle invasion is usually present [27] (Figure 39.33).

Other malignant bladder lesions include squamous cell tumors and metastatic lesions. Squamous cell tumors are often associated with a history of chronic infection, bladder calculi, or chronic catheter use. It may also be associated with bilharzial infection (Figure 39.34). These tumors are often nodular and invasive at the time of diagnosis.

Melanoma (Figure 39.35), breast adenocarcinoma, and several other tumors have been noted to metastasize to the bladder, often resulting in repeated bouts of gross hematuria. Locally advanced malignancies, typically of the colon, can also directly invade the bladder wall and eventually disrupt the bladder mucosa, resulting in an abnormal cystoscopic appearance and hematuria.

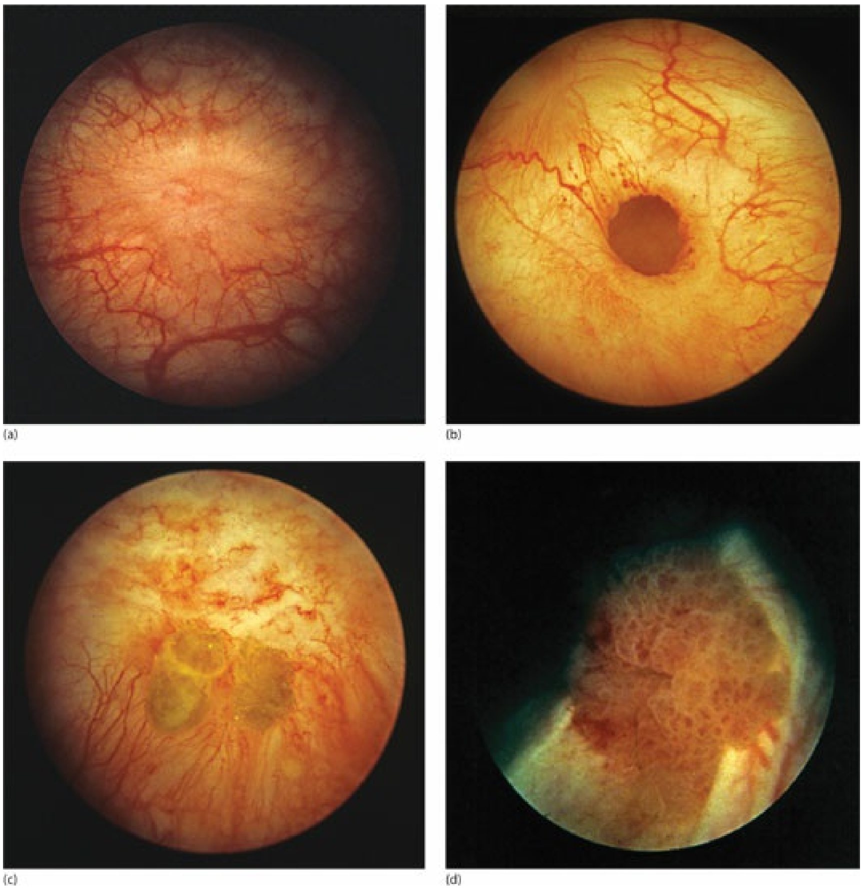


Figure 39.31 (a) Bladder scar after transurethral resection (TUR). (b) Healed ureteral orifice after TUR for bladder cancer. (c) Small stones growing in TUR—scar. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.) (d) Ureteral cancer from left orifice. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

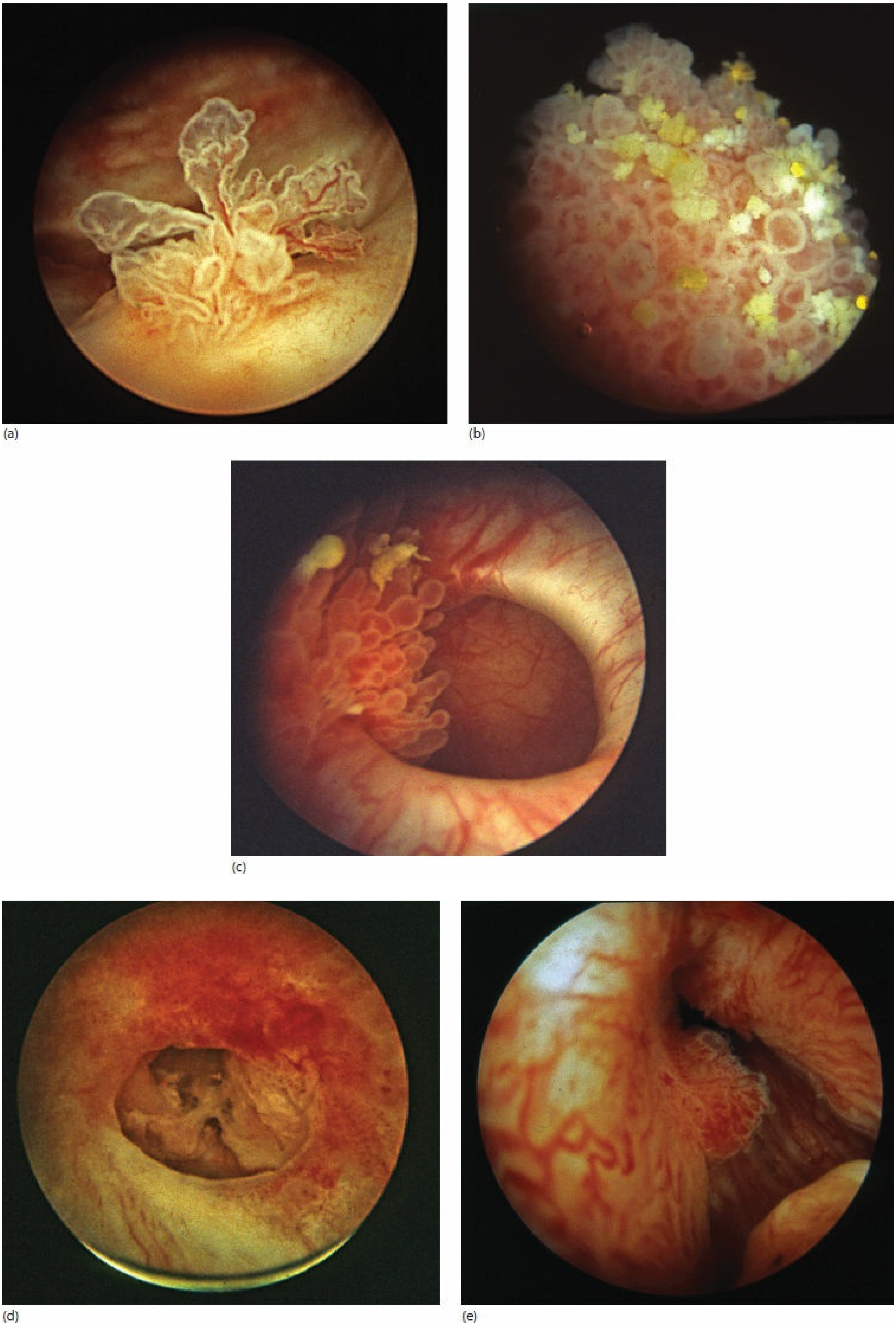


Figure 39.32 (a) Bladder cancer grade 1. (b) Grade 2 cancer—encrustations. (c) Grade 2 cancer—in a

diverticulum. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)(d) Grade 3 cancer in situ at diverticulum edge. (e) Urothelial cancer grade 2 in the prostatic part of the male urethra. This could be equally seen in females. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

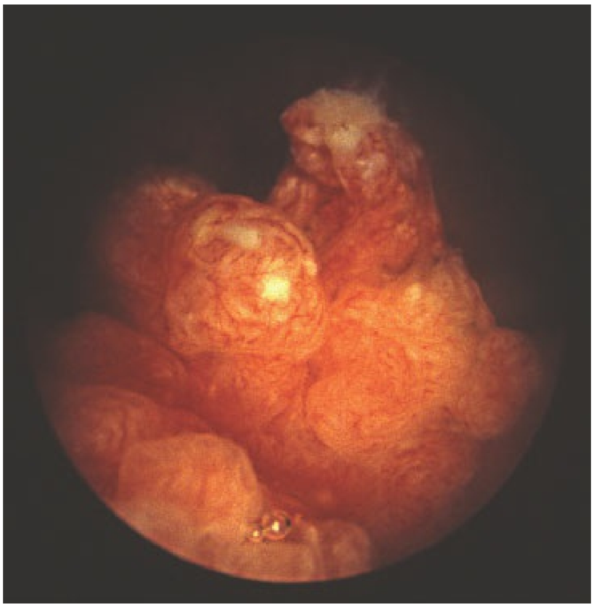


Figure 39.33 Primary adenocarcinoma of the bladder. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

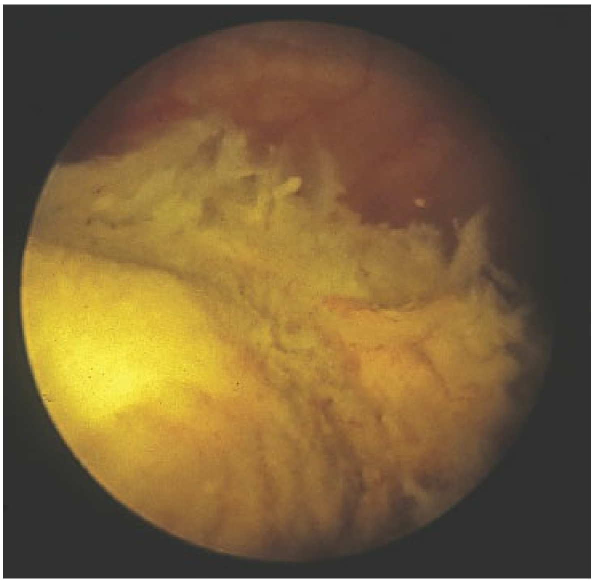


Figure 39.34 Bladder squamous carcinoma. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

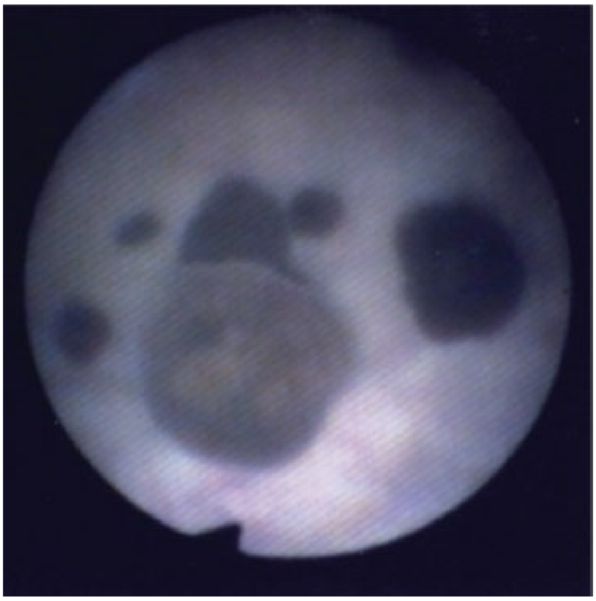


Figure 39.35 Metastatic melanoma to the bladder. (Courtesy of Dr. Y. Lotan, University of Texas Southwestern Medical Center, Dallas, TX.)

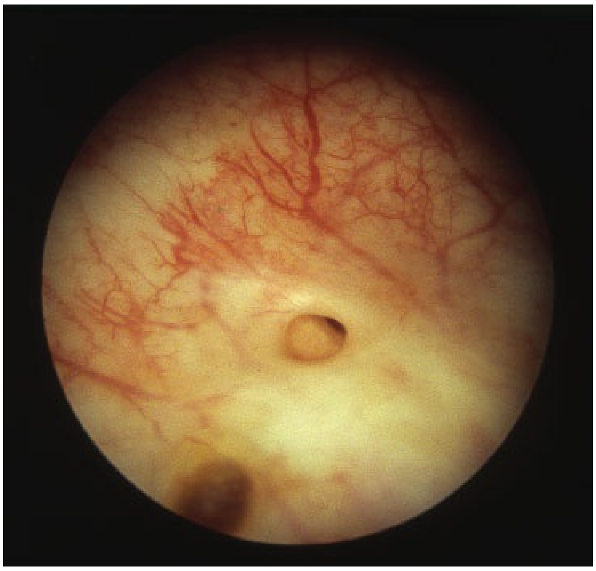


Figure 39.36 Abnormal refluxing of ureteral orifice and cystitis cystica. (From Schönebeck, J., *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

Ureteral Anomalies

Ureteral anomalies are not uncommonly found in patients undergoing diagnostic cystoscopy. Duplicated systems can occur bilaterally or unilaterally, with two orifices from the same renal unit typically being adjacent to one another. The medial and caudal-most of the ureteral orifices normally serve the upper pole system. Vesicoureteral reflux is often present in the ureter serving the lower pole system (a finding confirmed on cystography) (Figure 39.36). In women, ectopic ureters may also be found to drain into the urethra and vaginal vestibule, though most of these abnormalities will be found in childhood secondary to ongoing incontinence (Figure 39.37).

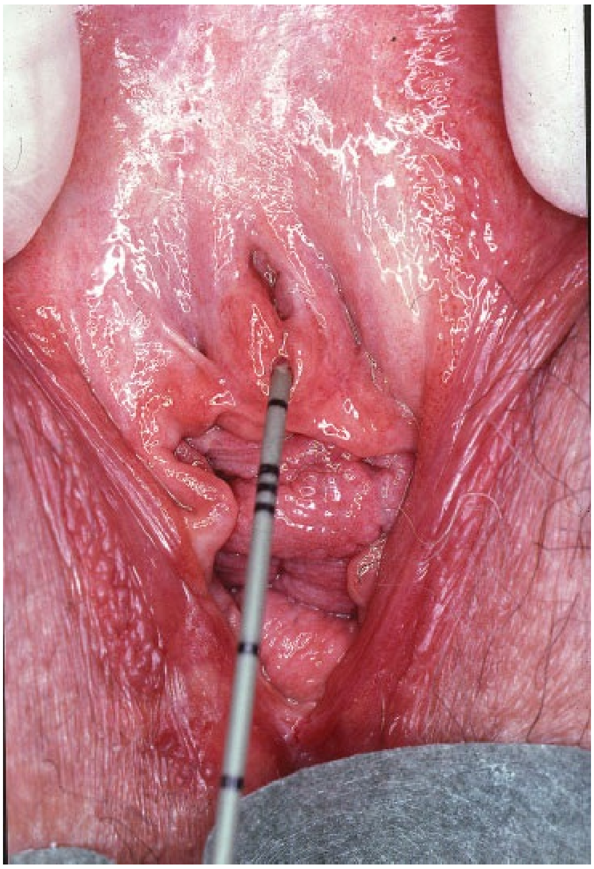


Figure 39.37 Ectopic ureteral orifice. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

Asymptomatic, single system ureteroceles are also not uncommon in adults, with the typical appearance being a thin layer of urothelium covering a bulging orifice in a normal location. Often, a pinpoint opening is noted on the membrane, and due to urinary stasis, ureteral stone formation can occur proximal to this opening, particularly in children. Occasionally, ureteroceles will be ectopic in location, at times presenting as far distally as the mid and distal urethra (Figures 39.38 and 39.39).

Uncommon Findings in Cystoscopy

Figures 39.40 through 39.56 illustrate uncommon findings in cystoscopy.

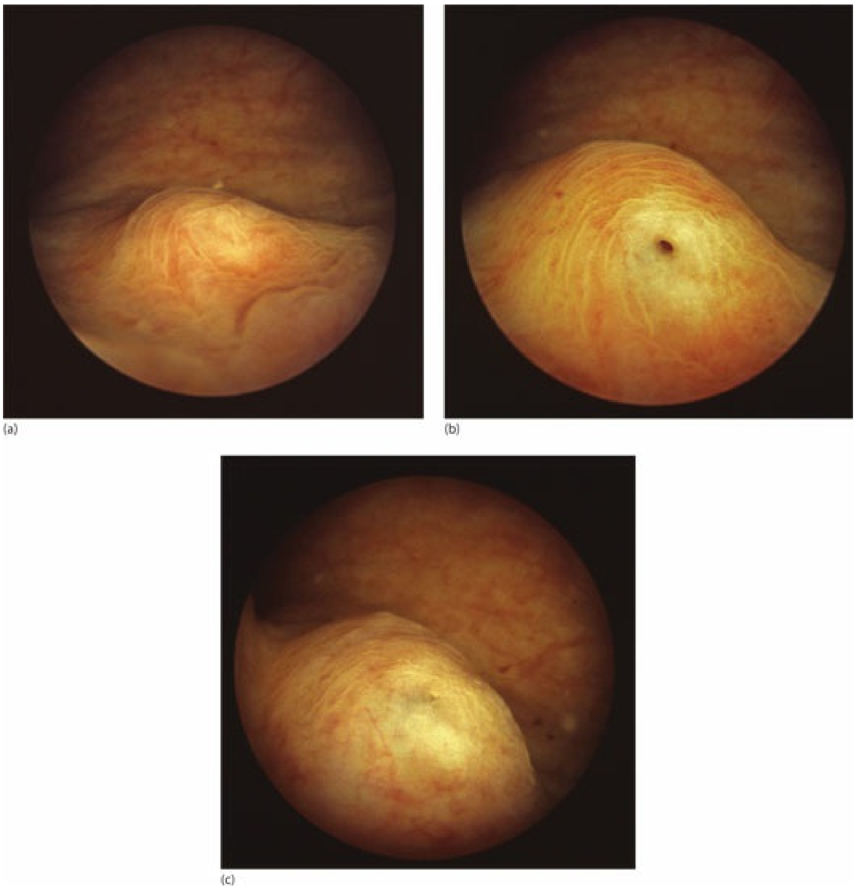


Figure 39.38 Small ureterocele: (a) empty, (b) half-filled, and (c) distended.

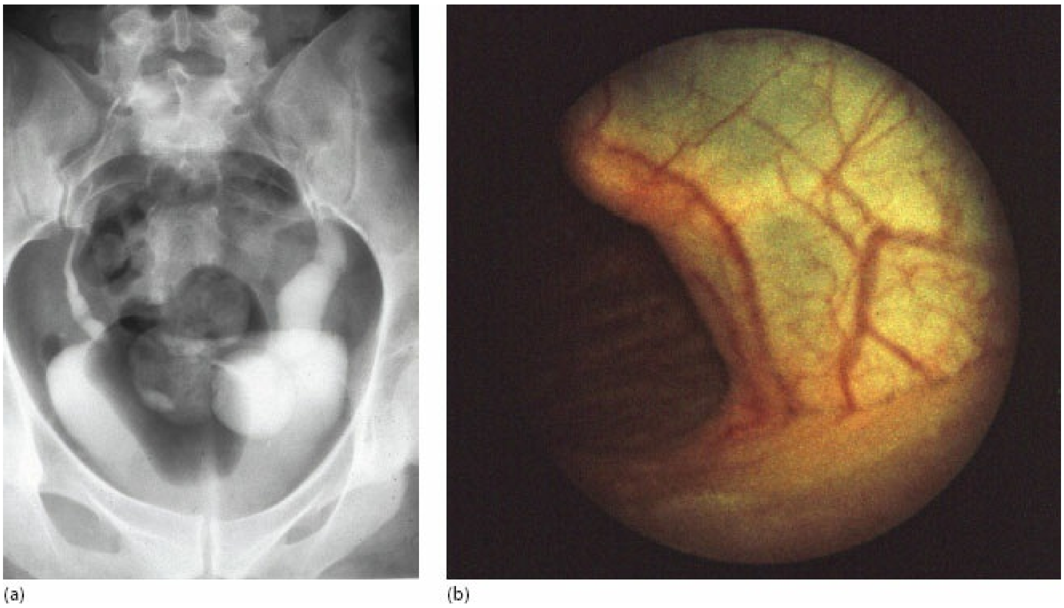


Figure 39.39 Ureterocele: (a) endoscopic and (b) intravenous urogram (IVU) image. (From Schönebeck, J., *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

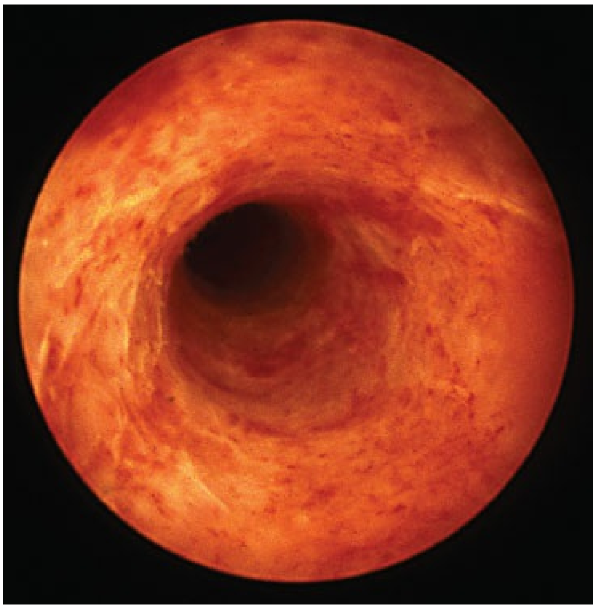


Figure 39.40 Catheter occasioned urethritis. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

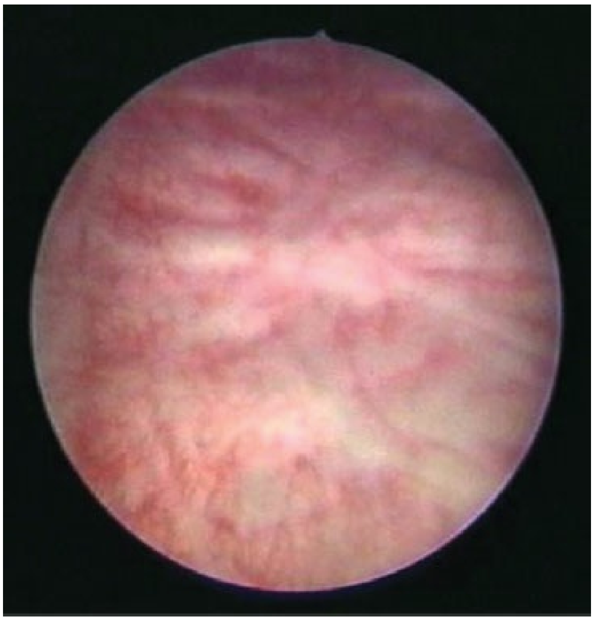


Figure 39.41 Acute cystitis with bladder trabeculation. (With kind permission from Springer Science+Business Media: *Manual Endourology: Training for Residents*, 2005, Hohenfellner R and Stolzenburg J-U.)

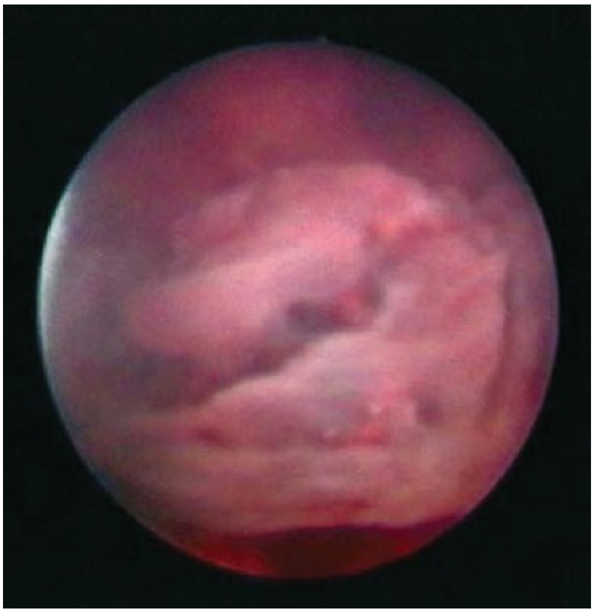


Figure 39.42 Bilharzial bladder showing extensive thick plaque of squamous metaplasia and leukoplakia close to squamous cell carcinoma. (With kind permission from Springer Science+Business Media: *Manual Endourology: Training for Residents*, 2005, Hohenfellner R and Stolzenburg J-U.)

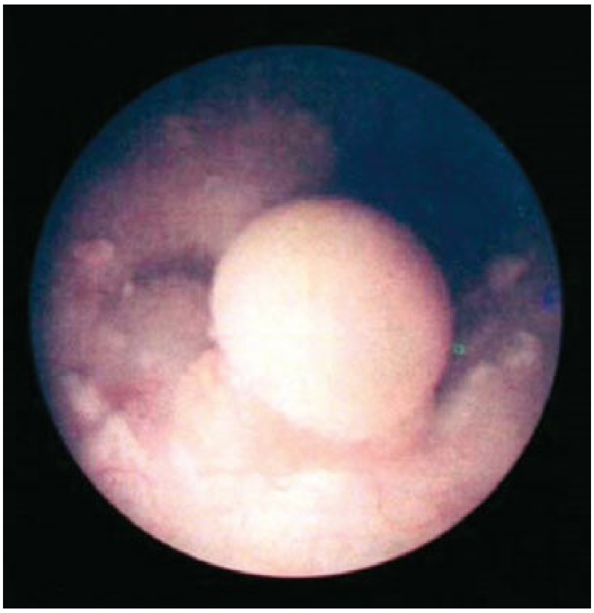


Figure 39.43 Multiple yellow-brown peppery cysts (cystitis cystica). (With kind permission from Springer Science+Business Media: *Manual Endourology: Training for Residents*, 2005, Hohenfellner R and Stolzenburg J-U.)

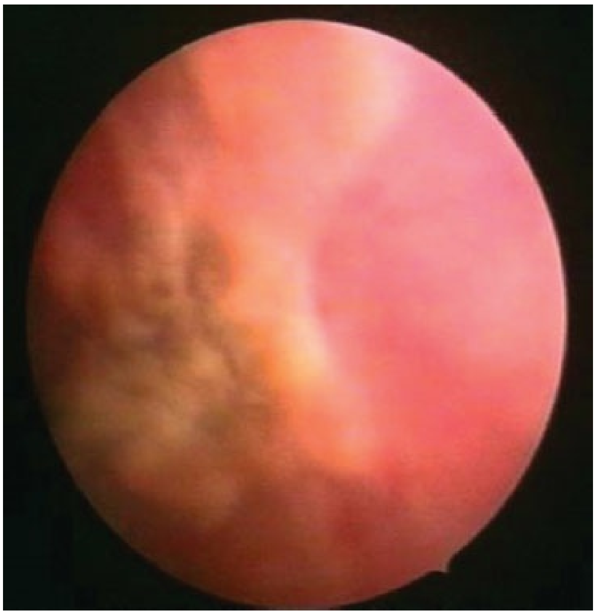


Figure 39.44 Residual tumor after radiotherapy with evidence of radiation cystitis (hemorrhagic cystitis). (With kind permission from Springer Science+Business Media: *Manual Endourology: Training for Residents*, 2005, Hohenfellner R and Stolzenburg J-U.)

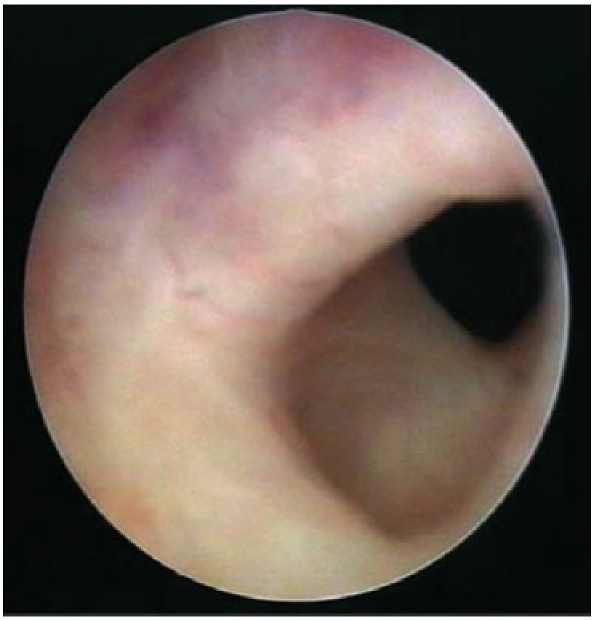


Figure 39.45 Bladder with history of large perforation showing an epithelized false diverticulum. (With kind permission from Springer Science+Business Media: *Manual Endourology: Training for Residents*, 2005, Hohenfellner R and Stolzenburg J-U.)

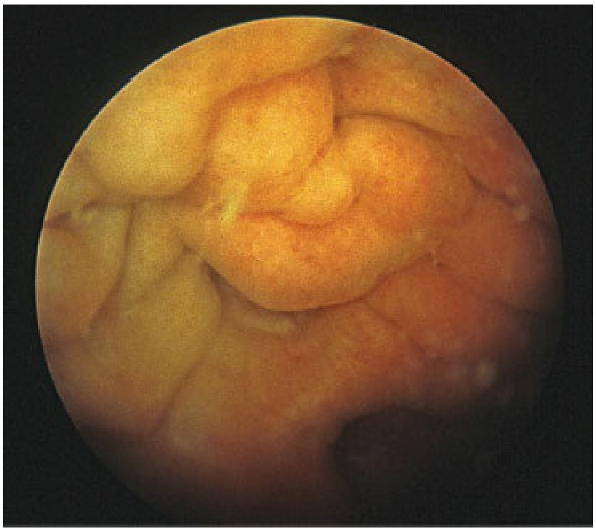


Figure 39.46 Thick-walled, contracted bladder caused by indwelling catheter. (From Schönebeck, J., *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

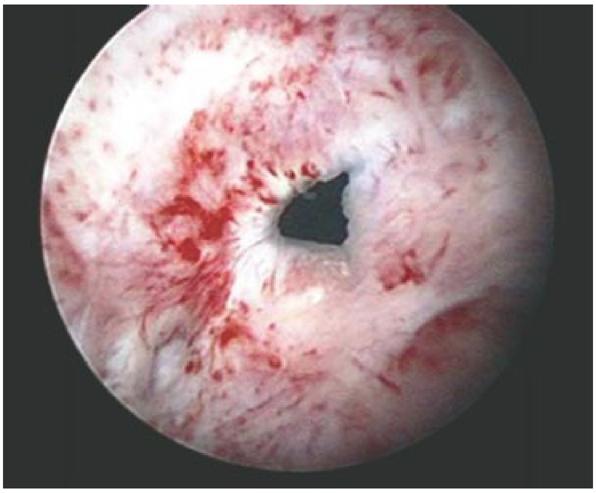


Figure 39.47 Bladder neck stenosis. (With kind permission from Springer Science+Business Media: *Manual Endourology: Training for Residents*, 2005, Hohenfellner R and Stolzenburg J-U.)

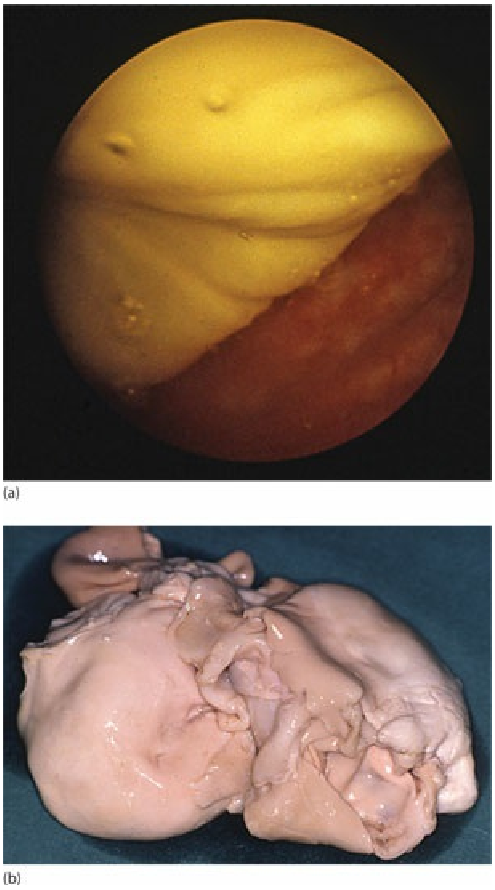


Figure 39.48 (a) Bladder bezoar—another uncommon occurrence is formation of a “fungus ball”—*Candida albicans*. (b) Bladder bezoar removed from the bladder. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

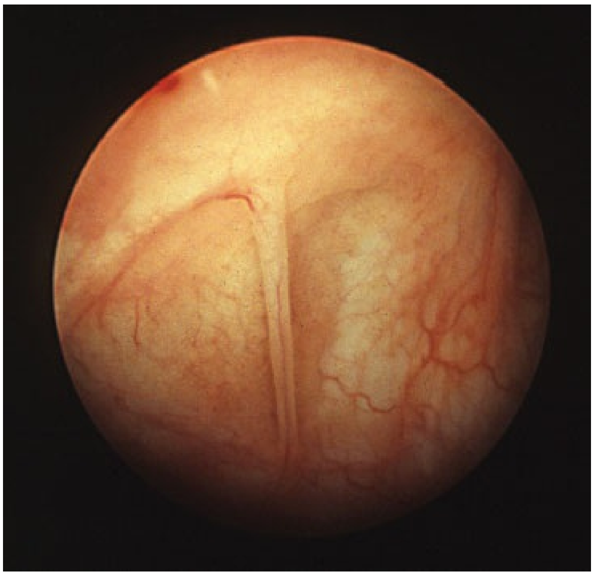
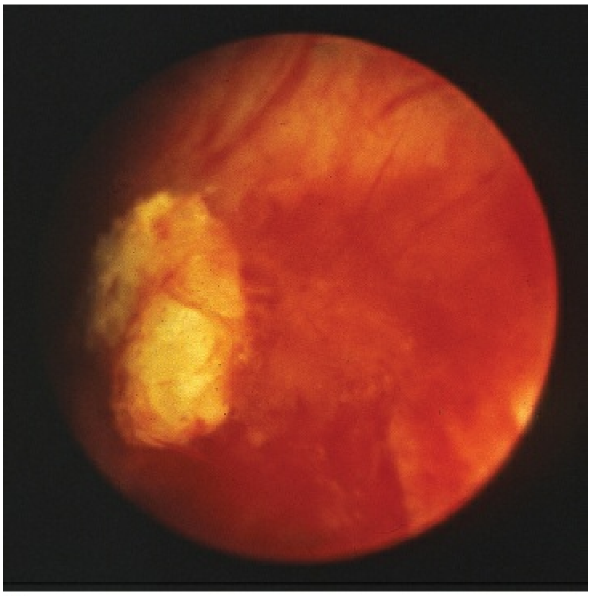


Figure 39.49 Cecocystoplasty—border cecum—bladder. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)



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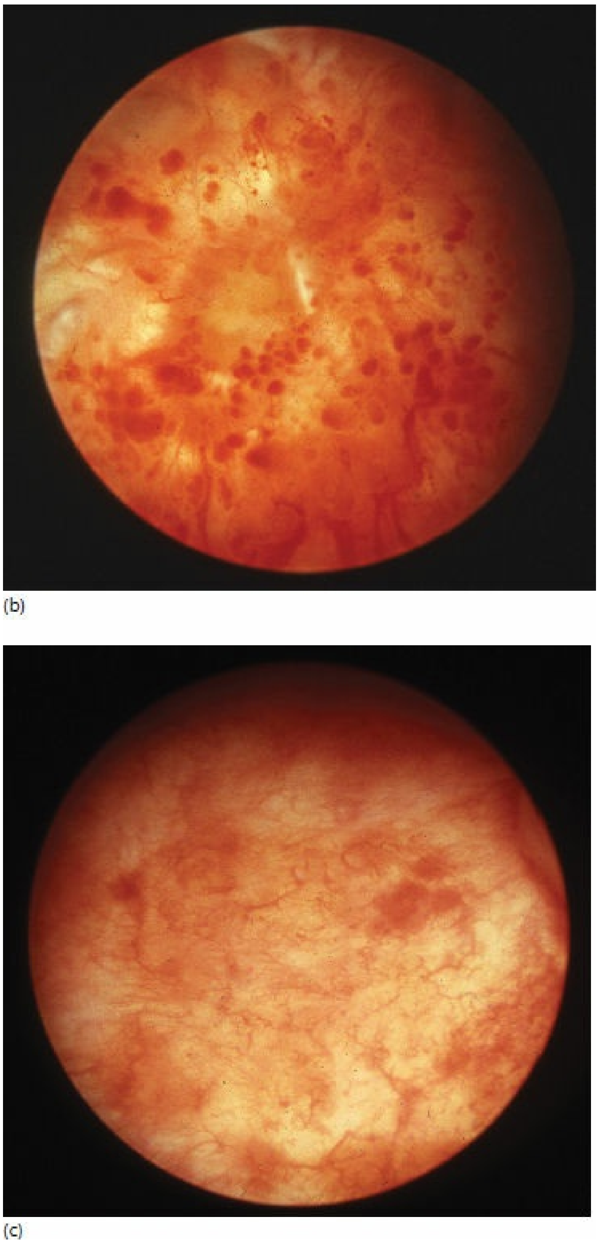

Figure 39.50 (a) Active bladder tuberculosis. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.) (b) Marked granulomatous changes after 5 months of treatment. (c) Healing bladder tuberculosis after 5 months of treatment. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

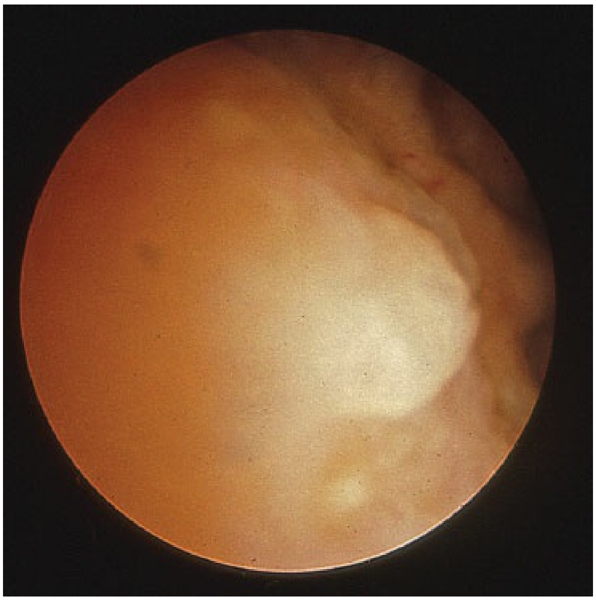

Figure 39.51 Bladder amyloidosis. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

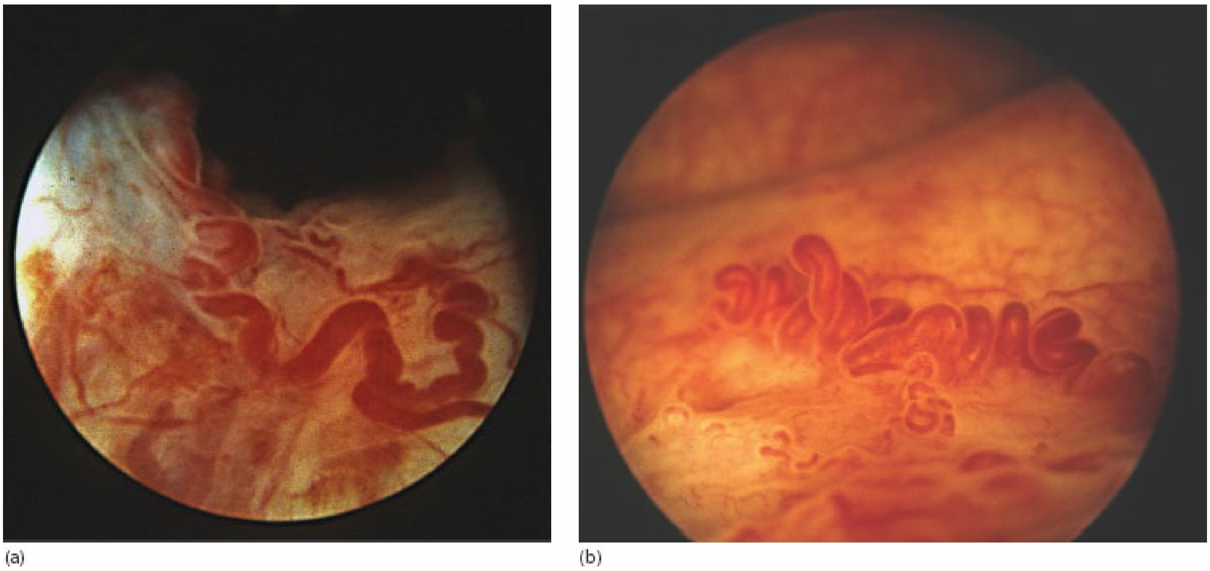

Figure 39.52 (a) Varicose veins at the internal opening of the urethra. (b) Normal bladder—varicose vessels. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

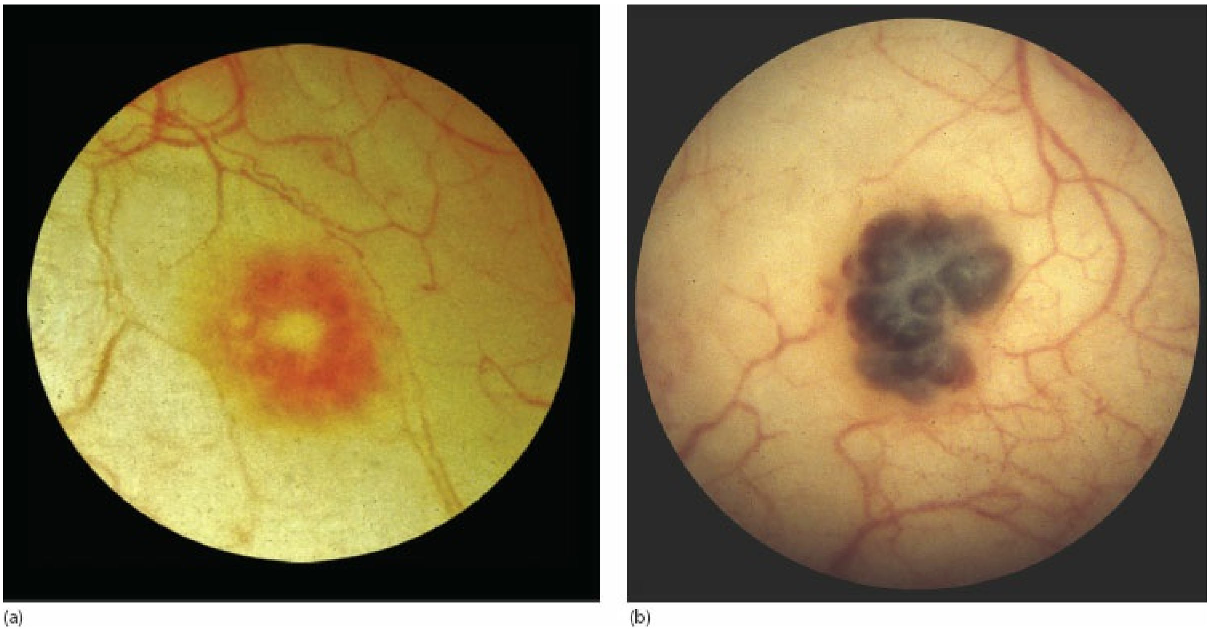

Figure 39.53 (a and b) Hemangioma—urinary bladder. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

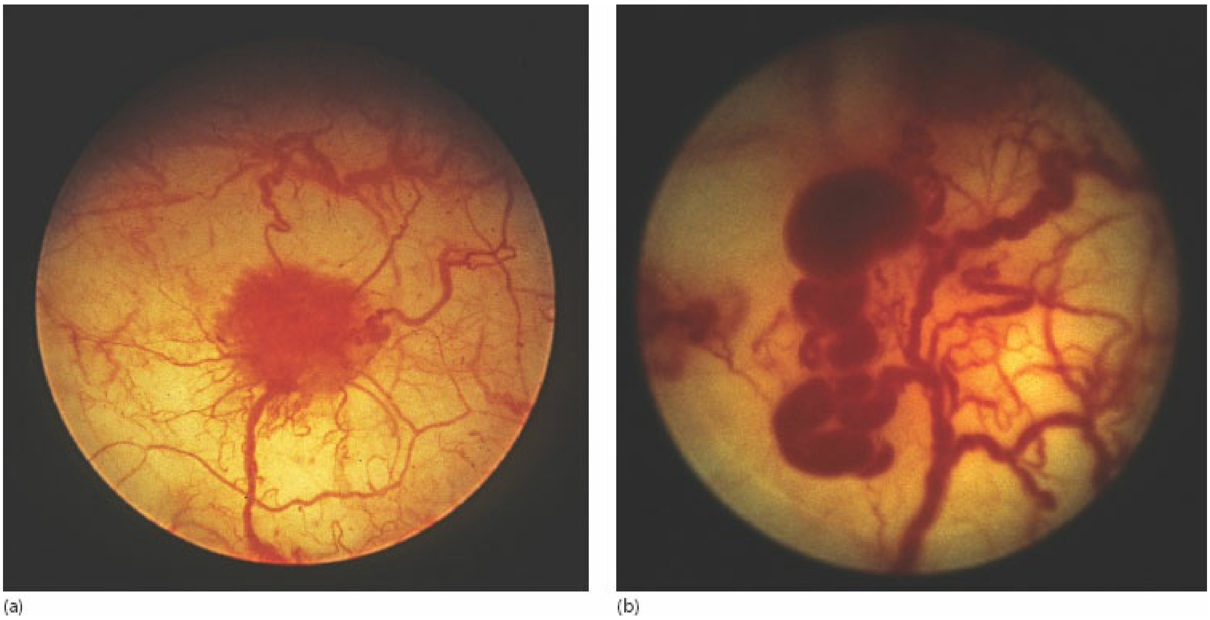

Figure 39.54 Bladder changes following radiotherapy especially for bladder cancer: (a) abnormal vessels after radiotherapy and (b) abnormal vessels—radiotherapy. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

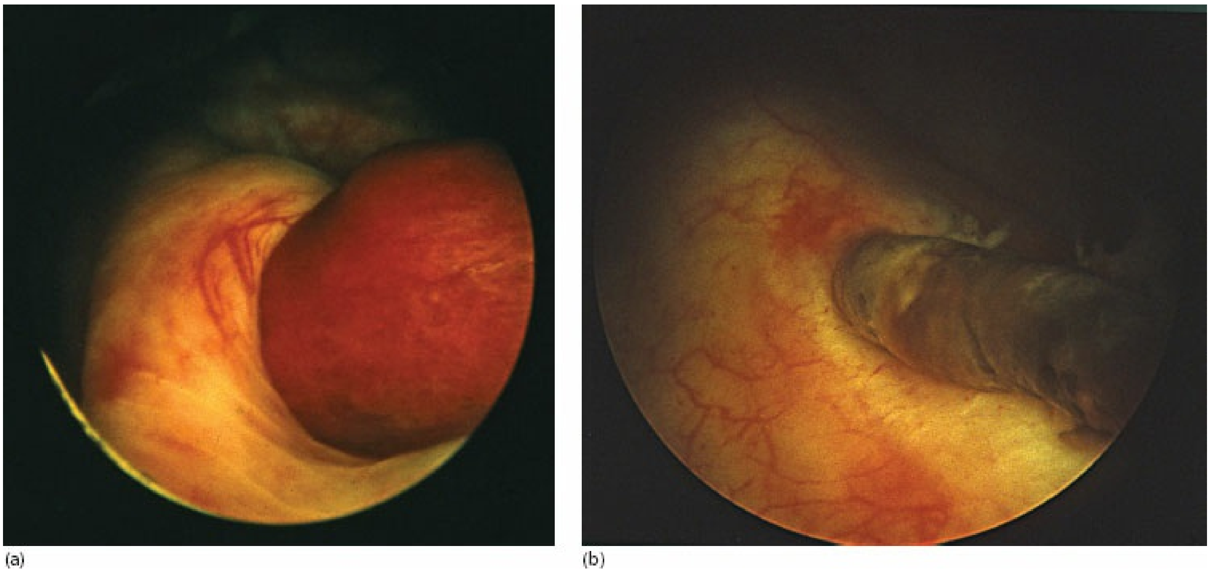

Figure 39.55 Blood clots: (a) fresh clot leaving the right ureter and (b) old clot (almost black) leaving the right ureter. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

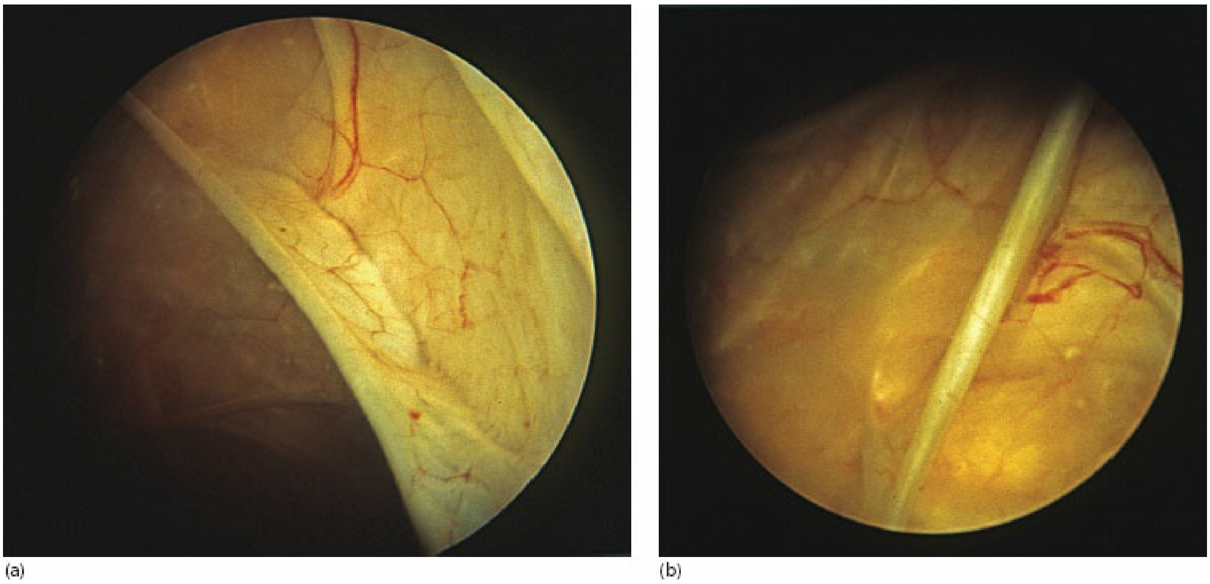

Figure 39.56 Bladder septum or membrane: (a) side view and (b) seen from above. (From Schönebeck J, *Digital Atlas of Cystoscopy*, Astra Tech, Molndal, Sweden, 2007, pp. 22–45.)

CONCLUSIONS

Endoscopy has revolutionized the treatment of urological disease and forms a cornerstone of modern practice. Technological developments have facilitated improved optics and smaller, more maneuverable instruments. This enables the treatment of increasingly complex pathology with less patient impact.

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40 Urinalysis

F.M.E. Wagenlehner and Ganesh Thiagamoorthy

URINALYSIS AND URINE CULTURE

Urinalysis is an essential noninvasive investigation and has been described since the era of the ancient Egyptians [1]. Basic urinalysis, conducted by the patient's bedside or in the office setting, allows for rapid assessment of urine to screen for a number of concerning pathologies including infection, diabetes mellitus, dehydration, malignancy, nephropathy, and renal stones. More detailed analysis can then be carried out in a laboratory to confirm diagnoses.

Analysis of urine should be based on standardized procedures, taking into account the areas of sample collection, transportation, and the actual analysis. One of the most detailed guidelines in this respect is the European urinalysis guideline that is still valid today [2].

Urine Collection and Testing

Specimens requiring investigation should be collected in a sterile manner into a clean container. In patients without catheters, urogenital cleansing prior to sample collection usually reduces and at least does not worsen the risk of contamination [3,4]. A recent comparative study showed using “paper soap” or “cleansing wipes” reduced the risk of contamination more than cleaning solely with water, but this has not yet been incorporated into clinical practice because of concerns regarding the effect of the soap on the viability of bacteria and chemical analysis [5,6]. Women should be asked to wipe the area between the labia from front to back and clean specifically over the urethra. Urine should be voided with their legs spread and with two fingers parting their labia. After passing some of the urine into the toilet, the collection device should then be at least half filled with the “midstream urine” sample prior to emptying the rest of their bladder into the toilet [7].

In women with indwelling catheters, if the catheter has been in situ for less than 2 weeks, a sample can be aspirated with a sterile syringe or using a cannula adapter after disinfecting the needleless sampling port. For specimens that are intended to be sent for microbiology, special device kits are now available that allow the urine sample to be transferred directly from the indwelling catheter to a Vacutainer tube containing preservative [8]. In cases where a urinary tract infection is suspected and the catheter has been in situ for more than 2 weeks, the catheter should be replaced to improve resolution of symptoms, and urine culture should be obtained from the freshly placed catheter prior to the initiation of antimicrobial therapy [9].

The components of urine such as bilirubin, urobilinogen, urothelial cells, microbial cells, or crystals begin to deteriorate soon after production, while commensal bacteria tend to overgrow altering glucose concentration and pH and preventing accurate diagnosis of pathogens [10]. In view of this, urinalysis should ideally be performed on-site within 2 hours of specimen production [11]. When this is not possible, a sample should be refrigerated within an hour or a preservative used [12]. Appropriate selection of preservation method may be critical since some preservatives interfere with enzymatic measurements.

Physical Examination

Urine may be globally screened by a trained assessor as part of a preliminary evaluation.

Color may be an indicator of concentration with increased pallor indicating increased hydration. The presence of brown, purple, red, or orange may, respectively, be secondary to raised bilirubin, the presence of infection, blood secondary to infection or malignancy, or ingestion of certain foods or drugs such as beetroot or rifampicin [13].

Turbidity increases with the presence of sediment and may be an indicator of infection, urinary crystals, or contaminants such as creams or vaginal discharge.

Odor is another factor that must be considered. Concentrated urine has a typical smell while overt urinary tract infections tend to have a specific foul-smelling ammonium odor. Ingestion of some foods, for example, asparagus, can also has a result in a characteristic smell.

Chemistry Examinations

Most chemistry examinations are performed with dipstick test strips. Routine dipstick urinalysis screens for leukocytes, nitrites, red blood cells, protein, glucose, ketones, specific gravity, and pH. “Test pads,” the small squares on test strips, are impregnated with specific chemicals that, when in contact with urine, undergo a chemical reaction resulting in a color change. The severity of the color change is then compared to the color on the chart, usually on the container to read the results. To reduce variation between users, optical readers are available that provide printed results. Abnormal urine color must be noted from the physical examination as this may lead to misinterpretation of the test pad color changes giving incorrect results [10].

Leukocytes are detected on the basis of indoxyl esterase activity released from lysed neutrophil granulocytes or macrophages. The detection limit is approximately 20×10^6 WBC/L.

Nitrites are found secondary to the activity of the nitrate reductase that reduces nitrate to nitrite, which is present in a variety of Gram-negative uropathogenic bacteria such as *Escherichia coli*. Nitrate reductase is however not produced by Gram-positive bacteria such as *Enterococcus* spp. and *Staphylococcus* spp. A positive nitrite test also requires nitrate in the patient’s diet (vegetables) to be excreted into urine and then incubated with nitrate reductase producing bacteria for at least 4 hours. Lower exposure times, e.g., in the case of patients with storage lower urinary tract symptoms leading to increased daytime frequency, could lead to false-negative results.

Red blood cells, hemoglobin or myoglobin in urine, are chemically detected by the pseudoperoxidase activity shown by the heme moiety of hemoglobin or myoglobin. Red blood cells or hemoglobin in urine might stem from prerenal, renal, or postrenal disease or hemolysis. Myoglobin in urine can be detected in cases of muscle necrosis, rhabdomyolysis, or myositis. The sources cannot be differentiated by chemistry investigation. A positive dipstick reading of red blood cells merits further microscopic examination to confirm or refute the diagnosis of asymptomatic microscopic hematuria.

Proteins in urine are a mixture of high- and low-molecular-weight proteins from plasma, kidney proteins such as Tamm–Horsfall protein, and proteins from the urinary and genital tract. Mucoproteins and low-molecular-weight proteins are less sensitively detected and Bence–Jones proteins are not detected. The test strip method mainly detects albumin at a concentration limit of 20 mg/L. Albumin concentrations less than 20 mg/L, termed “low-grade albuminuria,” may be suspicious for early glomerular damage. In order to screen for proteinuria resembling kidney damage in spot urine samples, the protein/creatinine ratio test has been designed. In morning urine samples, this technique compares favorably with 24 hours urine protein excretion with a threshold of 0.94 g/g creatinine to detect urine protein excretion of 1 g and 2.84 g/g creatinine to detect urine protein excretion of 3 g in 24 hours collections [14].

Glucose is found in urine when the volume of glucose filtered out of the blood stream by the glomerulus is greater than that that can be reabsorbed by the proximal renal tubule. The differentials for this include diabetes mellitus, pregnancy, Cushing’s syndrome, hepatobiliary, and pancreatic diseases.

Ketone bodies measured in the urine are acetoacetate and acetone and, to a lesser extent, β-hydroxybutyrate. Ketone bodies are elevated during diabetic hyperglycemia and ketosis, as well as after (overnight) fasting and inflammatory diseases of the bowel.

Specific gravity is measured using a chemical test and assesses the osmolality of urine compared to that of water. Specific gravity usually ranges between 1.003 and 1.035. A specific gravity close to 1.002 would be considered very dilute, while a level of 1.035 would be very concentrated.

Urinary pH is usually between 5.5 and 6.5 but can vary between 5 and 9, depending on diet and exercise. Urine pH is measured for diagnosis of acid–base disturbances. For example, in renal tubular acidosis or uric acid stone disease, urinary pH is constantly elevated or decreased, respectively. Bacteria metabolizing urea to ammonia, such as *Proteus mirabilis*, increase urine pH to 8.0 or higher.

Pregnancy tests are conducted on urine sample using specific test kits to measure human chorionic gonadotropin (hCG) secreted by the developing placenta. hCG is found at concentrations up to 10,000 IU/L in urine in early pregnancy and can be detected sensitively in urine in early pregnancy. The best urine sample for evaluation of hCG is the concentrated morning urine. A normally developing pregnancy will produce an hCG level of 25 IU/L 3–4 days after implantation. Most urinary pregnancy tests are sensitive to concentrations of 25 IU/L and therefore detect pregnancy up to 4 days prior to a missed period [15].

Particle Analysis

Particle analysis is the detailed assessment of urinary components either manually, mostly under a microscope, or via automated microscopy and flow cytometry [6]. It can be performed in unprocessed urine or using staining and can be performed in both centrifuged and noncentrifuged samples. There is a consensus that for most cases of routine examination, centrifugation is not necessary.

Some of the commonest particles found are white and red blood cells.

Leukocytes

Granulocytes are the most frequent leukocytes detected in the urine and are mainly observed as a response to urinary tract infection. In asymptomatic bacteriuria, granulocytes may also be seen, and their presence does not preclude the diagnosis of asymptomatic bacteriuria.

Macrophages also commonly appear in the urine of patients with urinary tract infection. In glomerulonephritis, interstitial nephritis, or interstitial cystitis, the major immune cellular components seen are granulocytes.

Lymphocytes in urine are more associated with viral diseases and renal transplant rejection.

Red Blood Cells

Red blood cells in urine, and their morphology, may reflect the origin of bleeding. Dysmorphic red blood cells are of an abnormal size or shape (erythrocytes usually have a diameter of 4–7 mm) and suggest renal disease, whereas normal morphology usually suggests the source to be the lower urinary tract. Accordingly, they can determine whether the subsequent diagnostic workup should be urological or nephrological.

Other Cells

Urothelial cells derive from the multilayered epithelium lining the urinary tract.

The appearance of squamous epithelial cells is a marker of contamination by poor collection technique. During pregnancy, epithelial cells in urine are increased regardless of quality of the collection technique.

Casts

Casts are particles formed in the distal tubules and collecting ducts and usually reflect the presence of renal disease. Within casts, plasma proteins, lipids, different types of cells, microorganisms, pigments, or crystals may be found.

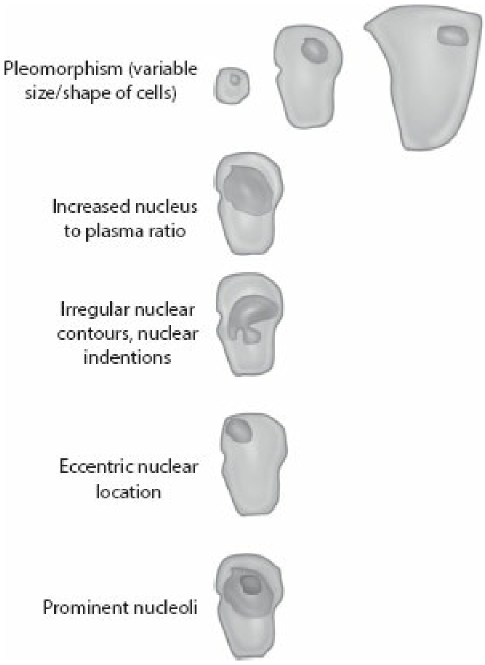
Pleomorphism (variable size/shape of cells)
Increased nucleus to plasma ratio
Irregular nuclear contours, nuclear indentions
Eccentric nuclear location
Prominent nucleoli

Figure 40.1 Schematic drawing of general cytomorphological features suggesting malignant cells.

Bacteria

Bacteria are detected at concentrations above 10^5 colony-forming units/mL (cfu) and centrifugation does not increase diagnostic accuracy. Applying Gram staining to centrifuged urine can increase diagnostic accuracy, but this is dependent on bacterial density.

Urine Cytology

Urine cytology is an important form of particle analysis used to investigate patients who are at risk or under surveillance for urothelial carcinoma. Several classification systems for urine cytology have evolved over the years [16–20]. General cytomorphological features suggesting malignant cells include nuclear hyperchromasia, irregular nuclear contours, abnormal chromatin texture, prominent nucleoli, eccentric nuclear location, nuclear indentations, increased nucleus-to-cytoplasm ratios, and high cellularity (Figure 40.1).

Urine cytology has a high sensitivity and specificity for high-grade urothelial lesions, such as carcinoma in situ, but low sensitivity and low negative predictive value in patients with low-grade urothelial tumors. Additional methods include fluorescence in situ hybridization techniques and various molecular approaches that are under evaluation currently.

Urine Culture

The aims of urine culture are to identify pathogens of urinary tract infection and estimate the concentration of bacteria and susceptibility to antimicrobials. The most commonly implicated bacteria in urinary tract infections are enterobacteria, such as *E. coli, Klebsiella* spp., *Enterobacter* spp., *Proteus* spp., non-fermenters such as *Pseudomonas* spp., and Gram-positive bacteria such as enterococci and staphylococci (*Staphylococcus saprophyticus*).

Dipslide testing does not reliably detect pathogen inocula of 10^4 cfu/mL or lower. However, in acute uncomplicated cystitis, colony concentrations of midstream urine samples are at concentrations of $\leq 10^3$ cfu/mL, so must be detected by additional tests such as plating on agar mediums, such as cystine lactose electrolyte deficient agar plates. A Gram-negative selective agar, such as MacConkey agar, can also be used.

Despite the presence of large numbers of bacteria, false-negative results may be obtained if patients have already commenced on antimicrobials. Special tests, such as the *Bacillus subtilis* test, help to detect antimicrobials in these circumstances.

Susceptibility testing allows the clinician to choose the correct antibiotic for treatment of urinary tract infections. There are several standardized methods available, such as disc diffusion, dilution, and epsilometer testing [21]. Susceptibility testing is performed according to international standards (Clinical and Laboratory Standards Institute or European Committee on Antimicrobial Susceptibility Testing). Susceptibility testing using automated systems has also been available for several years in most microbiological laboratories.

Fastidious organisms are prevalent in 13.7%–27.0% of patients with chronic lower urinary tract symptoms [22,23]. Three commonest fastidious organisms involved in chronic urinary tract infections are *Ureaplasma urealyticum*, *Mycoplasma hominis*, and *Chlamydia*. These organisms are more difficult to culture as they have complex nutritional requirements. To assess for fastidious organisms, laboratories must carry out either polymerase chain reaction testing or utilize culture mediums that enrich for a wider range of species and culture this for a longer than the usual duration of 7 days [23,24]. Due to the cost and time implications, most laboratories do not routinely screen for fastidious organisms. A single 3-month empirical course of a low-dose quinolone or tetracycline antibiotics can effectively treat 82% of fastidious organisms and a second 3-month course can treat 96% [25]. In view of the prevalence of these organisms in patients with chronic refractory lower urinary tract symptoms, it is important that fastidious organisms are considered and appropriate investigations conducted or empirical treatment initiated.

Novel Techniques

New “point-of-care” microbiology assessments are being developed that might enable susceptibility analyses of urine samples within 4–6 hours. This technology could avoid empirical broad-spectrum antibiotic usage and allow a more targeted approach.

CONCLUSION

In summary, urine dipstick with or without urine microscopy and culture is an important baseline test into the well-being of a woman. Although most commonly used to confirm the presence of infection, it has the ability to assess multiple other important diseases or concerns.

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Section V

Conservative and Minimally Invasive Therapies

41 The Role of the Continence Nurse

Angie Rantell

The role of the continence nurse (CN) is multifaceted and ever expanding. It has developed rapidly in the United Kingdom since the 1980s, and now most clinical commissioning groups (organizations set up to organize the delivery of health services in England) offer a continence service that is run by specialist nurses.

These specialists provide a comprehensive assessment of all patients with continence needs and, if applicable, will implement conservative and pharmacological management plans. CNs have a role in education and health promotion for patients and other health-care professionals (HCPs). They also act as counselors when dealing with the negative psychosexual, emotional, and social impact that incontinence can have on an individual's quality of life. Generally, CNs are the first HCPs that patients are referred to, following disclosure of an incontinence problem, which places them in a prime position to undertake further research into the field especially with regard to etiology, epidemiology, quality of life improvements, and assessment of successful management.

A survey in the United Kingdom [1] reported the benefits of better continence care including the following:

- Reduces admissions to permanent care settings—nursing homes, secondary care, and homes for disabled adults and children.
- Reduces costly emergency admissions to secondary care with urinary tract infections, pressure ulcers, and catheter-related infections.
- Reduces prolonged use of costly incontinence products through low-cost interventions such as physiotherapy and medication.
- Better continence care contributes to independent living and improved quality of life.

According to the National Health Service (NHS) Modernisation Agency, continence care is the total care package tailored to meet individual needs of patients with bladder and bowel problems. This chapter will further discuss the varied roles that CNs perform to be able to provide a continence care package for all patients.

RANGE OF NURSING ROLES WITHIN CONTINENCE CARE

When continence services were first introduced, they would often provide care for all patient groups. However, now with the expanding needs of these services, specialized areas have emerged. Table 41.1 shows the different nursing specialities within continence care. These subspecialities are essential to offer expert care to all patients in primary, secondary, and tertiary care.

There is also a distinct range of nursing roles within the field including nurse consultants, clinical nurse specialists, continence advisors, staff nurses, and health support workers. Some may work alone or as part of a larger multidisciplinary team.

Austin [2] undertook a postal survey of continence advisors working in one health region to assess the differences in their roles and, in total, 41 responded. All of them had clinical contact with patients. Of the continence advisors surveyed, 50% had been involved in research relating to their specialty. A high proportion of respondents were involved in the education of nurses, medical staffs, and other HCPs. Most were involved in producing standards, protocols, and guidelines and all had an organizational wide remit in an advisory role. Many were responsible for auditing the practice of others and 65% managed other staff within their team. For providing advice or approval regarding purchasing and supply of specialist products, 90% were responsible and half of them held their own budget. This paper demonstrates the many different roles that a CN must perform to provide a full service.

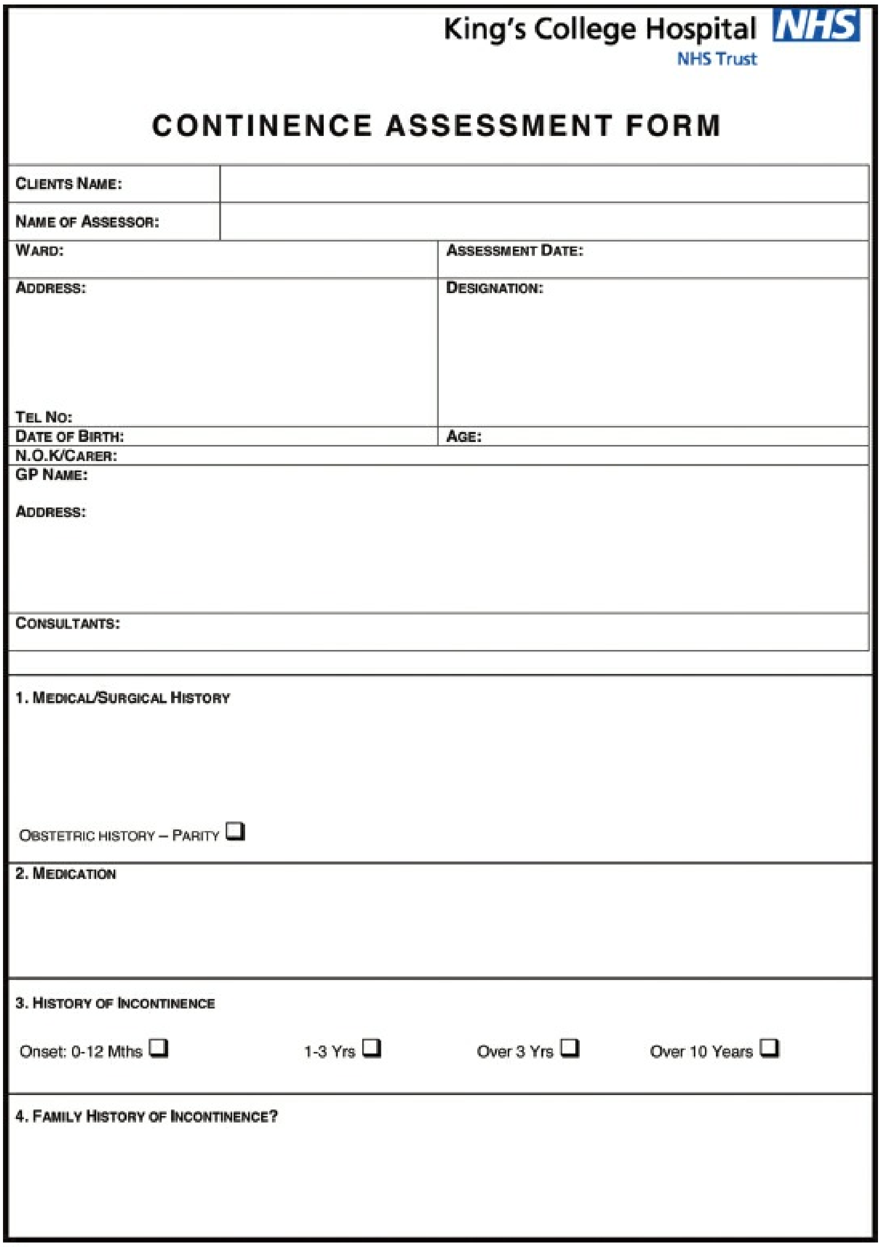
ASSESSMENT

Incontinence is a symptom of an underlying disorder. A complete continence assessment will help to identify possible causes by building a complete picture of bladder and bowel dysfunction. A thorough initial assessment is important to determine incontinence type and rule out infections or other causes [3]. According to Lloyd [4], the procedure of taking a patient history allows the patient to present their account of the problems and provides essential information to the practitioner. There are many different models of assessment that can be utilized for this; however, many units will have developed their own proforma to standardize assessment in their specialist area. These may not only be used for specialist assessment but can also be used to standardize continence assessment for general nurses and to help ensure appropriate referral for patients with continence issues. Figure 41.1 demonstrates a continence assessment proforma that is designed for general nurses to help identify and assess hospital in-patients with bladder or bowel dysfunction. The Royal College of Nursing (RCN) has also published a framework for the assessment of continence in care homes that provides key questions and suggestions where residents of a care home may have continence problems Royal College of Nursing, Continence care in care homes – A framework to gather and share key information, London, UK, RCN, 2007.

The quality of assessment will be greatly enhanced by the participation of the patient and carers to the assessment process ensuring that the patient's wishes are foremost and, wherever possible, her own words are used to reflect her needs [5]. For this to be put into practice, the CN needs to have excellent interpersonal skills to build a trusting and open relationship with the patients and carers, encouraging them to voice their feelings and views about their problems.

Table 41.1 Variety of Nursing Roles Involved in Continence Care

General continence nurse specialist
Urogynecology nurse specialist
Urology nurse specialists
Colorectal nurse specialist
Stoma nurse specialists
Pediatric continence specialist
Geriatric continence specialist
Neurology nurse specialist (e.g., stroke, multiple sclerosis, Parkinson's disease)



King's College Hospital NHS

NHS Trust

CONTINENCE ASSESSMENT FORM

CLIENTS NAME:	
NAME OF ASSESSOR:	
WARD:	ASSESSMENT DATE:
ADDRESS: TEL NO:	DESIGNATION:
DATE OF BIRTH:	AGE:
N.O.K/CARER:	
GP NAME: ADDRESS:	
CONSULTANTS:	

1. MEDICAL/SURGICAL HISTORY

OBSTETRIC HISTORY – PARITY ☐

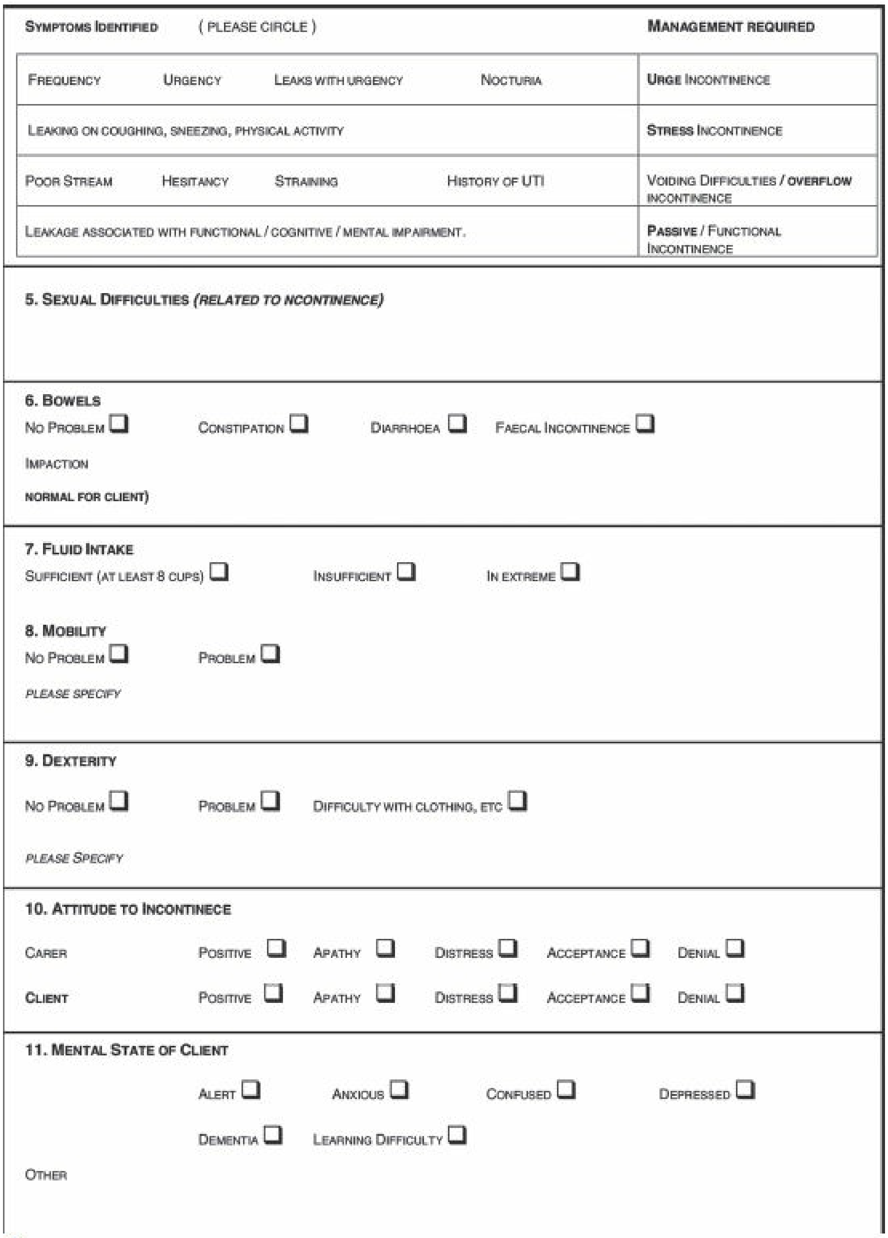
2. MEDICATION

3. HISTORY OF INCONTINENCE

Onset: 0-12 Mths ☐ 1-3 Yrs ☐ Over 3 Yrs ☐ Over 10 Years ☐

4. FAMILY HISTORY OF INCONTINENCE?

(a)



Symptoms Identified (PLEASE CIRCLE) **Management required**

Frequency Urgency Leaks with urgency Nocturia	**Urge** Incontinence
Leaking on coughing, sneezing, physical activity	**Stress** Incontinence
Poor Stream Hesitancy Straining History of UTI	Voiding Difficulties **/ overflow** incontinence
Leakage associated with functional / cognitive / mental impairment.	**Passive** / Functional Incontinence

5. Sexual Difficulties *(related to ncontinence)*

6. Bowels

No Problem ☐ Constipation ☐ Diarrhoea ☐ Faecal Incontinence ☐

Impaction

normal for client)

7. Fluid Intake

Sufficient (at least 8 cups) ☐ Insufficient ☐ In extreme ☐

8. Mobility

No Problem ☐ Problem ☐

Please specify

9. Dexterity

No Problem ☐ Problem ☐ Difficulty with clothing, etc ☐

Please Specify

10. Attitude to Incontinece

Carer	Positive ☐	Apathy ☐	Distress ☐	Acceptance ☐	Denial ☐
Client	Positive ☐	Apathy ☐	Distress ☐	Acceptance ☐	Denial ☐

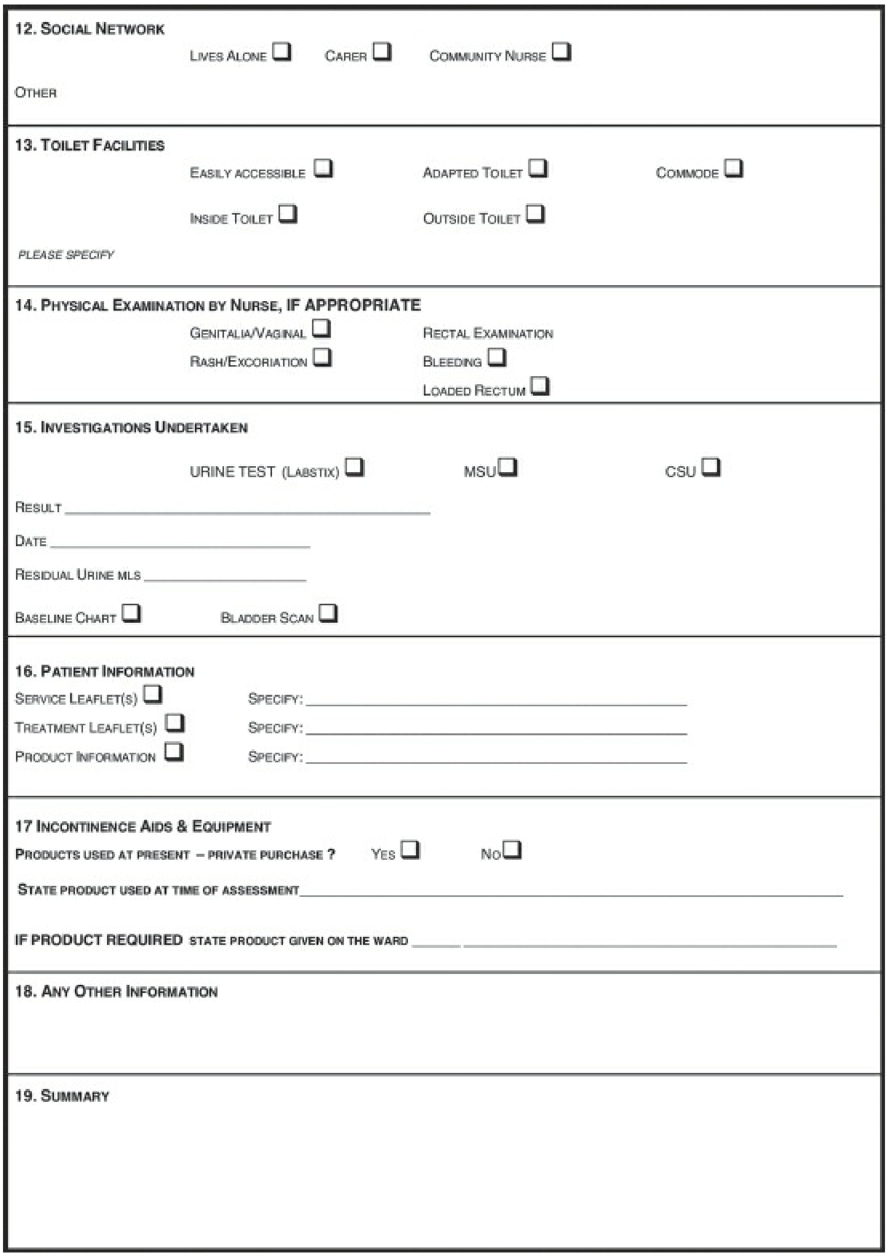
11. Mental State of Client

Alert ☐ Anxious ☐ Confused ☐ Depressed ☐

Dementia ☐ Learning Difficulty ☐

Other

(b)



12. Social Network

Lives Alone ☐ Carer ☐ Community Nurse ☐

Other

13. Toilet Facilities

Easily accessible ☐ Adapted Toilet ☐ Commode ☐

Inside Toilet ☐ Outside Toilet ☐

Please specify

14. Physical Examination by Nurse, IF APPROPRIATE

Genitalia/Vaginal ☐ Rectal Examination

Rash/Excoriation ☐ Bleeding ☐

Loaded Rectum ☐

15. Investigations Undertaken

URINE TEST (Labstix) ☐ MSU ☐ CSU ☐

Result ______________________________

Date ______________________

Residual Urine mls ________________

Baseline Chart ☐ Bladder Scan ☐

16. Patient Information

Service Leaflet(s) ☐ Specify: ______________________________

Treatment Leaflet(s) ☐ Specify: ______________________________

Product Information ☐ Specify: ______________________________

17 Incontinence Aids & Equipment

Products used at present – private purchase ? Yes ☐ No ☐

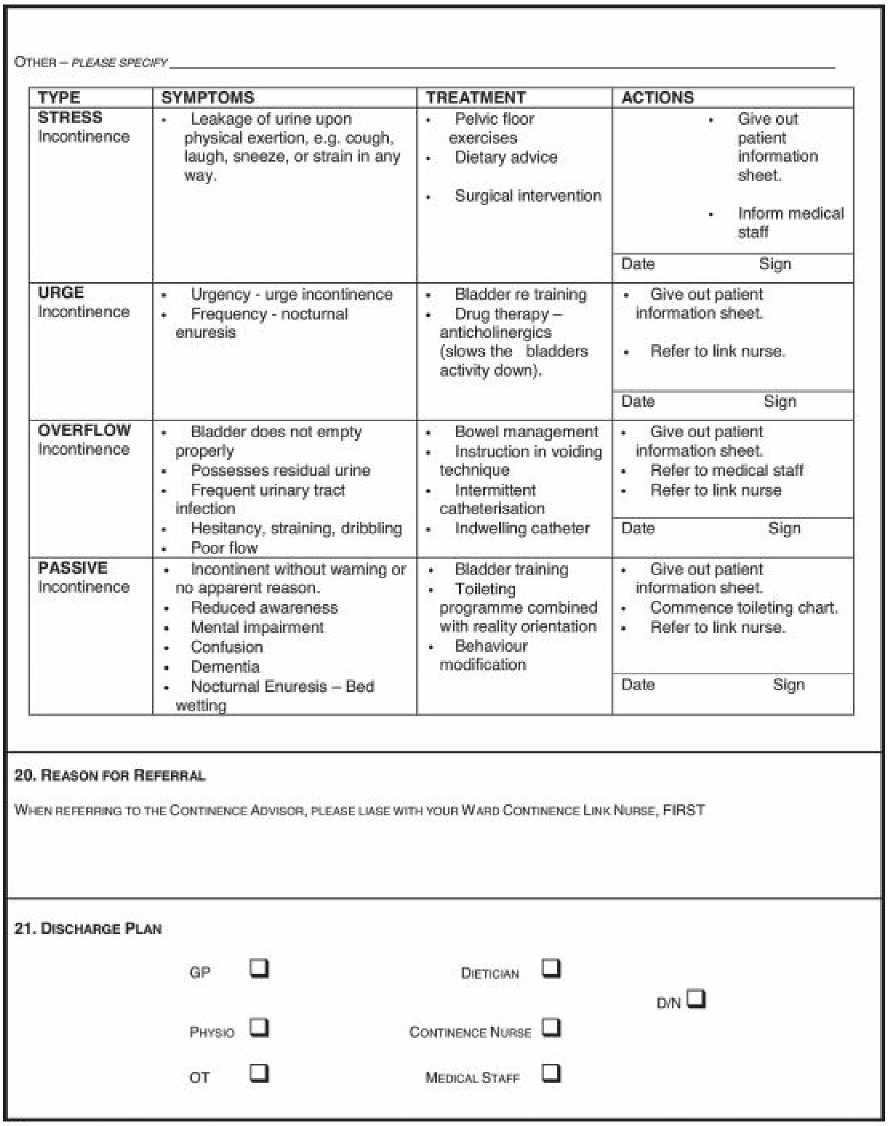
State product used at time of assessment______________________________

IF PRODUCT REQUIRED state product given on the ward _____ ______________________________

18. Any Other Information

19. Summary

(c)



Other – *please specify* ____________________

TYPE	SYMPTOMS	TREATMENT	ACTIONS
STRESS Incontinence	- Leakage of urine upon physical exertion, e.g. cough, laugh, sneeze, or strain in any way.	- Pelvic floor exercises - Dietary advice - Surgical intervention	- Give out patient information sheet. - Inform medical staff Date Sign
URGE Incontinence	- Urgency - urge incontinence - Frequency - nocturnal enuresis	- Bladder re training - Drug therapy – anticholinergics (slows the bladders activity down).	- Give out patient information sheet. - Refer to link nurse. Date Sign
OVERFLOW Incontinence	- Bladder does not empty properly - Possesses residual urine - Frequent urinary tract infection - Hesitancy, straining, dribbling - Poor flow	- Bowel management - Instruction in voiding technique - Intermittent catheterisation - Indwelling catheter	- Give out patient information sheet. - Refer to medical staff - Refer to link nurse Date Sign
PASSIVE Incontinence	- Incontinent without warning or no apparent reason. - Reduced awareness - Mental impairment - Confusion - Dementia - Nocturnal Enuresis – Bed wetting	- Bladder training - Toileting programme combined with reality orientation - Behaviour modification	- Give out patient information sheet. - Commence toileting chart. - Refer to link nurse. Date Sign

20. Reason for Referral

When referring to the Continence Advisor, please liase with your Ward Continence Link Nurse, FIRST

21. Discharge Plan

GP ☐
Physio ☐
OT ☐
Dietician ☐
Continence Nurse ☐
Medical Staff ☐
D/N ☐

(d)

Figure 41.1 Continent assessment form.

There are many components that are needed to perform a full continence assessment, and these will differ depending on local/national policies, as well as the CN's level of experience/expertise and the specialization within the field. It will also depend on the wishes of the patients and their desire for treatment or management. In 2000, the Department of Health [6] published a paper on good practice in continence services. This suggested key components that should be performed during a routine continence assessment. These are listed in Table 41.2.

SPECIALIST INVESTIGATION

CNs need a full understanding of different investigations that can be performed to assess and diagnose the causes of a patient's incontinence. They will not only be responsible for referring patients for further testing but also for performing investigations on their patients. Such investigations may be simple procedures such as urinalysis or more complex studies such as uroflowmetry, bladder scanning, subtracted cystometry, video cystourethrography (VCU), ambulatory urodynamics, flexible cystoscopy, anorectal physiology and manometry, and barium meals/enemas. To be able to perform these investigations, CNs may need specialist training in the procedures and may also need to gain further qualifications (e.g., good urodynamic practice). For CNs performing VCUs and barium studies, they may also have to be assessed and work within regulations for ionizing radiation (medical exposure), which can involve a theoretical exam and clinical assessment. This should be addressed in line with local policies.

Table 41.2 Key Components of a Continence Assessment

- Review of symptoms and their effect on quality of life.
- Assessment of the patient’s desire for treatment and possible alternative management.
- Examination of the patient’s abdomen for palpable mass or retention of urine.
- Examination of the perineum to identify prolapse and excoriation and assess pelvic floor contraction.
- Rectal examination to exclude fecal impaction.
- Urinalysis to exclude urinary tract infection.
- Assessment of manual dexterity.
- Assessment of the patient’s environment—access to the toilet.
- Use of a bladder diary/frequency/volume chart/bladder scan.
- Identification of conditions that may exacerbate the patient’s incontinence—medication, coughs, and drinking habits.

Source: Department of Health, Good practice in continence services, DH, London, U.K., 2000.

There are many different levels to which CNs will perform investigations depending on their level of expertise and training. Some may be technically experienced but unable to interpret the results of the tests in relation to the patient’s symptoms; however, the more experienced nurses will be able to assess, analyze, and interpret the results of any investigation that they perform.

Part of these investigations may involve internal examinations (vaginal and rectal). Prior to performing these examinations, it is essential to consider what information will be gained, whether it is a screening or diagnostic procedure and whether it is necessary at the time [7]. Informed consent should be gained verbally from all patients prior to investigation and, in some cases, written consent may also be necessary. Consideration should also be taken to ensure that the environment in which the assessment or investigation takes place is appropriate to meet the needs of the patient and the requirements of the investigation. Table 41.3 lists some of these environmental considerations.

Table 41.3 Environmental Considerations for the Assessment

The environment that the assessment takes place in should be
- Accessible
- Maintains privacy and dignity
- Hand washing facilities
- Male/female toilets
- Clean
- Warm
- Good lighting
- Appropriately equipped
- Free from distraction
- Safe for the patient and the nurse

Sensitive to religious and cultural needs

Source: Crouch A and Meurier C, *Vital Notes for Nurses: Health Assessment*, Blackwell Publishing Oxford, U.K., 2005.

DECISION-MAKING

Hamilton and Martin [9] state that “Information acquisition is not the end point for practitioners. Having the information is one thing but deciding on the implications of it and on what to do with the information is the essence of professionalism in nursing.” Specialist practice is the exercising of higher levels of judgment, discretion, and decision-making in clinical care [10].

Management of incontinence should take into consideration patients’ individual needs and preferences, and patients should have the opportunity to make informed choices about their care and treatment [11]. It has been shown that patient empowerment is the most dynamic, effective, and efficient approach to care [12]. This places choices and decisions into the hands of those with incontinence.

Working as autonomic practitioners, CNs play a large role in decision-making. This includes the analysis and interpretation of investigations along with clinical observations and the information gained from taking patients history to make a clinical diagnosis and appropriate management plan. Once a diagnosis has been made, CNs have a responsibility to fully inform patients and carers what type of incontinence they have and the treatment options available. With this knowledge, a management plan can be set based on the CN's recommendations and patients' choice and in line with local policies.

Kurtz et al. [13] developed the Calgary–Cambridge Observation Guide (CCOG) model of consultation. It facilitates continued learning and refining of consultation skills for nurses through five stages as described in Table 41.4.

Along with diagnosing, outlining, and implementing management strategies, CNs must also be able to make clinical decisions as to when patients need to be referred on for further investigation or more specialist care. This may be to a specialist within the field, e.g., urogynecologist/urologist or colorectal team for surgery or to a different specialty following abnormal findings during assessment or exacerbation of a preexisting comorbidity that may be impacting upon their incontinence (e.g., heart failure or diabetes).

Table 41.4 Five Stages of Calgary–Cambridge Observation Guide

1. *Explanation and planning*—giving patients information, checking that it is correct and that you both agree that the history has been taken.
2. *Aiding accurate recall and understanding*—making information easier for the patient using reflection.
3. *Achieving a shared understanding*—incorporating the patients perspective to encourage an interaction rather than a one way transmission.
4. *Planning through shared decision making*—working with patients to assist understanding and involving patients in the decision-making process.
5. *Closing the consultation*—explaining, checking, and offering a plan acceptable to the patients needs and expectations.

Source: Kurtz S et al., *Acad Med*, 78, 802, 2003.

CONSERVATIVE MANAGEMENT

The most recently published guidelines on urinary incontinence from the *5th International Consultation on Incontinence* (2013) [14] and NICE CG171 [11] recommend initial lifestyle interventions followed by conservative management, which is usually pelvic floor physiotherapy for stress urinary incontinence and behavioral therapy, such as bladder retraining for overactive bladder (OAB). CNs play a major role in the implementation of these conservative management strategies through patient education and health promotion. According to Kelly et al. [15], CNs can identify causes, create treatment plans, and empower patients with incontinence and be involved in all aspects of their care. It has also been demonstrated that this service can be provided by CNs in a more cost-effective manner [16].

PHARMACOLOGICAL MANAGEMENT

Many CNs are working not only as advanced practitioners but also as autonomic practitioners and this has been helped with the advances in nurse prescribing. Whether CNs are working as independent or supplementary prescribers or within the bounds of patient group directives, it means that patients can also access pharmacological treatment if appropriate for their type of incontinence through the nurse-led service. Long-term monitoring and adjustments of these medications can also be performed through the nurse-led service thus reducing waiting lists for medical teams with the specialty. Also, some general practitioners may not have an in-depth knowledge of the different medications available, their modes of action, and how to monitor progress so specialist nurses can advise other general health-care providers in these matters.

PADS, CATHETERS, AND ANTI-INCONTINENCE DEVICES

Management of incontinence with the use of pads, catheter, or nonsurgical devices is appropriate for some patients. CNs are responsible for assessing the need for these and providing the necessary education for patients using them as a coping strategy in either the short term while awaiting further treatment or surgery or the long term for people with intractable incontinence. Some CNs who hold a budget may also have a role in the negotiation of contracts and provision of these products in line with local policy and needs assessment.

For patients using long-term catheterization (intermittent, urethral, or suprapubic), CNs should focus on educating patients/carers in infection control procedures and should perform a periodic reassessment to confirm the continued need for catheterization. Further information and guidelines are available from the RCN Catheter Care—a guide for nurses [17]. There has also been a website developed by the International Consultation on Incontinence to guide health professionals and patients on available containment products and the evidence behind their use. This can be accessed at www.continenceproductadvisor.org/.

MINOR SURGERY

One of the expanding roles of all specialist nurses has been in the performance of minor surgery. For CNs, this has included performing procedures such as flexible cystoscopies, insertion of suprapubic catheters, intradetrusor injections of botulinum toxin A, and colonoscopies under local anesthetic or mild sedation. To perform this role, CNs must have an advanced level of understanding of anatomy and physiology and be experienced and proficient clinical decision makers. A formal assessment pathway to ensure competency must be performed by an appropriate medical professional to ensure safe practice in line with regulatory bodies and individual trust protocols. With the advent of more surgical devices for incontinence that can be inserted under local anesthetic, this role may soon expand further.

COUNSELING SKILLS

People with incontinence often adopt coping behaviors to manage or reduce their symptoms (e.g., toilet mapping, dietary, and fluid restrictions). Coping strategies and symptoms of incontinence can have a profound effect on health-related quality of life, negatively impacting on even simple daily activities. People with incontinence may be reluctant to travel, visit friends and family, or pursue leisure activities for fear of embarrassment [18]. The psychological burden of incontinence can be severe, leading to depression and low self-esteem. Furthermore, some coping strategies are not only inconvenient but can also have serious medical sequelae [19].

Despite the debilitating effects of OAB, almost half of symptomatic people do not seek health-care advice, often because of shame and embarrassment [20].

Barriers to treatment seeking can include

- Embarrassment
- Lack of knowledge about the condition and management
- Belief that incontinence is a normal part of aging and not a medical condition
- Availability of products to contain incontinence
- Fear of physical examinations, invasive testing, and surgery
- Low expectations regarding treatment

To overcome these barriers, CNs need to aim to improve patient education to allay fears and misconceptions and promote awareness of symptoms and treatments.

HEALTH PROMOTION

CNs are often in the prime position to provide information to patients and relatives/carers on health promotion. This may be in the form of diet and lifestyle advice (e.g., fluid and caffeine reduction), weight loss or smoking cessation, and information on what are considered to be normal bladder and bowel habits.

Continence is now becoming a more public subject. In the past, it has been considered a taboo that should not be discussed in public; however, with large numbers of women experiencing continence problems, it is the ideal time to improve awareness and knowledge. This has been achieved in many ways. For example, the International Continence Society has run a World Continence Week every year to actively promote continence awareness and the services and treatments offered and address any myths associated with the subject.

In modern times, with more and more women seeking information and help from the Internet, it provides HCPs and charitable foundations with the opportunity to provide accurate health promotion information to a wider audience.

Many of the charities associated with this field (e.g., the Bladder and Bowel Foundation and the

Overactive Bladder and Interstitial Cystitis Group) also provide user support groups where women with similar problems can share their experiences and help each other through the difficulties associated with the diagnosis and management of chronic conditions.

EDUCATION

Education forms a large part of the CNs' role. They educate not only patients but also carers, relatives, colleagues, and other HCPs. Patient education can often be the most difficult. Often, it has to be tailored to individual patient needs taking into account their degree of understanding, cultural sensitivities, and the level of knowledge that they need or wish to have. However, there is a growing trend toward "the expert patient" [21] where, it is possible that the patient with a chronic condition will actually know at least the same if not more on disease management than the HCP giving the care.

CNs are considered to have an in-depth knowledge and experience in the field and therefore act as clinical advisors and educators to other HCPs to raise awareness of continence issues in different medical settings. Table 41.5 sets out the responsibilities of the CNs with regard to education as suggested by the RCN [22].

MAXIMIZING COMPLIANCE

Compliance is a medical term that is used to indicate a patient's correct following of medical advice. It applies to medication, the use of surgical appliances, or attending courses of therapy. It is also known as adherence, persistence, or concordance. There are several reasons as to why we should promote compliance to therapy as shown in Table 41.6.

Poor adherence to medication represents a major challenge in the management of urinary incontinence [23]. There are many factors that can influence compliance with therapy and these are enumerated in Table 41.7. Before starting therapy, it is important to ensure that patients are counseled regarding the role of therapy, medication, or surgery. This should include information on the side effects, the estimated length of treatment, other therapies available, how medication will improve their symptoms and how long it may take to be able to notice these differences, postoperative recovery and risks, and benefits of each intervention. This may help the patient to make an informed decision about her treatment and improve compliance with treatment. Often, patients can become disillusioned with the expected outcome of treatment and this directly affects motivation and compliance that are paramount to the success of certain treatments. Regular assessment, good communication, and patient education are key skills for CNs to ensure that patients are making informed choices about their care and management. This is set out in The Code [24], which advises nurses to act as an advocate for those in their care, helping them to access relevant health and social care, information, and support. This will aid not only in maximizing compliance but also in overall patient satisfaction through their continence care package.

Table 41.5 Educational Responsibilities of Nurses Specializing in Continence Care

- Be involved with other members of the team in the assessment, planning, delivery, and evaluation of initial education to patients, their families, and carer about incontinence.
- Be involved in providing continuing education for all patients with incontinence and planning educational programs for the area. The nurse specialist should also be involved with the team in setting, reviewing, and monitoring standards of continence care in the health district.
- Participate in the planning and delivery of education about continence care for both nursing colleagues and those working in other disciplines. This may take place in the college of nursing, university, hospital, or community.
- Act as a source of expert advice for all who cope with incontinence—including patients, other nurses, health-care staff, and agencies that work with people with incontinence (e.g., local voluntary organizations).

Table 41.6 Why Promote Compliance to Therapy

- Reduce therapeutic failure
- Reduce wastage of resources
- Cost
- Improve patient satisfaction
- Increase efficacy of service provided

Table 41.7 Reasons for Nonadherence to Treatment

- Forgetfulness
- Purpose of treatment not clear
- Perceived lack of effect
- Side effects
- Instructions for administration not clear
- Complicated regimen
- Physical difficulty in complying
- Experiences since diagnosis
- Lack of time/money
- Health-care provision

MANAGEMENT

Aside from the clinical responsibilities of CNs, many staff in these posts will also have a management role within their trust. They may be leading or actively involved in the commissioning of integrated continence services and participating in regular policy reviews on nursing issues in their service (RCN). For new services, the CNs may be drafting policies in line with evidence-based practice and setting out the aims and needs of their service by developing a service model.

In primary care, CNs may hold a budget to provide containment products for their patients and, in secondary care, may be responsible for the standardization of products across the trust. In these roles, the CNs act as buyers to negotiate the best contracts as well as accountants managing budgets and trying to make cost improvements in line with set targets. They will also have to design policies to outline those patients who are entitled to such services and how needs are assessed and standardized. In the United Kingdom, the All Party Parliamentary Group [25] has developed guidelines written by CNs for service commissioners to help guide in the development of continence services.

As part of a standard management role, the CNs will also need to be proficient in tasks such as risk assessment, quality assurance, as well as having strong leadership skills and expertise in effective staff management.

CNs also have a role in the auditing of current services to ensure that they are working in line with the current evidence base and also of identifying and assessing the needs of the service and how these can be developed.

COORDINATION OF CARE

Some patients seen in continence clinics may require input from other services. As CNs have often performed the initial assessment, it is their role to make direct referrals to these other teams and they often play a pivotal role in the coordination of care between these specialties to ensure that care is integrated and continuous. Table 41.8 lists some of the other services that continence patients may need referral too.

RESEARCH AND AUDIT

As a consequence of the advanced nursing practice within continence care, more CNs are participating in further education by completing degrees such as master’s level and even doctorate programs. As part of these courses, they are undertaking innovative and original research into the field that previously had only been completed by the doctors. CNs are often best placed to recruit patients into clinical trials as they have more direct patient contact and are the first HCP that patients will meet along their pathway. With this in mind, CNs are in an ideal place to actively promote research and can collect a multitude of data with regard to initial presentation of symptoms, epidemiology, etiology, success of conservative and pharmaceutical management, and other aspects of care.

Table 41.8 Examples of Additional Services Needed by Continence Patients

- Urogynecologists
- Gynecologists
- Urologists
- Colorectal surgeons

- Gastroenterologists
- Geriatricians
- Psychologists
- Social workers
- Physiotherapists
- Occupational therapists
- Pharmacists
- General practitioners

For those who do not wish to undertake formal research, clinical audits can also be used to inform practice. For CNs with management duties, service audits may also be completed to assess how services are running, ensure that patient needs are being met, and as a scoping exercise when looking to further develop services.

COMMUNICATION

Communication is very important in the health-care setting. Smith [26] said that the ability to communicate effectively with patients, relatives, and other staff is essential if nurses are to build trusting relationships in which patients feel that they are accepted and understood. According to Payton [27], communication has two functions in health care. First, it is essential to establish and maintain effective interprofessional relationships with the patients, relatives, HCPs, and any other persons whom we come into contact with. The second function is the successful achievement of professional tasks, such as patient care, education, research, administration, supervision, and consultation. Wojnicki-Johansson [28] suggests that certain behaviors and devices have been found to facilitate and improve communication between nurses and patients such as the use of body language, eye contact, and touch. Nurses can facilitate successful and therapeutic patient contact through questioning, listening, summarizing, reflecting, paraphrasing, set induction, and closure [9]. CNs use these skills every day to assess, reassure, reduce anxiety, educate staff and patients, plan care, encourage critical thinking, liaise with other HCPs, and promote continence care.

MAINTAINING PRIVACY AND DIGNITY

In the field of continence, ensuring complete privacy and dignity can be difficult. Although basic environmental issues are often met in order for CNs to assess incontinence, we need to understand and know many personal pieces of information about the patient and often perform internal examinations. Some patients may find this information difficult to disclose to a nurse that they have never met before. It can therefore be difficult to CNs to strike a balance between protecting privacy and dignity and maintaining modesty while assessing, diagnosing, and managing incontinence. To compensate for this, every effort should be made to ensure all other areas of privacy and dignity are maintained, e.g., appropriate clinical area for review, appropriate use of chaperones during examination, and confidentiality.

CONCLUSIONS

The role of the CN does not just involve clinical care of the incontinence patient. These individuals aim to provide holistic care for patients and to act as educators and advisors to all other HCPs who encounter continence issues in their practice. As the scope of nursing practice continues to expand, CNs will further develop to meet these demands and their level of nursing expertise will increase, not only with regard to the clinical aspects of care but also in service development to ensure integrated services and optimal continence care packages for patients.

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42 Behavioral Therapies and Management of Urinary Incontinence in Women

Kathryn L. Burgio

Behavioral therapies are a group of interventions that improve bladder control by teaching patients skills for preventing urine loss or changing their daily habits. In clinical practice, behavioral interventions are usually comprised of multiple components, tailored to the individual needs of the patient, the characteristics of her symptoms, and her life circumstances. Behavioral treatment programs generally take one of two approaches. One approach focuses on improving bladder function by changing voiding habits, such as with bladder training or delayed voiding. Another basic approach targets the bladder *outlet*, such as with pelvic floor muscle training and exercise. Among the techniques included in behavioral treatment programs are self-monitoring with a bladder diary, pelvic floor muscle training techniques (including biofeedback or digital teaching), pelvic floor muscle exercise regimens, active use of pelvic floor muscles for urethral occlusion (stress strategies, the knack), urge control and suppression strategies, urge avoidance strategies, scheduled voiding (including bladder training), delayed voiding, teaching normal voiding techniques, fluid management, dietary changes to avoid bladder irritants (including caffeine), weight loss, and other lifestyle changes.

Although they are not curative in most patients, behavioral interventions are widely used because their efficacy is well established. They are safe and without the risks and side effects associated with some other therapies. However, they do depend on the active participation of a motivated patient and usually require some time and persistence to reach optimum benefit. Behavioral treatments have been recognized as effective by the 1988 Consensus Conference on Urinary Incontinence in Adults [1], the Guideline for Urinary Incontinence in Adults developed by the Agency for Health Care Policy and Research [2], the International Consultation on Incontinence (ICI) [3], and the American Urological Association Guideline on Diagnosis and Treatment of Overactive Bladder in Adults [4].

PATIENT EDUCATION

Because behavioral therapies are based on principles of learning, it is important that any behavioral program begin by providing basic patient education, so that she can understand the treatment process and the therapeutic goals. This education includes an explanation of the anatomy of the bladder and pelvic floor, how they function, and the mechanisms of urinary incontinence. Women need to understand that their behavioral program is based on changing their habits and learning new skills and that their results will depend on their active participation and daily practice. Further, understanding that improvement is often gradual facilitates adherence and realistic expectations about potential therapeutic outcomes.

BEHAVIORAL TRAINING AND PELVIC FLOOR MUSCLE TRAINING

Pelvic floor muscle training and exercise were first described by Margaret Morris in 1936 [5]. In her paper, she described tensing and relaxing of the pelvic floor muscles as an approach to the prevention and treatment of urinary and fecal incontinence. Pelvic floor muscle training was first popularized in the 1950s by Arnold Kegel, a gynecologist who proposed that women with stress incontinence lacked awareness and coordination of their muscles [6]. He also demonstrated that women could improve their stress incontinence through pelvic floor muscle training and exercise to improve strength and coordination [6,7]. Over the ensuing decades, this intervention has evolved both as a behavioral therapy and as a physical therapy, combining principles from both fields into a widely accepted conservative treatment for stress and urge incontinence. The literature on pelvic floor muscle training and exercise has demonstrated that it is effective for reducing stress, urge, and mixed incontinence in most outpatients who cooperate with training [8–20]. Pelvic floor muscle training and exercise is now a cornerstone of behavioral treatment for both stress and urge urinary incontinence [3].

Teaching Pelvic Floor Muscle Control

The goal of behavioral treatment for stress incontinence is to teach patients how to improve urethral closure and bladder neck support by voluntarily contracting pelvic floor muscles during whatever physical activities precipitate urine leakage. The first step in training is to properly identify the pelvic floor muscles and to contract and relax them selectively (without increasing intra-abdominal pressure on the bladder or pelvic floor). It is an essential and often overlooked step to confirm that patients have identified the correct muscles. Failure to find the pelvic floor muscles or to exercise them correctly is an important source of failure with this treatment modality. While it is easy for the clinician to give patients a pamphlet or brief verbal instructions to "lift the pelvic floor" or to interrupt the urinary stream during voiding, these approaches do not ensure that she knows which muscles to use before she is sent home to do daily exercises. Verification of proper muscle contraction can be accomplished by palpating the vagina during pelvic examination and giving her verbal feedback. Pelvic floor muscle control can also be taught using biofeedback or electrical stimulation.

Biofeedback is a teaching technique that helps patients learn control by giving them instantaneous, accurate feedback of their pelvic floor muscle activity. In his original work, Kegel used a biofeedback device he designed and named the perineometer [6]. It consisted of a pneumatic chamber (which was placed in the vagina) and a handheld pressure gauge, which visually displayed the pressure generated by circumvaginal muscle contraction. This device provided immediate visual feedback of pelvic floor muscle contraction to the woman learning to identify her muscles and monitor her practice.

Most biofeedback instruments in current use are computerized and display feedback visually on a computer monitor. Pelvic floor muscle activity can be measured by manometry or electromyography, using vaginal or anal probes or surface electrodes. Signals are augmented through the computer, and immediate feedback is provided on a monitor for visual feedback or via speakers for auditory feedback. When patients observe the results of their attempts to control bladder pressure and pelvic floor muscle activity, learning occurs by means of operant conditioning (trial and error learning). Biofeedback-assisted behavioral training has been tested in several studies, producing mean reductions of incontinence ranging from 60% to 85% [8,9,12,19–24].

A common problem encountered in learning to control the pelvic floor muscles is that patients tend to recruit other muscles, such as the rectus abdominis muscles or gluteal muscles, when they contract the pelvic floor muscles. Contracting certain abdominal muscles can be counterproductive, when it increases pressure on the bladder or pelvic floor, and therefore tends to push urine out rather than holding it in. Thus, it is important to observe for this bearing down Valsalva response and to help patients to exercise pelvic floor muscles selectively while relaxing these abdominal muscles.

Some practitioners recommend coordinated training of transversus abdominis muscles because it is thought that these muscles facilitate pelvic floor muscle contraction. This approach remains controversial, however, and a review article on this approach noted an absence of evidence for this type of training [25].

Daily Pelvic Floor Muscle Exercise

Once patients learn to properly contract and relax the pelvic floor muscles selectively, a regimen of daily practice and exercise is prescribed. The purpose of daily practice is twofold: to increase muscle strength and to enhance motor skills through practice. It has also been suggested that intensive strength training may increase resting tone and structural support of the pelvis by elevating the levator plate and enhancing the hypertrophy and stiffness of its connective tissues [26].

Exercise regimens vary considerably in frequency and intensity, and the optimal exercise regimen has yet to be determined. However, good results are generally achieved using 45–50 exercises per day [8,20]. To avoid muscle fatigue, it is usually recommended that patients space the exercises across the day, typically in 2–3 sessions per day. Patients may practice the exercises in the lying position at first, but it is important to progress them to sitting or standing positions as well so that they become comfortable and skilled using their muscles to avoid incontinence in any position.

Table 42.1 Instructions for Daily Pelvic Floor Muscle Practice

Do 45 pelvic floor muscle exercises EVERY day: 15 at a time, three times per day.

Do _____ lying down
Do _____ sitting
Do _____ standing

For each exercise, squeeze your pelvic floor muscles as quickly and as hard as you can.

Hold the squeeze for _____ seconds.

Relax completely after each squeeze for _____ seconds.

Remember to relax all the muscles in your abdomen when you do these exercises and continue to breathe normally.

To improve muscle strength, contractions should be sustained for 2–10 seconds [27,28], depending on the patient's initial ability. Exercise regimens should be individualized so that patients begin with a comfortable duration and gradually progress to 10 seconds [28]. Each exercise consists of muscle contraction followed by a period of relaxation using a 1:1 or 1:2 ratio [28]. This allows the muscles to recover between contractions. A template for individualized instructions for daily pelvic floor muscle exercise appears in Table 42.1.

One of the challenges of pelvic floor muscle training and exercise is motivating patients to adhere to the regimen and to sustain their efforts over time. It can be helpful to educate them that sustained improvement depends upon their continued exercise. Among the barriers to daily exercise are difficulty remembering to do the exercises and difficulty finding time [29,30]. To assist patients to remember their exercises, a variety of cues can be considered, including alarms or notes in prominent places in the home or car. Another approach is to teach them to integrate their pelvic floor muscle contractions into their daily lives or associate them with several daily activities. Once they are proficient, they no longer need to set time aside to concentrate on their exercises. Rather, they can do a few exercises during certain daily activities, such as taking a shower or sitting at a traffic light. Not only does this not add time to their busy schedules, but the activities eventually become cues, reminding them to exercise. This can improve adherence during active treatment and supports continued exercise during the maintenance phase when motivation tends to wane.

Using Muscles to Prevent Stress Incontinence

Although exercise alone has been known to improve urethral pressure and structural support and reduce incontinence [31], the best results seem to be achieved when patients contract their muscles consciously before and during coughing, sneezing, or any other activities that precipitate urine loss [16,26]. Initially, this new skill requires a conscious effort, but with consistent practice, patients can develop the habit of automatically contracting their muscles to occlude the urethra in situations of physical exertion. This skill has been referred to varyingly as the "stress strategy" [19], "counterbracing," "the knack" [32], perineal cocontraction, and "the perineal blockage before stress technique" [33].

Even when their muscles are weak, some women will benefit from simply learning how to control their pelvic floor muscles and use them to prevent urine loss. In one trial, women were taught to voluntarily contract pelvic floor muscles before or during a cough and demonstrated reduction in leakage after only 1 week of training [32]. Pelvic floor muscle precontraction has been recommended, not only during coughing but also during any daily activity that results in increased intra-abdominal pressure [34]. The strength that is needed to occlude the urethra and prevent urine leakage is not known, and some women will still need a more comprehensive program of pelvic floor muscle rehabilitation to increase strength in addition to learning this skill.

The literature on pelvic floor muscle training and exercise has demonstrated that it is effective for reducing stress, urge, and mixed urinary incontinence in most outpatients who cooperate with training. Systematic reviews and the ICI (2013) concluded that there is Grade A evidence for pelvic floor muscle training and that it should be offered as first-line treatment to women with stress, urge, or mixed incontinence [3,35–37].

BEHAVIORAL TRAINING FOR URGE INCONTINENCE

Historically, pelvic floor muscle training and exercise was used almost exclusively for the treatment of stress incontinence. It is now established as a central component in the treatment of urge incontinence and overactive bladder as well. Initially, it was observed that detrusor contraction could be inhibited by pelvic floor muscle contraction that was induced by electrical stimulation [38–40]. Then, in the 1980s, Burgio and colleagues demonstrated that voluntary pelvic floor muscle contraction can be used not only to occlude the urethra but also to inhibit detrusor contraction [8,20] (see Figure 42.1). Pelvic floor muscle control and exercise is taught in the same way as it is for stress incontinence. What differs is how women with urge incontinence are taught to use their muscles to manage urgency and prevent urine loss.

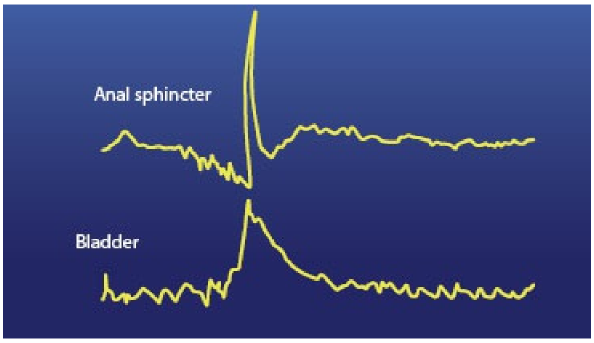


Figure 42.1 Urodynamic tracings showing detrusor inhibition associated with anal sphincter contraction.

Using Muscles to Prevent Urge Incontinence: Urge Suppression Strategies

Most patients with urge incontinence feel compelled to rush to the toilet to void. This behavior can make incontinence more likely, because it increases intra-abdominal pressure on the bladder and increases the feeling of fullness, and when the patient reaches the vicinity of the toilet, she is exposed to visual cues that can trigger incontinence. Behavioral training teaches patients a new way to respond to the sensation of urge. Although it may seem counterintuitive at first, the urge suppression strategy encourages patients to pause, sit down if possible, relax the entire body, and contract pelvic floor muscles repeatedly to diminish urgency, inhibit the detrusor contraction, and prevent urine loss. After the urge sensation subsides, they are to proceed to the toilet at a normal pace [41].

Detrusor inhibition using pelvic floor muscle contraction can be taught and documented in the clinic. A handout for teaching patients about the urge suppression strategy appears in Figure 42.2. Patients are then encouraged to practice this urge suppression technique to manage urge and prevent incontinence episodes in their daily lives.

The home program for urge incontinence follows the same daily exercise regimen as for stress incontinence. In addition, it is often helpful for women with urge incontinence to practice interrupting or slowing the urinary stream during voiding once per day. Not only does this provide practice in occluding the urethra and interrupting detrusor contraction, it does so in the context of the urge sensation, when patients with urge incontinence need it most. Some clinicians express concern that repeated interruption of the urinary stream may lead to incomplete bladder emptying in certain groups of patients. Therefore, caution is recommended when using this technique with patients who may be susceptible to voiding dysfunction.

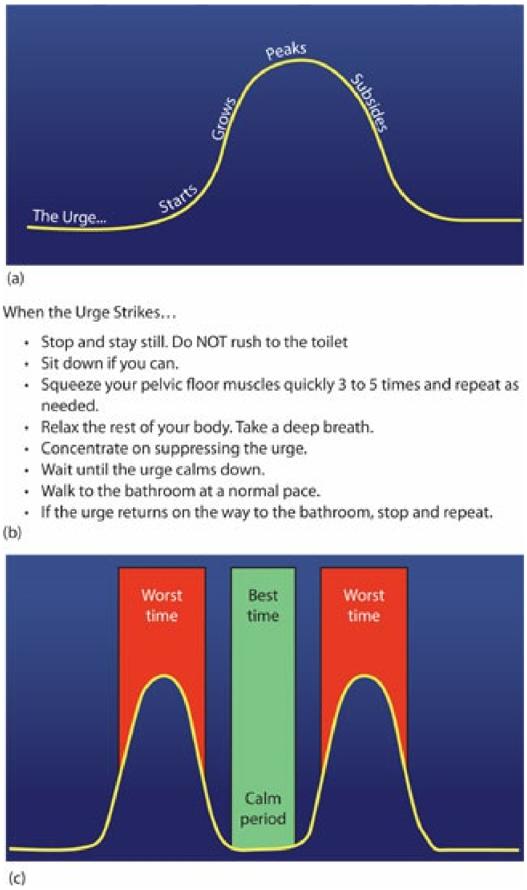
Behavioral training for urge incontinence has been tested in several clinical series utilizing pre–post designs. Mean reductions of incontinence range from 76% to 86% [8,22,24,42]. In randomized controlled trials using intention-to-treat models, mean reductions of incontinence range from 60% to 80% [20,21]. This urge suppression strategy can be combined with bladder training or delayed voiding as one of several coping techniques that can help patients postpone voiding.

VOIDING HABITS AND SCHEDULES

Decreasing Voiding Frequency

Bladder Training

It has long been thought that habitual frequent urination can over time contribute to reduced bladder capacity and lead to detrusor overactivity, which in turn causes urgency and urge incontinence. Bladder training is a behavioral intervention that was developed to break the cycle of urgency and frequency using consistent, incremental voiding schedules. When it was first introduced, it was known as bladder drill. Bladder drill was an intensive intervention, often conducted in an inpatient setting, in which women were placed on a strict expanded voiding schedule for 7–10 days to establish a normal voiding interval [43,44]. Urgency and anxiety about possible urine loss were sometimes managed with Valium. Bladder training is a sequel to this procedure that increases the voiding interval more gradually, over a longer period of time, and is conducted in the outpatient setting [45–55].



When the Urge Strikes...

- Stop and stay still. Do NOT rush to the toilet
- Sit down if you can.
- Squeeze your pelvic floor muscles quickly 3 to 5 times and repeat as needed.
- Relax the rest of your body. Take a deep breath.
- Concentrate on suppressing the urge.
- Wait until the urge calms down.
- Walk to the bathroom at a normal pace.
- If the urge returns on the way to the bathroom, stop and repeat.

Figure 42.2 (a) The urge suppression strategy. (b) Urge wave. (c) When to void. (From Burgio, K.L. et al., *Staying Dry: A Practical Guide to Bladder Control*, Johns Hopkins University Press, Baltimore, MD, 1989. With permission.)

Patients are given instructions to void at predetermined intervals, and over a period of several weeks, the voiding interval is gradually increased. This is believed to increase bladder capacity and decrease overactivity, resulting in improved bladder control. To follow this regimen, patients must resist the sensation of urgency and postpone urination. Several behavioral techniques have been used to help patients control the urge to urinate while they wait for their next scheduled void. The traditional approach has been to suggest various techniques for relaxation or distraction to another activity [52]. Patients are encouraged to distract themselves from the bladder by engaging in a task that requires mental but not physical effort, such as reading, calling a friend, or making a to-do list. Self-statements such as “I am in control of my bladder” and “I can wait” are also helpful. More recently, the urge suppression strategy (described earlier), i.e., repeated contractions of the pelvic floor muscles, has been adopted in bladder training as another way to control urgency and detrusor contractions while the patient waits to void.

Bladder training programs have differed widely in terms of the instructional approach, intensity of clinical supervision, scheduling parameters, strategies for controlling urgency, frequency of schedule adjustments, criteria for increasing the voiding interval, length of treatment, and use of adjunctive treatments. At present, there is no evidence for determining which parameters are most effective. However, the ICI recommends that clinicians should provide the most intensive bladder training supervision that is possible within service constraints [3]. Guidelines for conducting bladder training are presented in Table 42.2.

Several clinical series studies and randomized trials have demonstrated efficacy of outpatient bladder training or a mixture of inpatient and outpatient intervention [45–55]. The classic study of outpatient bladder training is a randomized clinical trial that demonstrated a mean 57% reduction in frequency of incontinence in older women [52]. In this trial, bladder training reduced not only incontinence associated with detrusor overactivity but also incontinence associated with sphincter insufficiency, possibly because patients acquired a greater awareness of bladder function or that the exercise of postponing urination increased the use of pelvic floor muscles. A subsequent trial compared bladder training to oxybutynin; 73% of women in bladder training were reported to be “clinically cured” [53].

Table 42.2 Guidelines for Bladder Training

- Review voiding diary with the patient, noting the various voiding intervals.
- Identify with the patient the longest voiding interval that is comfortable for her.
- Patient Instructions: Empty your bladder…
  - First thing in the morning
  - Every time your voiding interval passes during the day
  - Just before bed
- Teach coping strategies for occurrence of urge.
  - Self-statements (affirmations)
  - Distraction to another task
  - Relaxation
  - Urge suppression strategy (using pelvic floor muscle contraction)
- Gradually increase interval
  - When patient is comfortable for at least 3 days
  - By 30-minute intervals or clinical judgment based on patient confidence

Delayed Voiding

Another approach to helping patients to increase control and expand the interval between voids is delayed voiding. Unlike bladder training, delayed voiding does not involve putting patients on a predetermined voiding schedule. Instead, patients are taught urge suppression strategies and instructed to use them when they have an urge to void. When the urge subsides, instead of going to the bathroom immediately, they are encouraged to wait 5 minutes before voiding.

Even a mild urge to void can prompt a trip to bathroom in a woman with urge incontinence, due to the fear of urine loss. However, most patients can be convinced to try a 5-minute delay, especially when they are in safe circumstances such as at home alone. Many are surprised to find that even with a brief delay, the urge subsides or disappears altogether. This enhances their sense of control and builds confidence to gradually increase the delay time to achieve a normal frequency.

Increasing Voiding Frequency (Timed Voiding)

It is quite common for health-care providers to advise patients with incontinence to simply increase their frequency of urination as a way to avoid a full bladder and its increased risk of incontinence. While increased frequency of urination can have an immediate benefit in terms of avoiding incontinent episodes, the long-term result is most likely counterproductive because the patient can lose the ability to accommodate larger volumes and tolerate bladder fullness. In addition, it feeds the cycle of urgency and frequency thought to perpetuate overactive bladder and exacerbate urge incontinence in the long run.

Increasing the frequency of voiding is generally reserved for patients who void infrequently (<5 times per day). Infrequent voiding may reflect a lifelong pattern of urge suppression (e.g., in teachers or nurses) or can be the result of reduced bladder sensation. Often, these patients have never considered voiding more frequently because they do not have an urge to void. It may also be due to dementia or other cognitive impairments in patients who are unable to inhibit bladder contraction and unable to learn new skills for bladder control. A timed voiding schedule can prompt them to void before urgency with leakage occurs. It is possible for many patients to identify times in their day when they are at increased risk of incontinence, for example, 2 hours after morning coffee or during exercise, and they can plan strategic voids before those times.

BLADDER DIARY

The bladder or voiding diary is a widely used tool in the evaluation and monitoring of incontinence in women. It provides information on the timing of symptoms and events that helps the clinician to understand the type, severity, and circumstances of urine loss and plan appropriate components of behavioral intervention. The diary is less recognized for its value in the treatment phase when it can be reviewed periodically to track the efficacy of various treatment components and guide the intervention. In research, it provides a validated measure of the frequency of voids and incontinence episodes and has also been used to measure the number and severity of urgency episodes.

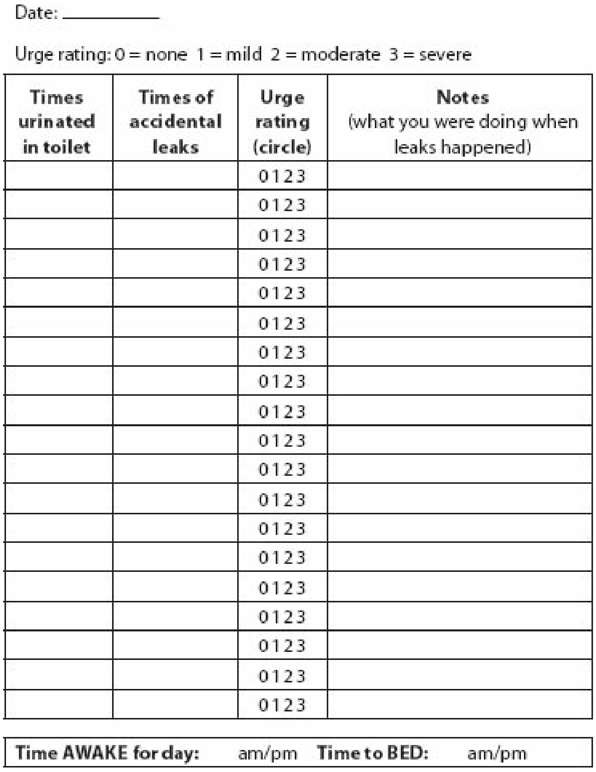
In addition to its value for the clinician, completing a daily diary can have direct benefit to the patient. Its self-monitoring effect enhances the patient's awareness of voiding habits and patterns of incontinence. It encourages patients' recognition of how their incontinence is related to their activities, for example, their physical activities or drinking patterns. In particular, understanding clearly the immediate precipitants of urine leakage optimizes the patient's vigilance and readiness to implement the continence skills learned through behavioral treatment.

To have a reliable sample of the patient's habits, it is useful for her to complete a diary for 5–7 days [56]. At a minimum, she should record the time of each incontinent episode and the circumstances or reasons for the urine loss [41]. In behavioral treatment, the circumstances of each incontinent episode noted in the diary can be reviewed with the patient and used to develop instructions that are specific to that patient's situation. Through the process of reviewing the bladder diary, patients can identify certain times when they are more likely to have incontinence and activities that seem to trigger incontinence. Most commonly, patients can be made more aware of the antecedents of stress incontinence (e.g., coughing, sneezing) and develop the habit of contracting their pelvic floor muscles in preparation for these situations.

In addition to documenting incontinence, it is also very useful to have the patient record the times she urinates both during the day and at night. These recordings can be used to identify patients who urinate too frequently and to establish appropriate voiding intervals for interventions like bladder training and delayed voiding. A record of voided volumes provides a practical estimate of the patient's functional bladder capacity in their daily lives. Because it is more burdensome to measure voided volumes, they are usually collected for only 24–48 hours.

There are many different formats for bladder diary in use. One example of a bladder diary form is presented in Figure 42.3. The form should be modified as needed to collect information most pertinent to each patient's symptoms. For example, columns can be added as needed to record voided volumes and type and volume of fluid intake, in order to identify polydipsia as a cause of lower urinary tract symptoms.

Many clinicians are skeptical of the bladder diary, partly because of reports that patients have not completed them in real time, but rather just before the visit in the waiting room. Despite these anecdotes, we have observed that most patients are capable of using the diary correctly if they are educated about its purpose and how it will be used. Sending a blank diary to patients along with other routine forms in preparation for their first visit may not accomplish this. To improve the chances of obtaining a useful diary, it is best to look at the diary with the patient in person, review its parts, and explain how and when to fill it out. Patients should be encouraged to carry the diary with them at all times and to make entries as soon as it is feasible. Some patients prefer that the diary be small enough to fit in a purse. Alternatively, they can be given explicit permission to fold it. Further, it seems to be helpful to tell the patients that it is okay to get it dirty or spill on it, such that we expect to see coffee stains and ragged edges.



Date: ________

Urge rating: 0 = none 1 = mild 2 = moderate 3 = severe

Times urinated in toilet	Times of accidental leaks	Urge rating (circle)	Notes (what you were doing when leaks happened)
		0 1 2 3	
		0 1 2 3	
		0 1 2 3	
		0 1 2 3	
		0 1 2 3	
		0 1 2 3	
		0 1 2 3	
		0 1 2 3	
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		0 1 2 3	
		0 1 2 3	
		0 1 2 3	
		0 1 2 3	

Time AWAKE for day: am/pm **Time to BED:** am/pm

Figure 42.3 Sample bladder diary.

Equally important is how the diary is handled when the patient returns it to the clinician. If we merely collect the diary and put it in the chart, we can devalue this carefully collected information in the patient's eyes. If she does not believe that her diary entries will be used to understand her condition and inform decisions about her treatment, she is not likely to put effort into daily recording in the future. If the clinician takes an interest in her diary entries by reviewing each day's events, we communicate that the information is useful in guiding her treatment, and this encourages continued accurate recordings.

LIFESTYLE CHANGES

Lifestyle changes are generally used as adjuncts to a primary behavioral intervention in selected cases. Lifestyle changes include fluid management, caffeine reduction, weight loss, avoiding bladder irritants, and bowel management.

Fluid Management

Fluid management is a common practice used to make it easier for patients to control their bladders. Assessment may involve the patient completing a fluid intake diary, and recommendations include alterations in the volume or type of fluids that patients consume. Many patients with incontinence restrict fluid intake as a self-management technique to help prevent incontinence by avoiding bladder fullness. In some cases, particularly among older women, this results in an inadequate intake of fluid and places them at risk of dehydration. It is important to recognize these cases and encourage patients, for their overall health and well-being, to consume an adequate amount of fluid each day, such as the often recommended 6–8 glasses of fluid each day [57]. It is thought by some clinicians that this will also dilute the urine making it less irritating to the bladder.

It should be noted that avoiding fluid intake in the evening hours can be helpful for reducing nocturia. Similarly, it can be very helpful for some patients to restrict fluids for a time when toilet access will be limited, such as before a church service. Women using such targeted fluid restriction should be reminded to compensate for these missed fluids earlier or later to ensure that their total daily fluid intake is adequate.

In patients who consume an abnormally high volume of liquids, fluid restriction is often appropriate. Some patients maximize their fluid intake deliberately in the belief that they need to "flush" their kidneys, to avoid dehydration, or in an effort to lose weight. It is not uncommon to see women carry a water bottle throughout the day taking frequent drinks for health reasons. In these cases, reducing excess fluids can relieve problems with sudden bladder fullness and urgency.

Caffeine Reduction

Caffeinated beverages in particular can exacerbate incontinence because in addition to its diuretic effect, caffeine is a bladder irritant for many people. Research has demonstrated that caffeine increases detrusor pressure [58] and that it is a risk factor for detrusor instability [59,60]. Evidence also exists that reducing caffeine intake helps to reduce episodes of incontinence [61–63].

Although it is very difficult for most coffee drinkers to completely eliminate it from their diet, provided with the knowledge that caffeine may be aggravating their incontinence, many will be willing to reduce their intake or to eliminate it for a few days as a trial. Reducing caffeine intake can be done gradually by mixing decaffeinated beverages with caffeinated beverages in increasing increments. For example, coffees can be mixed to consist of ¼ decaffeinated coffee in week 1, ½ in week 2, ¾ in week 3, and full decaffeinated coffee in week 4.

Avoiding Bladder Irritants

Many clinicians recommend, even as a first-line approach, restricting certain foods and beverages that are believed to irritate the bladder, including sugar substitutes, citrus fruits, spicy foods, and tomato products. Although there is little scientific evidence on dietary factors, there are many cases in which these substances appear to be aggravating incontinence, and reducing or eliminating them has provided clinical improvement. A diary of food and beverage intake can sometimes be useful in identifying which substances are irritants for individual patients. Rather than recommending that all patients restrict their intake of these substances, a diary or trial restriction can help to identify which patients are sensitive and may chose to reduce their intake.

Weight Loss

Obesity is an established risk factor for urinary incontinence. Women with higher body mass index are not only more likely to develop incontinence, but they also tend to have more severe incontinence than women with lower body mass index. Research on the relationship between body mass index and incontinence reports that each five-unit increase in body mass index increases the risk of daily incontinence by approximately 60% [64,65].

Intervention studies of morbidly obese women report significant improvement in symptoms of incontinence with weight loss of 45–50 kg following bariatric surgery [66–68]. Similarly, significant improvements in continence status have been demonstrated with as little as 5% weight reduction in more traditional weight loss programs [69]. The most definitive randomized trial of weight loss for incontinence was the Program to Reduce Incontinence with Diet and Exercise (PRIDE) study. PRIDE compared an intensive 6-month group-administered, weight loss program of diet, exercise, and behavioral modification to a structured education control program in overweight and obese women with incontinence [70]. Both groups received a booklet describing a step-by-step self-administered behavioral program to reduce incontinence. The weight loss program, which resulted in a mean weight loss of 8%, showed significantly greater reductions in number of incontinence episodes compared to the control group, which had a mean weight loss of 1.6% (47% vs. 28%).

Because moderate weigh loss is an achievable goal for many women, it is rationale to recommend weight loss as a first-line treatment or as part of a comprehensive program to treat incontinence in overweight and obese women.

Bowel Management

Fecal impaction and constipation have been cited as factors contributing to urinary incontinence in women, particularly in nursing home populations [71]. In severe cases, fecal impaction can be an irritating factor in overactive bladder or obstruct normal voiding, causing incomplete bladder emptying and overflow incontinence. Disimpaction relieves symptoms for some patients, but it can recur in the absence of a bowel management program. Bowel management may consist of recommendations for a normal fluid intake and dietary fiber (or supplements) to maintain normal stool consistency and regular bowel movements. When hydration and fiber are not enough, stool softeners or enemas may be used to stimulate a regular daily bowel movement, preferably after a regular meal such as breakfast to take advantage of postprandial motility.

ENCOURAGING PATIENT PARTICIPATION AND ADHERENCE

Most behavioral therapies for incontinence are based on self-management models, and their success depends on the active participation of a motivated patient. This reliance on patient behavioral change is perhaps the main limitation of this treatment approach. Like any new habit or skill, changing daily bladder habits and learning new skills require effort and persistence over time. It can be challenging for women to remember to use their muscles strategically in daily life as well as to maintain a regular exercise regimen for strength and skill. Unlike with some therapies, progress with behavioral treatment is often gradual. This gradual change makes it difficult for patients to appreciate even steady improvement over time and represents the primary challenge for behavioral treatment—how to sustain the patient's motivation for a long enough time that she will experience noticeable change in her bladder control.

A key ingredient in addressing this challenge is to maintain contact with the patient during this period of time when her benefit is not yet appreciable. Rather than leaving the patient on her own, it is essential that clinicians support the patient's efforts to persist by scheduling follow-up appointments to review and reinforce her progress, encourage persistence, identify and address barriers, and make any needed adjustments to her daily regimen. In addition, when initiating behavioral treatment, it is important to make it clear to the patient that her improvement, as with any new skill, will likely be gradual, with good days and bad days, and that it will depend on her consistent practice. The patient who expects this course of treatment will be better prepared to persist over time so that results can be achieved and maintained long term.

Little research has examined the durability of behavioral treatments in the long term, but studies are promising in that many patients are able to sustain improvements in bladder control over time [72–74].

WHO IS A CANDIDATE FOR BEHAVIORAL THERAPY?

Most patients who engage actively with behavioral treatment for incontinence experience some degree of improvement, yet there is considerable variation in outcomes. Little is known to help us predict which patients will respond best to behavioral treatment. Most studies examining predictors of success have found that outcomes are not related to the type of incontinence or urodynamic diagnosis [13,52,55,75,76]. Some studies show that patients with more severe incontinence have greater improvements [52,72], but others conclude that patients with more severe incontinence have poorer outcomes [22,72,76] or no relationship between severity and outcome [24,55,75,77]. Evidence on the effect of age is also inconsistent [22,24,52,77]. Current evidence indicates that outcomes are not associated with patient race, parity, body mass index, cystocele, uterine prolapse, hysterectomy, hormone therapy, use of diuretics, or urodynamic parameters [76]. There is little information in the usual clinical evaluation of a patient with incontinence that would indicate the likelihood of her success or failure with behavioral treatment. Thus, given that behavioral therapies are virtually without risk and most adherent patients experience symptom improvement, offering behavioral treatment as first-line therapy is appropriate for any woman with urinary incontinence.

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43 Physiotherapy for Urinary Incontinence

Bary Berghmans

INTRODUCTION

Worldwide, urinary incontinence is a common and distressing health problem with often huge social consequences. In Western countries approximately 10% of all adult women report leakage at least weekly [1]. Increasing prevalence of 20%–30% during young adult life to 30%–40% around the menopause to 30%–50% in the elderly has been reported by some authors [2,3]. Others report a prevalence of any urinary incontinence of 22% [4] to 29% [1] in older women, severe urinary incontinence in 7% [1]. Among nursing home residents, this percentage increases to 42%–72.5% [4,5]. Urinary incontinence is associated with nursing home admission from the community [6].

Although there is no consensus yet about what constitutes significant urinary incontinence [7], incontinence is predominantly a problem among women: 10% of them suffer from weekly incontinence, 25%–45% from occasional leakage [7]. Pooled overall prevalence rates in men are from 4.81% to 32.17%, with the prevalence increasing with age [1,8].

The annual incidence of "monthly" or "any" urinary incontinence varies between 1% and 19%, for "weekly" urinary incontinence between 1.2% and 4% [1], and the yearly remission is reported between 2% and 5% [1].

Mainly due to shame, taboo, and unawareness of treatment possibilities, only a minority of people suffering from incontinence seek professional help [9,10]. In daily general practice, patients usually go for help when the loss of urine leads to mental, physical, or social problems or discomfort for the patient or his or her social environment. Because of more and better patient information, in the Netherlands now about half of the women suffering from urinary incontinence consult a medical doctor [10].

Several forms of urinary incontinence such as stress incontinence, mixed incontinence, and incontinence due to detrusor overactivity (DO) can be differentiated [11]. Symptoms of the latter are urgency, frequent micturition, nocturia, and/or urgency incontinence [11].

In women, the most prevalent form is stress incontinence, being responsible for 49% of all cases of isolated stress urinary incontinence (SUI) [1]. Isolated urgency urinary incontinence is the second most prevalent cause of urinary incontinence (1%–7%) [1]. Combinations of the aforementioned symptoms of stress and urgency incontinence are considered to reflect mixed incontinence [12]. Its prevalence is 7.5%–25% [1].

A patient suffering from stress incontinence usually has a normal voiding frequency (less or equal than eight times in 24 hours) and bladder volume and has mean micturitions between 200 and 400 cc/void, but with neither urgency nor micturition. The patient generally complains of losing small amounts of urine during exertion.

A patient with urgency incontinence usually loses more urine (up to the complete content of the bladder) than a patient with stress incontinence. On the other hand, the patient may void less than 150 mL urine during micturition, suggesting a reduced functional capacity of the bladder.

Incontinence has several treatment options such as physiotherapy, drug treatment, and surgical procedures. Most patients can be treated to a satisfactory level [13]. In several countries, guidelines have been published [13–20]. For the time being, little is known about the implementation of these guidelines and their use in daily practice [16].

For patients with incontinence, physiotherapy is often considered as first-line treatment due to its noninvasive character, the results in terms of symptom relief, the possibility of combining physiotherapy with other treatments, the low risk of side effects, and the moderate to low costs. Important restrictions are that the success depends on the motivation and perseverance of both the patient and the physiotherapist and the time needed for therapy [16].

In this chapter, we review and discuss the diagnosis, analysis, evaluation, and therapeutic possibilities of physiotherapy for stress incontinence, urgency incontinence, and mixed incontinence.

MEDICAL DIAGNOSIS

For women with urinary incontinence, the International Consultation on Incontinence (ICI) distinguishes between initial management and, in case of failure, specialized management [21,22]. For initial management, the ICI (2013) recommends a simple clinical assessment leading to a *presumed* medical diagnosis. First-line health-care providers such as general practitioners (GPs) should use simple diagnostic tools like structured history taking; micturition or voiding diaries (to assess drinking habits, voiding pattern, type, pattern and volume of urine loss, impact), filled in by the patient; and physical examination [23–25]. To help the GP to improve his or her accuracy of medical diagnosis, also short questionnaires for the triage of women with urinary incontinence to quickly differentiate between stress, urgency, and mixed incontinence are developed and methodologically tested [26]. An example of such a questionnaire is the two-item Stress/Urge Incontinence Questionnaire (S/UIQ) [26].

S/UIQ and Classification System

S/UIQ

1. How many times in the last 7 days have you had an accidental leakage of urine onto your clothing, underwear, or pad during an activity such as coughing, sneezing, laughing, running, exercising, or lifting?
2. How many times in the last 7 days have you had an accidental leakage of urine onto your clothing, underwear, or pad with such a sudden strong need to urinate (United States)/pass water (United Kingdom) that you could not reach the toilet in time?

Incontinence Symptom Classification System with S/UIQ

- SUI ≥ 4; UUI = 0 pure SUI
- SUI > 0; SUI > UUI; UUI > 0 stress predominant mixed urinary incontinence
- SUI > 0; SUI = UUI balanced mixed urinary incontinence
- SUI > 0; UUI > 0; UUI > SUI urge predominant mixed urinary incontinence
- UUI ≥ 4; SUI = 0 pure urge urinary incontinence

SUI, stress urinary incontinence episodes per week; UUI, urge urinary incontinence episodes per week.

For the GP, who, in many countries throughout the world, is the first physician the patient is referred to for consultation, the use of these simple tools still associated with difficulty in finding the exact cause of the urinary incontinence. Specialists, like the urologist or the gynecologist may fall back on specific diagnostic tests such as urodynamic evaluation.

Usually, GPs have no access to such tests, and therefore, GPs must rely on their history taking, physical examination, and questionnaires like the S/UIQ.

However, because of its invasive character and doubts about its usefulness, reliability, and validity, the need for urodynamic testing is currently being discussed. Recent high-quality evidence showed that, even in cases of surgery for women with *uncomplicated*, demonstrable SUI, preoperative office evaluation alone was not inferior to evaluation with urodynamic testing for surgical outcomes at 1 year [27].

This suggests that for GPs urodynamic tests are—by and large—only needed if there is doubt about the type of incontinence and, consequently, about the necessity and choice of treatment.

These suggestions are supported by reports concluding that under optimal conditions (after GP training), the sensitivity and specificity of the GPs history taking and physical examination to detect urodynamic stress incontinence are 78% and 84%, with a positive predictive value of 87% [24]. Using simple diagnostic tools such as the S/UIQ, these percentages even can be enhanced [22]. A meta-analysis of primary care diagnostic methods of urinary incontinence (initial management) showed a sensitivity of 0.92 (95% confidence interval [CI] 0.91–0.93) and a specificity of 0.56 (0.53–0.60) to correctly identify women with urodynamic stress incontinence [28]. A clinical history for the diagnosis of DO was found to be 0.61 (0.57–0.65) sensitive and 0.87 (0.85–0.89) specific [28].

Unfortunately, in busy daily practice, and for these variably trained GPs, such optimal conditions can usually not be maintained over a prolonged period of time. Moreover, the symptoms of incontinence may be vague and less clear-cut as compared to that which is written in textbooks. Altogether, this may impair the reliability of history taking and physical examination [13].

In case of a referral to a pelvic physiotherapist, an as accurate as possible medical diagnosis is very important to determine the severity and impact of the complaints of the patient and to estimate the success or failure aspects of pelvic floor physiotherapy [29]. But in the initial management of urinary incontinence in women, in a lot of cases, the *presumed* medical diagnosis lacks accuracy, confronting the physiotherapists with heterogeneity or complexity of indications and unclear grade of severity, which might result in a minor degree of success or even failure.

Probably because of its unpredictable prognosis and appearance of symptoms, like losing all content of the bladder because of irresistible urgency, urgency incontinence due to DO has a greater impact on quality of life than stress incontinence [30–32].

Especially younger people describe DO as very intrusive [33,34].

After a childbirth, stress incontinence sometimes goes together with a total denervation of the pelvic floor muscles or with great damage to surrounding connective and structural tissue.

In such cases, physiotherapy has normally little or no effect.

Also in patients with DO as a result of an infection or a spinal cord lesion, the effect of physiotherapy is not likely to be satisfactory [35].

Next to pregnancy and birth dysfunction, incontinence can also develop as a result of a neurological problem and/or a trauma. For the majority, the pathophysiology of the health problem(s) determine(s) prognosis and result of treatment [36,37].

Whether or not there is a causal relationship between the grade of pelvic organ prolapse (POP) and (stress) urinary incontinence has yet to be determined. Some authors consider that POP and SUI share similar pathophysiologies and might be etiologically connected [38]. DeLancey et al. (2007) showed, in a study of 151 women with prolapse and 135 controls with normal support determined by POP quantification examination, that women with prolapse have reduced pelvic floor muscle strength and generated less vaginal closure force during pelvic muscle contraction than controls, potentially leading to urinary incontinence [39].

Hagen et al. (2004) reported that, in the United Kingdom, physicians referred a number of women with a presumed diagnosis of both POP and urinary incontinence to the pelvic physiotherapist and that 92% of the physiotherapists assessed and treated the combination of these two pelvic floor dysfunctions [40]. Although there are no guidelines for the treatment of POP available so far, more recent randomized clinical trials (RCTs) show that, compared to no treatment, pelvic physiotherapy is effective in women with POP (stages I–III) of any type and urinary incontinence [41–43].

Also, other etiological and prognostic factors such as age, hysterectomy, estrogen depletion during menopause, chronic diseases such as diabetes mellitus, immobility, obesity, and number, duration, and mode of delivery play a role in incontinence [43].

In the Royal Dutch Society for Physiotherapy (KNGF) guidelines on adult SUI, a systematic review of the literature up to 2011, including only prospective studies, has been included [16]. Thirty-nine studies were found to meet the inclusion criteria. Using the Evidence-Based Richtlijn (Guideline) Ontwikkeling (Development) (EBRO) criteria, these studies were first evaluated in terms of quality [16]. The conclusions were that it has been demonstrated (level of evidence A2) that there is an increased risk of SUI after pregnancy if SUI was already present before the pregnancy [44] and after the pregnancy if SUI was present during the pregnancy [45]. Similarly, there is an increased risk of developing SUI after vaginal delivery [46]. The risk of developing SUI rises with the age of the mother at the time of her first delivery [46]. If a woman has SUI 3 months after giving birth, there is an increased risk that she will also have SUI later on [44]. The risk of developing SUI increases with increasing BMI (>25) [47] and among morbidly obese women (BMI > 30) [48]. More details on etiological and prognostic factors of success of pelvic physiotherapy can be found in the KNGF guidelines [16]. If, and to what extent, there is a causal relationship between these factors and the incidence of incontinence is by far not clear yet [49,50].

Still, identification of relevant etiological and prognostic factors that might hinder—locally and/or in general—recovery and compensation and whether or not these factors can be influenced by physiotherapy is important, because these might have consequences for the strategy, routing, and outcome of treatment.

So, following relevant guidelines recommendations, the referral to a pelvic physiotherapist should contain the following data [16]:

- Date of referral and personal patient data
- An as accurate as possible medical diagnosis
- Severity of urine loss and patient's experience and impact of the complaints of the patient
- Diagnostic findings: capacity to contract, either voluntarily or involuntarily, and relax the pelvic floor muscles and indication of (level of) pelvic floor muscle strength
- Presence of and grade of prolapse and/or other relevant urogynecological health problems
- Data of the voiding diary
- Requested intervention and, if applicable, former interventions
- Potential (causal) (risk) factors and prognostic factors (e.g., rupture after vaginal delivery, a neurological damage of the pudendal nerve, diabetes mellitus, earlier urogynecological surgery)
- Use of medication (related to incontinence interfering with treatment)

PHYSIOTHERAPEUTIC DIAGNOSTIC PHASE

Based on the medical diagnosis of the referring physician, the physiotherapist starts his or her physiotherapeutic diagnostic process. The aim is to assess, analyze, and evaluate the—often unclear [16]—nature and severity of the urinary incontinence problem and to determine whether and to what extent a physiotherapeutic intervention can be effective. What is the nature of the underlying pathology? Are there any local or general obstructing factors for recovery and improvement, and to what extent can these factors be influenced by physiotherapy?

Using the International Classification of Functioning [50] (Table 43.1), the physiotherapist tries to influence the *consequences* of the health problem on three different levels: organ level (impairment level, e.g., urine loss while coughing), personal level (disability level, e.g., sanitation), and social–societal level (restriction of participation, e.g., social isolation).

The taking of a systematic history aims to establish and record

- The confirmation of the type of incontinence (Is it really a case of stress urinary incontinence?) (See Table 43.2)
- The severity of the health problem by noting impairment(s), disability(ies), and restrictions in participation
- The likely nature of the underlying pathology by noting causal factors (e.g., in stress incontinence trauma during vaginal delivery[ies])
- Local factors, which may prevent the recovery and improvement (e.g., prolapsed uterus)
- General or systematic factors, which may prevent recovery and improvement (e.g., diabetes mellitus)
- Personal factors (e.g., what efforts does the patient make to alleviate stress or urgency incontinence)

The type of incontinence will become clear during history taking and can, if necessary, be confirmed using the incontinence questionnaire (3IQ) test. A presumptive diagnosis of SUI can be established using a short questionnaire for primary care, which allows rapid and valid discrimination of the main types of urinary incontinence, for example, SUI vs. urgency (urinary) incontinence.

Table 43.1 Definitions of the International Classification of Functioning Terms: Impairment, Disability, and Restriction in Participation

Impairment	Loss or abnormality of psychological, physiological, or anatomical structure or function at organ level. With respect to the classification of disorders in the storage and voiding of urine and feces, this means the impairment stress incontinence, or detrusor overactivity.
Disability	Restriction or loss of ability of a person to perform functions/activities in a normal manner. With respect to the classification of disabilities of voiding and stool, this means the disability involuntary loss of urine.
Restriction in participation	Disadvantage due to impairment or disability that limits or prevents fulfillment of a normal role (depends on age, sex, sociocultural factors) for the person.

Source: WHO-Publication, *International Classification of Functioning, Disability and Health* (*ICF*), World Health Organization, Geneva, Switzerland, 2001.

Table 43.2 3IQ Test

During the last 3 months, have you leaked urine (even a small amount)?

Yes (please continue with questions 2 and 3) or no (questionnaire completed).

During the last 3 months, did you leak urine (check all questions that apply)?

1. When you were performing some physical activity, such as coughing, sneezing, lifting, or exercise?
2. When you had the urge or the feeling that you needed to empty your bladder but you could not get to the toilet fast enough?
3. Without physical activity and without a sense of urgency?

During the last 3 months, did you leak urine most often (check only one)?

1. When you were performing some physical activity, such as coughing, sneezing, lifting, or exercise?
2. When you had the urge to empty your bladder but you could not get to the toilet fast enough?
3. Without physical activity and without a sense of urgency?
4. About equally as often with physical activity as with a sense of urgency?

Definitions of type of urinary incontinence are based on the responses to question 3:

1. Most often with physical activity → stress only or stress predominant urinary incontinence
2. Most often with the urge to empty the bladder → urgency only or urgency predominant urinary incontinence
3. Without physical activity or sense of urgency → other cause
4. About equally with physical activity and sense of urgency → mixed urinary incontinence

The 3IQ test is a useful measurement instrument, which can establish the presence of SUI with a sensitivity of 0.86 (95% CI = 0.79–0.90) and a specificity of 0.60 (95% CI = 0.51–0.68) and can establish urgency (urinary) incontinence with a sensitivity of 0.75 (95% CI = 0.68–0.81) and a specificity of 0.77 (95% CI = 0.69–0.84) (Table 43.2) [51].

A physical examination of the patient is important in order to verify and support the patient profile gained from the patient's history. To conduct the physical examination, a number of diagnostic tests are available to the physiotherapist. The severity of the stress, urgency, or mixed incontinence depends not only on the condition of the pelvic floor and the bladder but also on the posture, respiration, movement, and the general physical and psychological condition [52,53]. Information on the severity of stress, urgency, or mixed incontinence can also be obtained by studying the voiding diaries mentioned earlier with relevant data about incontinence. Also subjective self-report, quality-of-life questionnaires, and/or symptom questionnaires, such as the "PRAFAB"-score (which combines the most important objective and subjective elements of the degree of urinary incontinence), are helpful [54]; *p*rotection (use of pads), *a*mount of urine loss, *f*requency of the complaint, *a*djustment in behavior due to the complaint, and *b*ody image as a result of the urine loss are the five elements of the PRAFAB-score. With such questionnaires, it is possible to illustrate the degree of incontinence in a reproducible manner [54]. Especially in patients with stress incontinence, a pad test can be useful to test the extent and severity of the involuntary loss of urine [55].

The objective of physical examination is to understand

- The functionality of the pelvic floor in rest and during activities in terms of coordination, tonus, endurance, and strength
- The possibility and degree of contraction (with or without awareness) and relaxation of the pelvic floor muscles
- The influence of other parts of the body on the function of the pelvic floor, by inspection at rest and while moving

For qualification and quantification of strength of contraction, level of relaxation, coordination, endurance, repeatability, and displacement, manual assessment of the function of the pelvic floor muscles is the most commonly performed technique by physiotherapists. It is done either by digital intravaginal (Figures 43.1 and 43.2) or intra-anorectal palpation with the patient in supine position [16]. To test maximal strength, the patient is instructed to contract the pelvic floor muscles as hard as possible. Muscular endurance is tested by asking the patient to sustain a near to maximum contraction for at least 10 seconds repeatability to repeat as many as possible maximal contractions followed by complete relaxation during 15 seconds. Digital palpation is also used to determine pelvic floor muscle (over, under) activity, pelvic floor muscle activity differences and differences between the left and the right side of the pelvic floor (Figure 43.3).

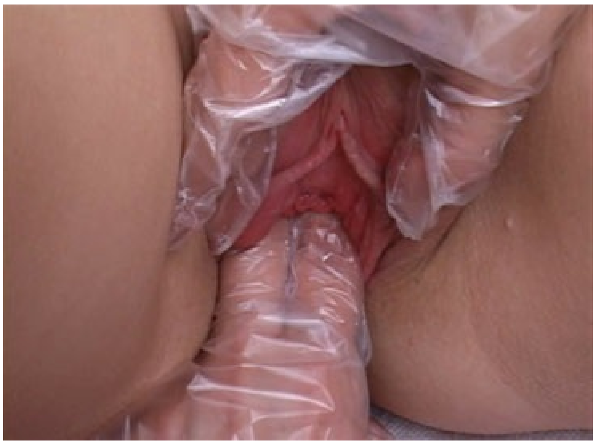


Figure 43.1 Assessment of the pelvic floor and contraction of the levator ani muscles.

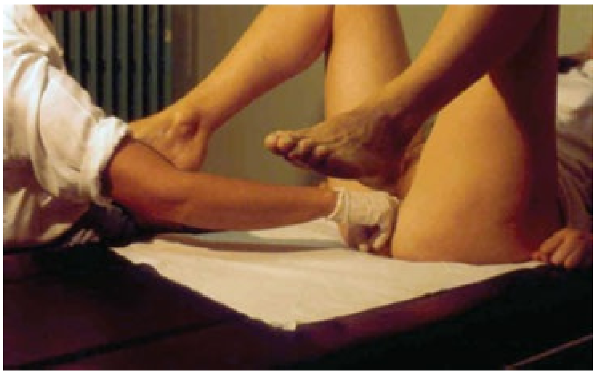


Figure 43.2 Pelvic floor muscle training for stress urinary incontinence (and mixed urinary incontinence [MUI] with predominant stress factor): (1) explain correct PFM contraction; (2) practice before checking ability to contract; (3) first intensive guidance in office to perform conscious and selective PFM contractions to prepare for pelvic floor muscle training [PFMT] at home; (4) set up individual home training program; (5) follow up with weekly or more often supervised training. The first part of PFMT can involve digital palpation to support and control PFM contractions during coughing and lift of one or two legs (as shown), followed by more functional exercises such as lifting weights, sitting down, or standing up. (By kind permission of IRPP, Lille, France.)

With pelvic floor muscle palpation, vaginal squeeze pressure and inward/upward lift of the pelvic floor muscles can be registered. For assessment of contraction of the levator ani muscles, the pelvic physiotherapist inserts first his or her index, if possible followed by his or her middle finger from below inside the vagina until he or she feels the levator ani muscles.

To assess a conscious contraction, the patient is instructed to contract the pelvic floor muscles (“withhold a flatus; contract the anus inward; stop the urine”). An unconscious contraction (the pelvic floor muscles [PFM] contraction that takes place preceding an abdominal pressure rise, for instance, due to a cough, to prevent loss of urine, sometimes called reflex contraction) is assessed by asking the patient to (deeply) cough and to perform a Valsalva maneuver. In all cases, a correct contraction is a simultaneous circumferential squeeze around the physiotherapist’s index or index and middle finger and inward/upward movement or elevation of the levator ani muscles. To quantify the (static and dynamic) strength of a voluntary or reflex contraction, the International Continence Society and the International Association of Urogynecology recommend the use of the tool in Figure 43.3 [11].

The strength of the PFM contraction is graded as

- Absent, no contraction at all
- Weak, i.e., weak contraction (pelvic floor [PF] lift not possible)
- Normal, i.e., moderate contraction (PF lift is possible)
- Strong, i.e., good contraction (PF lift is possible)

Pelvic floor muscle relaxation should be tested after a contraction. Therefore, the investigator should always start with a contraction and then ask for relaxation. Relaxation is graded as absent, partial (i.e., incomplete and/or delayed), or complete (Figure 43.2).

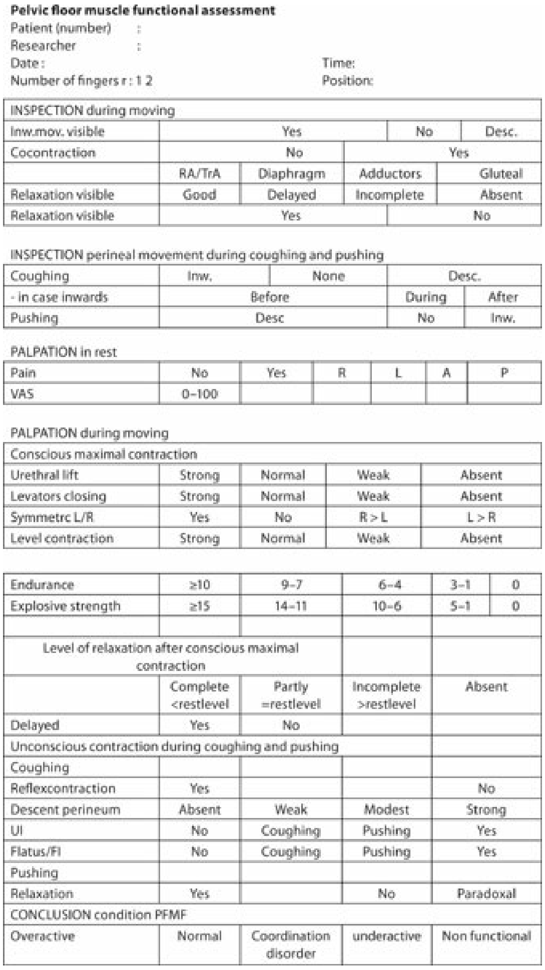
The strength of the pelvic floor muscles can also be measured by a vaginal squeeze pressure device connected to a manometer (pressure manometry, perineometer) [56] or pelvic floor dynamometer (a kind of strain gauge device for the pelvic floor to measure precisely forces produced during a pelvic floor muscle contraction independently of the evaluator's judgment) [57]. These methods are complicated to perform, demand clinical experience and skills in order to produce a methodologically high-quality result or are not yet clinically available [58].

More recently, an increasing number of pelvic physiotherapists assess pelvic floor function with perineal ultrasound. Dynamic evaluation of pelvic floor function includes position and elevation or descent of the bladder neck. Also, the puborectalis muscle at rest as well as pelvic floor precontraction, voluntary pelvic floor maximal and submaximal contractions, hold during respiration and sneezing or coughing, stabilization of the urethra, and hold of bladder neck position during coughing or abdominal maneuvers can all be evaluated. However, although pelvic floor imaging using ultrasound becomes more and more popular, diagnostic ultrasound is reported to be well known for its operator-dependent nature and should only be used after appropriate and effective education [59].

A limitation of the different measurement methods common to all clinic-based measurements of pelvic floor muscle function is that they are performed in the supine position or other standard positions. One should keep in mind that this might not reflect functional or usual activity of the pelvic floor during daily life activities as a response to increased abdominal pressure [58].

After the history taking, physical examination, and functional tests, analysis and evaluation of the results of physiotherapeutic diagnostic phase and relevant medical data will complete this process. The diagnosis of the referring provider can be confirmed or changed, and the indication for physiotherapy ascertained. Therefore, answering the following questions is necessary:

- Is referral diagnosis likely?
- Are there any urinary incontinence–related health problems?
- What is the nature of the stress incontinence, urgency incontinence, or mixed incontinence?
- What is the severity and the extent of the health problem?
- Is there a dysfunction of the pelvic floor?
- What caused this dysfunction?
- Are there currently any local factors that may prevent recovery or improvement, and can physiotherapeutic intervention have an influence on these factors?
- Are there any general factors that may prevent recovery or improvement?
- Is physiotherapy indicated?



Pelvic floor muscle functional assessment

Patient (number) :

Researcher :

Date : Time:

Number of fingers r : 1 2 Position:

INSPECTION during moving				
Inw.mov. visible	Yes	No	Desc.	
Cocontraction	No	Yes		
	RA/TrA	Diaphragm	Adductors	Gluteal
Relaxation visible	Good	Delayed	Incomplete	Absent
Relaxation visible	Yes	No		

INSPECTION perineal movement during coughing and pushing

Coughing	Inw.	None	Desc.	
- in case inwards	Before	During	After	
Pushing	Desc	No	Inw.	

PALPATION in rest

Pain	No	Yes	R	L	A	P
VAS	0–100					

PALPATION during moving

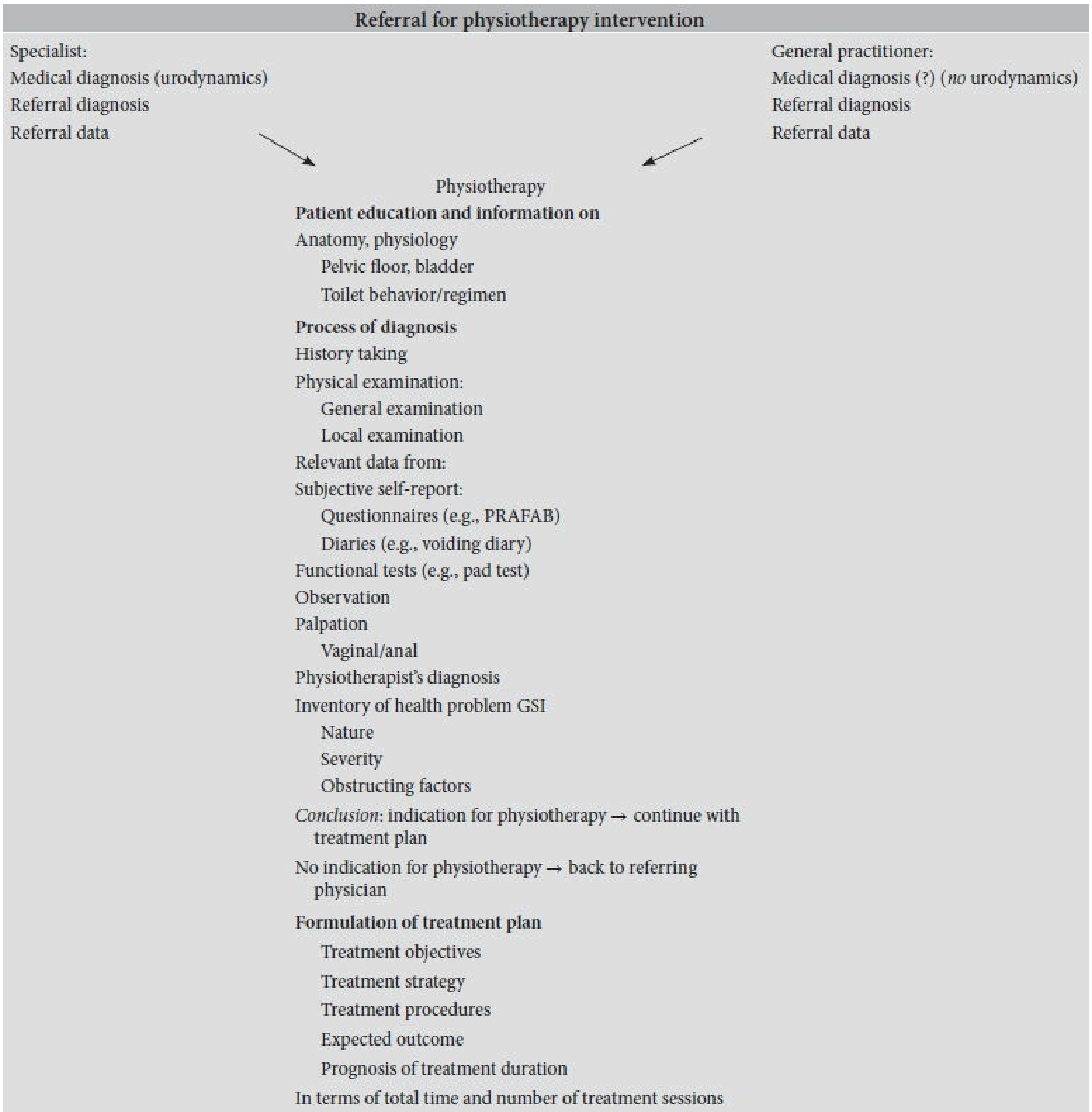
Conscious maximal contraction				
Urethral lift	Strong	Normal	Weak	Absent
Levators closing	Strong	Normal	Weak	Absent
Symmetrc L/R	Yes	No	R > L	L > R
Level contraction	Strong	Normal	Weak	Absent

Endurance	≥10	9–7	6–4	3–1	0
Explosive strength	≥15	14–11	10–6	5–1	0
Level of relaxation after conscious maximal contraction					
	Complete <restlevel	Partly =restlevel	Incomplete >restlevel	Absent	
Delayed	Yes	No			
Unconscious contraction during coughing and pushing					
Coughing					
Reflexcontraction	Yes			No	
Descent perineum	Absent	Weak	Modest	Strong	
UI	No	Coughing	Pushing	Yes	
Flatus/FI	No	Coughing	Pushing	Yes	
Pushing					
Relaxation	Yes		No	Paradoxal	
CONCLUSION condition PFMF					
Overactive	Normal	Coordination disorder	underactive	Non functional	

Figure 43.3 Pelvic floor muscle functional assessment.

A given severity of the health problem at referral has an impact on the prognosis and the evaluation of the likely effect of the physiotherapeutic intervention.

Table 43.3 Flowchart of Referral and Physiotherapeutic Process



Referral for physiotherapy intervention

Specialist:	General practitioner:
Medical diagnosis (urodynamics)	Medical diagnosis (?) (*no* urodynamics)
Referral diagnosis	Referral diagnosis
Referral data	Referral data

Physiotherapy

Patient education and information on

Anatomy, physiology
- Pelvic floor, bladder
- Toilet behavior/regimen

Process of diagnosis

History taking

Physical examination:
- General examination
- Local examination

Relevant data from:

Subjective self-report:
- Questionnaires (e.g., PRAFAB)
- Diaries (e.g., voiding diary)

Functional tests (e.g., pad test)

Observation

Palpation
- Vaginal/anal

Physiotherapist's diagnosis

Inventory of health problem GSI
- Nature
- Severity
- Obstructing factors

Conclusion: indication for physiotherapy → continue with treatment plan

No indication for physiotherapy → back to referring physician

Formulation of treatment plan
- Treatment objectives
- Treatment strategy
- Treatment procedures
- Expected outcome
- Prognosis of treatment duration

In terms of total time and number of treatment sessions

It is important to take into account other prognostic and patient variables, such as age, obesity, and vaginal childbirth, which will have their impact on the process of intervention.

In Table 43.3, a flowchart for the referral and physiotherapeutic diagnostic process is given.

INTERVENTION PHASE

As a general rule, the least invasive and the least troublesome treatment procedure should be considered as a first choice. After analysis and evaluation, the physiotherapist formulates his treatment plan. He or she estimates whether full recovery can be achieved or only compensation of the complaints is possible. Also, he or she determines his or her strategy, procedure, methods of treatment to reach the goal, and whether or not he or she has the skills and capability to do the job.

Approach and treatment modalities will be different for patients with stress incontinence, DO, or mixed incontinence, but all these low-risk interventions involve educating the patient and providing positive reinforcement for effort and progress [17,43].

Patient education embraces all relevant concepts (e.g., what is the function of the bladder) and information for the patient. Comprehension on the part of the patient will promote the motivation to start on other stages of treatment. The interplay between patient and physiotherapist is very important in this process. Before starting the specific therapy modalities on the pelvic floor, it is important to know and appreciate the position and the function of the pelvic floor and how to contract and relax the pelvic floor muscles. To achieve satisfactory results from intervention (in the long term), information and supervision by the physiotherapist throughout the intervention phase are essential, especially concerning the adequate use of the pelvic floor muscles during daily life activities and efforts and behavior of micturition.

Stress Urinary Incontinence

Physiotherapeutic treatment modalities for SUI are PFMT with or without biofeedback, electrical stimulation, magnetic stimulation, and/or vaginal cones.

The biological rationale for PFMT in the management of stress incontinence is that a strong and fast pelvic floor muscle contraction will clamp the urethra, increasing the urethral pressure, to prevent leakage during an abrupt increase in intra-abdominal pressure [60]. If the pelvic floor muscles are normally innervated and sufficiently attached to the endopelvic fascia, and, if by contracting her pelvic muscles before and during a cough, a woman is able to decrease that leakage [61], then simply learning when and how to use her pelvic muscles may be an effective therapy. In such cases, the subject needs to train to use this skill during those activities that transiently increase abdominal pressure [62]. DeLancey has also suggested that an effective pelvic floor muscle contraction may press the urethra against the pubic symphysis, creating a mechanical pressure rise [30]. Pelvic floor muscle contraction also supports the pelvic organs [30]. Timing might be one of the most important elements; in healthy continent women, activation of the PFM before or during physical exertion seems to be an automatic anatomic response, so it is, in essence, an unconscious contraction [63,64]. This PFM “reflex” contraction is a fast feedforward loop and might precede the bladder pressure rise by 200–240 milliseconds [65,66], something that might have been lost in SUI women. Also Bø has suggested that a well-timed, fast, and strong pelvic floor muscle contraction may prevent urethral descent during intra-abdominal pressure rise [67,68]. So pelvic floor muscle training is especially focused on adequate timing, strength improvement, and coordination of the periurethral and the pelvic floor muscles.

Appropriate treatment with PFMT should always include an assessment of pelvic floor muscle contraction and relaxation, because the effect of PFMT is dependent on whether the contractions and relaxations are performed correctly [68].

Repeated correct contractions of the pelvic floor, strengthening the pelvic floor muscles in a regular, intensive, and long-lasting training program, are essential for effective improvement through PFMT [68–70].

Extrapolation of exercise prescription guidelines suggests that pelvic floor muscle training should include short- and long-duration exercises, based on diagnostic findings, as both type I and type II muscle fibers need to be exercised with overload strategies. The frequency and the number of repetitions of exercises should be selected following assessment of the pelvic floor muscles. Daily regimes of increasing repetitions to the point of fatigue seem to be recommended (8–12 *maximal* pelvic floor muscles contractions, 1–3 seconds to 6–8 seconds hold/relax, three extra quick peak contractions superimposed on the maximal contraction, three times a day for at least 6 months [70]). A process of patient awareness of isolated contractions to fully automatic controlled function of the pelvic floor during multiple complex tasks is required [16].

It is very important to select relevant starting positions tailored to the individual patient while training. In addition, functional activities must be incorporated into the training program as soon as possible [43]. An individually tailored home exercise program manageable during daily life activity is essential [68].

Because the total urethral closing mechanism also depends on a competent intrinsic urethral sphincter (in case of incompetence, this is termed intrinsic sphincter deficiency [ISD]), there is no guarantee that improvement of timing, absolute strength, and endurance of the pelvic floor, with respect to the extrinsic part of the total urethral closing mechanism, will fully restore continence [62].

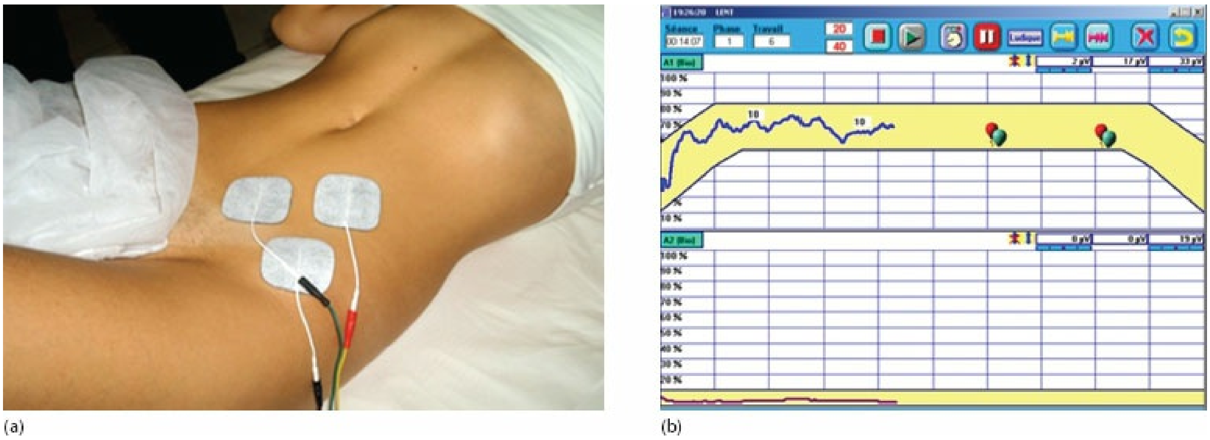
Meanwhile, there is sufficient evidence that PFMT is effective in the reduction of involuntary loss of urine in patients with stress incontinence, which is sustained for the long term [71–74].

In general, intensive training showed better results than a low intensity program [43,75,76].

Twenty-five percent of females are still dry after 5 years, while two-thirds of them indicate by follow-up that they are very satisfied with their present state and that they wish no further intervention.

Biofeedback refers to a range of audiovisual techniques whereby information regarding “hidden” physiological processes, in this case pelvic floor muscles contractions and relaxations, is displayed in a form understandable to the patient, to permit self-regulation of these events [43]. For instance, biofeedback can be used to teach a patient with SUI to selectively contract their pelvic floor muscles. A sensor or electrode is introduced into the vagina or rectum, to record the vaginal or rectal pressure or the ani electromyogram (EMG) signal of the sphincter muscle. The patient receives visual or acoustic information about the pressures measured and/or the EMG signals, enabling them to see what force is being generated by the pelvic floor muscles and whether this force has reached its maximum.

Recently, wireless biofeedback devices have been developed, introducing new technology and training program strategies (Figure 43.3). With the help of wireless biofeedback, numerous actions related to involuntary urine loss during daily activities can be mimicked, also enhancing the patient's motivation and adherence. Further studies to validate these promising innovative techniques and applications are needed. Recent research has investigated the use of extracorporeal ultrasonography to show patients with SUI whether they are producing the correct type of lift (in an inward and upward direction) of the pelvic floor during contraction [77].



(a) (b)

Figure 43.4 Electromyogram (EMG) biofeedback. (a) EMG biofeedback, here registered by surface electrodes, can be used to visualize on-screen; (b) selective pelvic floor muscle activity (blue line) together with control of any synergistic abdominal muscle activity (red line). (From Berghmans B et al., in: *Atlas of Bladder Disease*, Staskin D (Ed.), Springer, New York, 2009.)

Dietz et al. used suprapubic external ultrasonography for this purpose [78]. They concluded that this form of biofeedback takes little time (an average of 5 minutes) and is effective as well as efficient and as such is a useful strategy to teach patients to produce the right contractions.

Ultrasonography can also be used to estimate the volume (thickness) of the pelvic floor. But this type of biofeedback cannot be used to measure muscle strength [58,78]. Further research will be needed to assess methodological aspects of this type of biofeedback, such as its validity and reliability [58].

Biofeedback is not a treatment on its own. It is an adjunct to pelvic floor muscle training.

Biofeedback is based on operant conditioning and a cognitive learning process. An incontinence patient can be taught, with the aid of biofeedback, to be selective in the use of the pelvic floor muscles (Figure 43.4).

Usually, at the onset of therapy with biofeedback, the motor unit activity (EMG) or the intravaginal/anal pressure of the pelvic floor muscles (manometry) at rest, during a maximal pelvic floor muscles contraction (Pmax) and relaxation after Pmax are measured.

In an RCT comparing a group using PFMT with biofeedback and a group without biofeedback, Berghmans et al. [55] demonstrated quicker progress in the first group. In the long term, for the treatment of stress incontinence, biofeedback in combination with PFMT seems equally effective as only PFMT [55,79–81].

Nevertheless, in patients with urinary incontinence who have insufficient or no awareness of the pelvic floor muscles and therefore are not able to voluntary contract or relax their pelvic floor muscles or have very poor quality (intensity) of contraction at initial assessment, biofeedback is suggested to be an important strategy to quicken up and restore this awareness [43,55,67,82]. However, further large, high-quality RCTs are required in order to proof this hypothesis [43,55].

Electrical stimulation is generally provided by clinic-based electrical equipment (i.e., those that need to be plugged into a wall socket) or portable battery-powered stimulators (Figure 43.5).

Although relevant studies poorly report the biological rationale underpinning the application of electrical stimulation for the treatment of SUI [43], the aim of electrical stimulation in this setting appears to be to improve the function of the pelvic floor muscles, while for patients with urgency incontinence, the objective seems to be to inhibit DO.

For stress incontinence electrical stimulation is focused on the restoration of the reflex activity through stimulation of the fibers of the pudendal nerve with the purpose to create a contraction of the pelvic floor muscles [83]. Electrical stimulation is suggested to lead to a motor response by patients for whom a voluntary contraction is not possible as a result of an insufficient pelvic floor, on the condition that the nerve is (partly) intact [84].

Although electrical stimulation appears to be better than placebo, its effect in stress incontinence has not been sufficiently demonstrated due to inconsistency in study protocols [43,72].

There are many differences in potential clinical application that have not yet been investigated. For example, some clinicians suggest that “active” electrical stimulation (i.e., the patient voluntarily contracts the pelvic floor muscles during stimulation) is better than “passive” electrical stimulation, but the effect of these two approaches has not yet been evaluated [43,72]. Equally, it may be that some populations or subgroups of patients benefit from electrical stimulation more than others.

Figure 43.5 Wireless biofeedback equipment for urinary continence: POD universal, which is an external device for registration wireless connected medical machine. (Courtesy of Vivaltis, Montpellier, France.)

Although to date there is still insufficient evidence, in clinical practice, we suggest using electrical stimulation in patients with stress incontinence, who—during assessment—were not capable of performing an active voluntary contraction of the pelvic floor muscles. The following parameters may be used as a starting point:

- *Pulse shape*: bipolar rectangular square wave
- *Frequency*: 50 Hz
- *Pulse duration*: 200 microseconds
- *Duty circle*: ratio 1:2
- *Intensity of current*: maximal tolerance
- Two times/week office bound, two times/day at home, until voluntary contraction by the patient himself or herself is possible and adequate

Magnetic stimulation has been developed for stimulating both central and peripheral nervous systems noninvasively [85]. Magnetic stimulation has been applied to pelvic floor therapy and the treatment of urinary incontinence and was reported in treatment of this condition for the first time in 1999 by Galloway et al. [86]. Contrary to electrical stimulation, extracorporeal magnetic innervation (ExMI) aims to stimulate the pelvic floor muscles and sacral roots without insertion of an anal or vaginal probe [87,88]. For treatment, the patient is positioned in a chair. Within the chair's seat is a magnetic field generator (therapy head) that is powered and controlled by an external power unit. Conventional stimulators deliver, at frequencies of 10–50 Hz, repetitive pulses of current between less than 100 microseconds [66] and 275 microseconds [65] in duration. Size and strength of the magnetic field are determined by adjusting this amplitude by the physiotherapist [86]. A concentrated steep gradient magnetic field is directed vertically through the seat of the chair. When seated, the patient's perineum is centered in the middle of the seat, which places the pelvic floor muscles and sphincters directly on the primary axis of the pulsing magnetic field. Because of this, all tissues of the perineum can be penetrated by the magnetic field. Galloway indicated that no electricity, but only magnetic flux, enters the patient's body from the device [86]. Goldberg indicated that, in contrast to electrical current, the conduction of magnetic energy is unaffected by tissue impedance, creating a major advantage in its clinical application compared to electrical stimulation. In that way, structures, such as sacral roots or pudendal nerves, might therefore be magnetically stimulated without patient's discomfort or inconvenience of probe insertion for electrical stimulation [87].

Therefore, advantages of ExMI seem to be that it is performed through full clothing, entailing no probes, skin preparation, or physical or electrical contact with the skin surface. On the other hand, the need for repeated office-based treatment sessions represents an inherent disadvantage. In contrast to electrical stimulation units, this kind of technology lacks portability, and, because both the depth and width of magnetic field penetration is proportional to coil diameter, the present technology according to Goldberg is best suited for stimulation of a field, rather than a narrowly focused target such as the sacral roots or the pudendal nerve [87].

Magnetic stimulation of the sacral nerve roots and pelvic floor is suggested to be effective for SUI [87,88] although the mechanism of action on the continence mechanism is not fully understood [88]. Some authors suggested that in SUI it stimulates pelvic floor musculature causing external sphincter contraction [89], acting as a kind of a passive pelvic floor muscle exercise [90], and an increase of maximal urethral closing pressure [91]. Stimulation of sympathetic fibers maintaining smooth muscle tone within the intrinsic urethral sphincter seems to be involved in this mechanism of action [92,93]. Previous studies suggested a stimulation frequency of 50 Hz to be the most effective for urethral closure [86].

There is only limited evidence of the effect of magnetic stimulation treatment in women with SUI. There was considerable variation in diagnostic groups, the regimen, protocols, intensity, and duration of treatment. Sample sizes were small, and outcomes were contradictory. Only short-term results were available. At the moment, there is not enough evidence of the efficacy of magnetic stimulation to recommend this therapy in women with SUI [86].

In women with stress incontinence, weighted vaginal cones in combination with PFMT are sometimes used [72,94,95]. All cones are identical in size, but have increasing weight. The idea is that the stronger the pelvic floor muscles grow, the higher weight of a cone can be held in place and therefore continue to stimulate the pelvic floor muscles to hold the cone inside the vagina. A review by Herbison et al. provided some evidence that weighted vaginal cones are better than no active treatment but on the other hand add no benefit to a pelvic floor muscle training program alone [43,95]. Vaginal cones may add benefit to a training protocol if subjects are asked to contract around the cone and simultaneously try to pull it out in lying or standing position while performing their pelvic floor muscle exercises in the way described earlier [96].

Because of the lack of evidence about their efficacy and doubts regarding the theoretical basis of this treatment modality, Bo et al. stated that widespread use is not recommended [94].

On the other hand, in the latest update of their Cochrane Collaboration Review, Herbison and Dean suggest that, based on the sparse evidence that weighted vaginal cones are better than no active treatment, these could be offered as one treatment option, if women find them acceptable [97].

Guidelines for Stress Urinary Incontinence

In the KNGF guidelines for stress incontinence, the following problem areas are differentiated [16]:

- Stress incontinence with a dysfunction of the pelvic floor
  - With awareness of the pelvic floor.
  - Without awareness of the pelvic floor.
  - The function of the pelvic floor is compromised by dysfunctions in the respiratory or the locomotive tract.
- Stress incontinence without a dysfunction of the pelvic floor
- Stress incontinence (with or without a dysfunction of the pelvic floor) in combination with general factors that inhibit or delay improvement or recovery

Stress Incontinence with a Dysfunction of the Pelvic Floor

The primary aim of treatment is to obtain a good awareness of the pelvic floor muscles. During the treatment, the following techniques are used: digital palpation either by the patient herself or by the physiotherapist and electrical stimulation and/or biofeedback in combination with pelvic floor muscles training. If the patient is aware of contraction and relaxation of the pelvic floor muscles, the therapy continues with the use of PFMT only. If a pelvic floor dysfunction coexists with dysfunctions of the respiration or the locomotive tract or with inadequate toilet behavior, these issues need to be addressed additionally. The ultimate aim of the treatment is a complete restoration of the functionality of the pelvic floor.

Stress Incontinence without a Dysfunction of the Pelvic Floor

Without a dysfunction of the pelvic floor, an ISD is likely. Here, pelvic floor training can only provide some degree of compensation at the most. A complete cure is merely impossible.

Stress Incontinence in Combination with General Factors That Inhibit or Delay Improvement or Recovery

In this case, physiotherapy will aim at the reduction of these negative general factors. Avoiding specific situations by the patient, impaired social participation, and feelings of shame related to involuntary urine loss can be reduced by the physiotherapist using relevant information, education, counselling, and care.

In Table 43.4, an algorithm of the process of therapy for stress incontinence in women is given.

Table 43.4 Algorithm of Process of Therapy for Stress Incontinence in Women

- Process of therapy
  - Therapeutic training/management for distinguished problem areas
    - GSI + dysfunction pelvic floor + *no* awareness of pelvic floor:
      - Digital palpation by patient and/or physiotherapist
      - Electrostimulation (intravaginal/extravaginal) + PFMT
      - Biofeedback + PFMT
  - Objective: restoration of awareness of the pelvic floor
    - If awareness restored → see 1b
    - Unsatisfactory results → back to referring physician
    - GSI + dysfunction pelvic floor + awareness of the pelvic floor:
      - PFMT + home exercises; isolated contractions of the pelvic floor → with awareness of pelvic floor, single tasks → double tasks → multiple tasks → automatic controlled tasks; optional: vaginal cones
  - Objective: total recovery (of the functionality of the pelvic floor)
    - Unsatisfactory results → back to referring physician
    - GSI + dysfunction pelvic floor + function pelvic floor malinfluenced by disorders of tractus respiratorius or other parts such as tractus motorius, toilet regimen, toilet behavior
      - PFMT + home exercises
      - Exercises to achieve adequate respiration, postural exercises
    - Relaxation exercises, lift instruction
  - Objective: reduction or elimination of malinfluence disorders, improvement functionality of the pelvic floor
    - Unsatisfactory results → back to referring physician
    - GSI + *no* dysfunction of the pelvic floor
    - PFMT + home exercises; optional: vaginal cones
  - Objective: compensation. Expectation: total recovery not likely

Unsatisfactory results → back to referring physician
GSI + general obstructing factors
Objective: maximal possible reduction of these negative factors
Unsatisfactory results → back to referring physician
Evaluation
Treatment results (changes in), patient's health status, course of action of physiotherapist
Concluding treatment period and reporting to referring physician

Detrusor Overactivity

In this condition, the patient has no or insufficient control over involuntary detrusor contractions, which can result in involuntary urine loss [97]. Physiotherapy for DO consists of patient information and education, toilet training, bladder (re-)training (BlT) or behavioral therapy, PFMT with or without biofeedback, electrical stimulation, and magnetic stimulation. All physiotherapeutic modalities can be used alone or in combination with each other or in combination with medication.

Patient information and education is provided about the lower urinary tract function, the function of the pelvic floor, and the way to contract and relax the pelvic floor.

The goal of toilet training is to change inadequate toilet behavior and regimens, i.e., aiming at the aspects of the micturition process itself.

BlT aims to restore normal bladder function using patient education together with a scheduled voiding regimen in order to increase the time interval between two consecutive voidings [98,99]. It consists of four components. The first is an educational program that addresses lower urinary tract function. The next component involves training to inhibit the sensation of urgency and to postpone voiding. The third is to urinate according to a timetable in patients with an interval less than 2 hours between two consecutive micturitions in order to reach an interval of at least 3 hours between two consecutive voidings and to reach larger voided volumes. The fourth step is reinforcement of patient motivation by the physiotherapist.

Especially in those patients whose functional capacity of the bladder is too small, a BlT program can provide normalization of bladder capacity. So far, the exact working mechanism of BlT remains unclear [43,99,100]. Improvement of cortical inhibition over involuntary detrusor contractions [101], central modulation of afferent sensory impulses or cortical facilitation over urethral closure during bladder filling [102], and behavioral changes leading to an increase of "reserve capacity" of the lower urinary tract system [103] have been proposed.

The efficacy of bladder training in women with DO varies from 12% to 90% [43]. From the few trials available, the ICI concluded that there is scant level 1 evidence that BlT may be an effective treatment for women with UUI and MUI (level of evidence: 1). If there is no reduction in incontinent episodes after 3 weeks of bladder training, the ICI recommends reevaluation and the consideration of other treatment options [43].

Specific PFMT *probably* facilitates and restores the detrusor inhibition reflex (DIR) by selective contraction of the pelvic floor muscles. PFMT consists of PFME and general or specific relaxation exercises. Different from the mechanism in stress incontinence, in patients with DO, selective contractions of the pelvic floor muscles during therapy are focused on the inhibition of involuntary detrusor contractions (reflex inhibition) [104].

In many patients with DO, there is concurrent high pelvic floor muscle tone [105]. The level of activation is so high that selective contraction of the pelvic floor muscles in order to achieve reciprocal inhibition of the bladder is very difficult or not possible [106]. Teaching selective contraction and relaxation of the pelvic floor muscles is then an important first step. Once this is achieved, selective contraction of the pelvic floor muscles focuses on facilitation of the DIR. After testing a patient's ability to hold contractions for at least 20 seconds by digital palpation by the physiotherapist, patients are instructed to do so, followed by a relaxation period of 10 seconds. A more functional training program (pelvic floor exercises during daily living activities) completes the exercise program.

Combinations of BlT and PFMT are also used in patients with DO. In the study by Berghmans et al., this kind of program was called lower urinary tract exercises [84].

Similar to that seen in patients with stress incontinence, with DO, and with insufficient or no awareness of the pelvic floor, biofeedback can be used to learn to control muscle functions such as reduction of an increased muscle activity or a better timing and coordination of contraction or relaxation

[55].

Wyman et al. suggested that a combination of biofeedback, PFMT, and bladder training was more effective immediately after the therapy than a separate application of each treatment modality [103].

In patients with DO, electrical stimulation theoretically stimulates the DIR and pacifies the micturition reflex, resulting in a decrease of overactive bladder dysfunction [83].

Electrical stimulation aims to inhibit involuntary detrusor contractions through selective stimulation of afferent and efferent nerve fibers in the pelvic floor. This activity results in contraction of the para- and periurethral musculature either directly or via spinal reflexes [84].

Although sometimes external electrodes have been used, electrical stimulation is mostly applied vaginally or anally through plug mounted electrodes [25,43]. A patient is instructed to use the maximal tolerable level during stimulation. In relevant studies, the following treatment characteristics were used: frequency modulation of 0.1 second trains of rectangular biphasic 200 microseconds [84,107] or 400 microseconds [108] long pulses that varied stochastically between 4 and 10 Hz [84] or with a fixed frequency of 10 Hz [107,108]. Acute electrical stimulation can be applied (mostly 1–2 times a week during 20 minutes) or chronic electrical stimulation (daily at home, e.g., every 6 hours 20 minutes).

Besides office-based electrical stimulation, portable electrical stimulation devices for self-care by patients themselves at home have been developed [84] (Figure 43.6).

Magnetic stimulation of the sacral nerve roots and pelvic floor is suggested to be an effective treatment modality for urgency urinary incontinence [87,88]. The mechanism of action to improve or restore urgency urinary incontinence is still not fully clear [88]. Using low-frequency stimulation (e.g., 10 Hz) [91] for the treatment of urgency urinary incontinence, magnetic stimulation might suppress DO through at least two autonomic effects: by activation of pudendal nerve afferents blocking parasympathetic detrusor motor fibers at the spinal reflex arc or by activation of inhibitory hypogastric sympathetic neurons or by a combination of both mechanisms [93]. Modulation of pudendal nerve afferent branches stimulating an inhibitory spinal reflex at the S3 nerve root is also suggested to play a role in this mechanism of action [93].

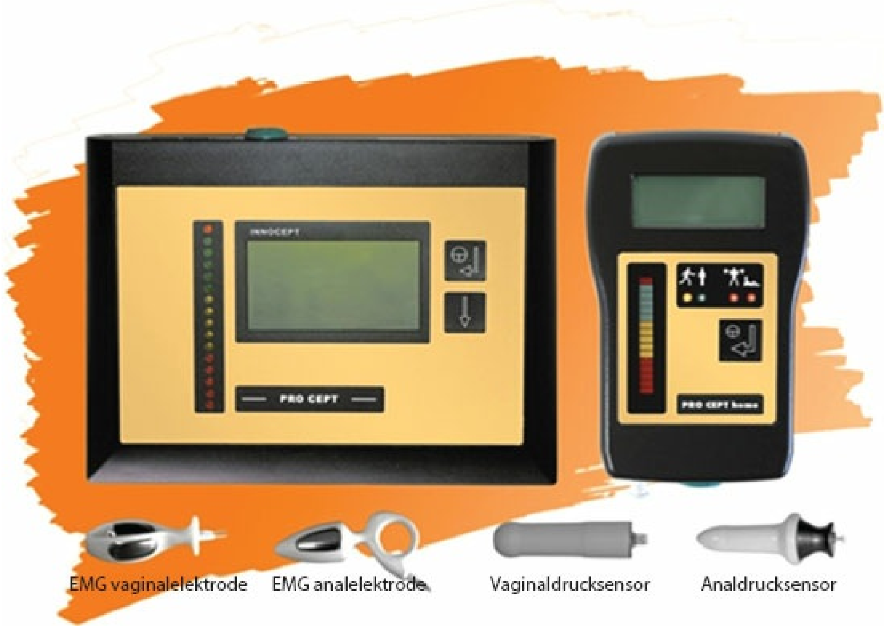


Figure 43.6 Office-bound and home devices for electrical stimulation. (By permission of Biobedded MgbH, Gladbeck, Germany.)

Only sparse evidence of the effect of magnetic stimulation vs. no treatment, placebo or control treatment in women with urgency urinary incontinence, is available. So far, only short-term results have been reported. At the moment, there is not enough evidence for the efficacy of magnetic stimulation in women with urgency urinary incontinence to recommend this therapy.

In summary, with regard to the evidence for the different treatment modalities for DO, the following conclusions can be made: the efficacy of bladder training in women with DO is still pending and varies from 12% to 90% [43]. Despite a positive trend in several studies [84,108] with reported success rates around 45%–50%, today there is still insufficient evidence for the efficacy of PFMT programs with or without biofeedback in patients with DO [25,43,84]. Three high-quality RCTs show that acute and chronic electrical stimulations, office and home based, are effective in 70% of all cases [84,107,108]. This treatment modality may be the treatment of first choice in patients with DO [43,84,107,108].

Mixed Incontinence

The physiotherapeutic diagnostic and therapeutic process focuses on the predominant symptom of the mixed urinary incontinence: stress vs. urgency. If the symptoms of urgency/frequency appear to be dominant, mostly the aim will be to reduce and improve these factors. In these cases, if the physiotherapist erroneously starts with addressing the stress component, this can provide a negative influence on the urgency component, potentially introducing more severe urgency/frequency. Reduction or improvement of the latter symptoms will provide a solid base for the subsequent treatment of the stress component. The choice of therapy modalities depends on the nature, extent, and severity of the health problem and is based on the analysis and evaluation of the physiotherapeutic diagnostic process.

PATIENT EDUCATION IN PHYSIOTHERAPY PRACTICE

In order to achieve a permanent positive result from physiotherapy, patients have to incorporate the newly acquired abilities into daily life. The physiotherapist is the most important mentor in this behavioral modification. Patient education is a very important aspect of this kind of care, and a professional attitude toward providing patient education is required. Van der Burgt and Verhulst developed a model for allied health professions as an instrumental tool for patient education [109]. This model is a combination of the ASE model and the so-called steps model of Hoenen et al., developed for individual patient education [110]. In the ASE model, the premise is that the interplay between *a*ttitude, *s*ocial influence, and own *e*fficacy determines the willingness to modify behavior (Figure 43.7).

In the model of van der Burgt and Verhulst, a number of stages are distinguished, such as thinking, feeling, and doing. In patients with urinary incontinence, this model can be transformed into an exchange of information and explanation (thinking); in awareness and feeling of the pelvic floor, posture, and movement (feeling); and in training of the pelvic floor and promotion of short- and long-term compliance (doing). The standardized patient education model of van der Burgt and Verhulst can be seen as an example of how to facilitate best practice and thus can provide physiotherapists with a framework upon which to base patient education in urinary incontinence.

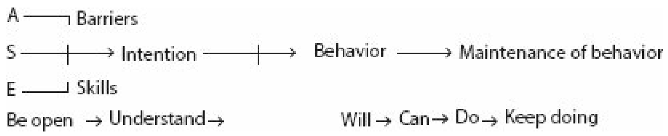


Figure 43.7 Parallels between the ASE model and the Steps model. (From van der Burgt M and Verhulst F, Gedragsmodellen, in: Van der Burgt M and Verhulst F, eds., *Doen en blijven doen*, Bohn Stafleu Van Loghum, Houten, the Netherlands, p. 31, 1996.)

CONCLUSION

Pelvic physiotherapy often appears to be effective in the treatment of incontinence.

For this reason, physiotherapy is a valuable treatment option in the management of patients with urinary incontinence.

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44 Pessaries and Devices: Nonsurgical Treatment of Pelvic Organ Prolapse and Stress Urinary Incontinence

Catherine S. Bradley

INTRODUCTION

Pessaries, or devices placed in the vagina to support the uterus or vaginal walls, have been used for thousands of years to treat pelvic organ prolapse (POP). Hippocrates documented the use of pomegranates soaked in vinegar as vaginal pessaries, and ring pessaries made of wood, cork, silver, and gold were described in the early 1700s [1,2]. In the nineteenth century, the development of pessaries made out of vulcanized rubber allowed safer long-term use [2]. Pessaries remained the treatment of choice for POP through the early 1900s when over 100 types of pessaries were available, but their use declined in the following decades as developments in aseptic techniques and anesthesia made surgical correction more feasible.

Pessaries are currently considered the primary nonsurgical treatment option for POP and an important treatment option for stress urinary incontinence (SUI). However, opinions on pessary use, pessary training, and pessary management continue to vary widely among clinicians. Several surveys of gynecologists and urogynecologists in the United States and United Kingdom suggest most (77%–87%) offer pessary treatment for prolapse, but a significant minority are not involved in pessary care or offer pessaries only to women who are not surgical candidates [3–5]. While the majority of gynecologists surveyed in one U.S. study offered pessary fitting for POP, most reported they received minimal training in pessary use and few believed pessaries were an effective treatment for SUI [6].

Many experts now recommend pessaries as a long-term treatment option for any woman with POP and SUI seeking nonsurgical therapy, not just for women for whom surgery is not an option [7]. However, evidence on the effectiveness of pessaries and other mechanical devices for the treatment of POP and SUI remains limited.

PESSARIES FOR PELVIC ORGAN PROLAPSE

Pessaries used for treating POP can be loosely grouped into supportive and space-occupying pessaries. Supportive pessaries (Figure 44.1) are held in place by levator muscle tone, while space-occupying pessaries (Figure 44.2) keep prolapse reduced by filling the vagina. Most pessaries today are made from medical-grade silicone, which is nonallergenic, nontoxic, and latex-free. This material does not absorb odors, and it can be sterilized and lasts for several years.

Effectiveness of Treatment

Prospective research on the effectiveness of pessaries for POP treatment is sparse. In fact, experts have identified an “urgent need” for randomized controlled trials focusing on the effectiveness of pessaries as well as on aspects of pessary management [8]. In 2007, Cundiff et al. [9] published the only randomized trial focusing on pessary therapy for POP. This multicenter, randomized crossover trial compared outcomes of women with symptomatic POP treated with two common types of pessaries. Women were randomized to initial treatment with a ring with support pessary or with a Gellhorn pessary. After 3 months of treatment, participants were fitted and treated with the other type of pessary. The primary outcome was change in prolapse symptoms, assessed using validated questionnaires. The percentage of participants who successfully fit with at least one pessary is 92%, and 60% continued the pessary therapy for 3 months (there were no differences seen between pessary types). Using a strict criterion for defining clinically significant improvement in quality of life scores, both pessaries were found to be equally effective in decreasing POP-related symptom bother as well as bother from obstructive and irritative urinary and colorectal symptoms [9].

Three short-term, prospective cohort studies of urogynecology patients (n = 80–203, follow-up from

4–12 months) also demonstrated significant improvements in pelvic floor symptoms when POP was treated with a pessary [10–12]. About 75% of patients were successfully fit with a pessary, and 43%–56% continued use through 4–12 months follow-up [10,11,13,14]. In one study, prolapse symptom improvement (assessed using a validated questionnaire) best predicted pessary continuation [11]. All three studies found overall improved prolapse and urinary symptoms after pessary treatment. Clemons et al. [12] found women with baseline urinary symptoms (stress incontinence, urge incontinence, and voiding difficulty) had moderate improvement (in 45%, 46%, and 53%, respectively). However, among women without urinary symptoms at baseline, 21% developed new stress incontinence symptoms, which was associated with treatment dissatisfaction.

Long-term pessary treatment outcomes were studied in a 5-year, prospective observational study of patients choosing pessary treatment for POP [15]. Of 246 patients who chose pessary treatment, 187 retained the pessary at the 4 weeks follow-up visit and were entered into follow-up. After 5 years, 53 (28.3% of the entire cohort or 35.1% of the 151 who completed 5-year follow-up) were considered treatment successes due to reduced prolapse symptoms and patient desire to continue pessary use.

Finally, two recent observational studies provide some information about treatment outcomes in patients choosing pessary treatment compared to surgery. Abdool et al. [16] performed a prospective, observational study of 359 women who selected pessary treatment and 195 women who selected surgery for POP. The majority of pessary users wore ring pessaries (83%), and 95% of the prolapse surgeries were vaginal-approach native tissue repairs. Women who selected pessary treatment were on average older (68 vs. 60 years). At 1-year follow-up, both groups had significant improvements in prolapse, urinary, bowel, and sexual symptoms. The extent of symptom improvement was similar in the pessary and surgery groups when controlled for age. However, the study had significant loss to follow-up (32% of the pessary group and 45% of the surgery group). This loss to follow-up and the observational study design limit the impact of these results.

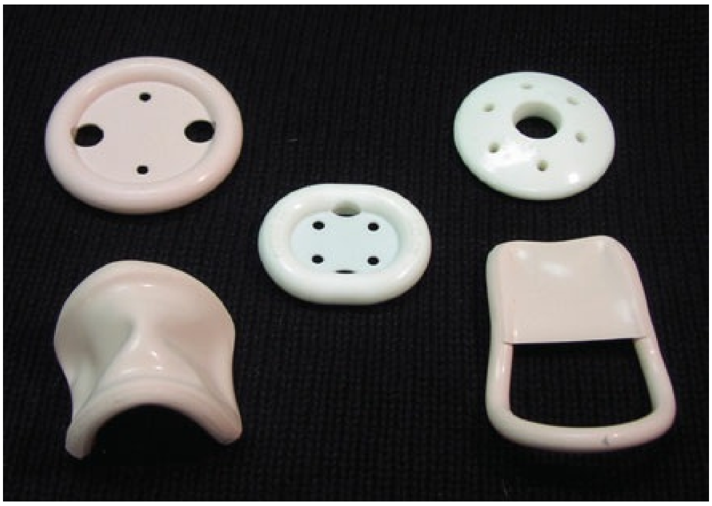

Figure 44.1 Support pessaries used to treat pelvic organ prolapse. *Top row*: (left) ring with support (Courtesy of Milex, Inc., Chicago, IL.); (right) Shaatz (Courtesy of Mentor Corporation, Santa Barbara, CA.). *Middle row*: oval with support (Courtesy of Mentor Corporation, Santa Barbara, CA.). *Bottom row*: (left) Gehrung (Courtesy of Milex, Inc., Chicago, IL.); (right) Hodge (Courtesy of Milex, Inc., Chicago, IL).

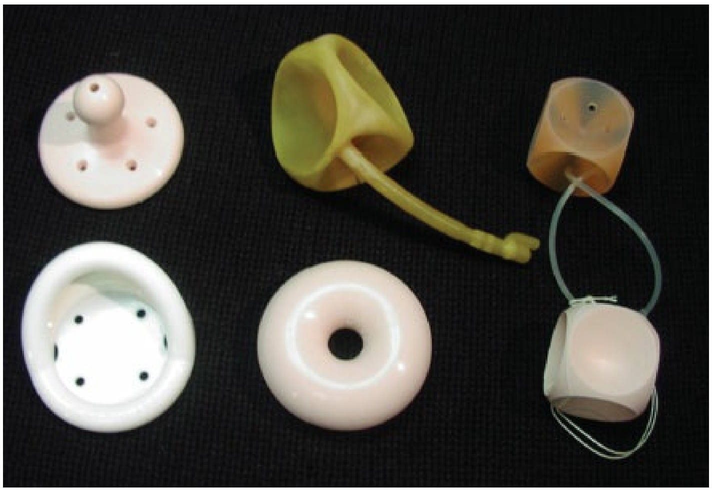

Figure 44.2 Space-occupying pessaries used to treat pelvic organ prolapse. *Top row*: (left) Gellhorn (Courtesy of Mentor Corporation, Santa Barbara, CA.); (middle) inflatoball (Courtesy of Milex, Inc., Chicago, IL.); (right) cube with drainage holes (Courtesy of Mentor Corporation, Santa Barbara, CA.). *Bottom row*: (left) Marland; (middle) donut; (right) cube (All three by courtesy of Milex, Inc., Chicago, IL).

In a smaller but well-designed prospective study, Mamik et al. [17] compared short-term (3 month) treatment outcomes in women choosing surgery or pessary treatment for POP, including goal attainment, patient global impression of improvement, body image, and symptom change. Both patient groups had similar characteristics at baseline, and both treatment groups improved 3 months after treatment. In contrast to the study by Abdool et al. [16], the surgery treatment group had higher goal attainment, higher global impression of improvement, and better symptom improvement.

In summary, research published to date suggests that pessary therapy for POP will improve or resolve most prolapse symptoms as well as many bladder, defecatory, and sexual symptoms. The development of new stress incontinence occurs in a minority of patients, but it is associated with pessary discontinuation. Most women interested in pessary treatment can be successfully fitted with a pessary, and 40%–60% will continue its use for greater than 6–12 months. More studies are needed to compare outcomes after pessary treatment versus surgery before conclusions can be reached regarding comparative effectiveness.

Pessary Fitting

Rates of successful pessary fitting in the literature range from 41% to 92%, with variable definitions used for success [9,10,14,18,19]. Often, more than one visit and the use of two or more pessaries are required for fitting. Among 1216 patients with POP and UI referred to a pessary clinic, Hanson et al. [19] initially fitted 1043 (86%) with a pessary, but only 744 (62%) continued to wear the pessaries for greater than 1 month. Half of the patients required two or more visits for fitting and a median of two pessaries was tried. Clemons et al. [14] successfully fitted 73% of patients with POP with a pessary, defined as a successful fit and planned continued use of the pessary after a 1 week follow-up visit. Thirty percent of patients required two visits and on average two pessaries were tried per visit to achieve a successful fit.

Patient characteristics that predict a successful pessary fitting are inconsistent across studies [10,14,18–20]. For example, conflicting results have been reported for age and POP stage in predicting pessary fitting success [14,20]. The type of support defect (e.g., anterior, posterior or apical) is also not consistently associated with fitting failure. In several studies, prior hysterectomy and prior reconstructive surgery were more common in those with pessary fitting failure [10,18,19]. Possible anatomic predictors include a wide introitus (>4 fingerbreadths), short vaginal length (<7 cm), and larger genital-hiatus-to-vaginal-length ratio [14,20]. Among postmenopausal women, use of vaginal estrogen therapy may increase fitting success rates [19].

Pessary types used for POP vary among published reports. Many pessary providers report tailoring their choice of pessary to specific support defects [3], but this practice is based on limited evidence. Conventional wisdom states that support pessaries will be more successful in women with milder degrees of POP, while space-occupying pessaries may be required in women with advanced POP and in those with a wide genital hiatus or a weak perineal body [21]. In support of this assertion, one study found only 36% of women with Stage IV prolapse were able to be fit with a support pessary, compared to 80% of women with Stages II and III prolapse ($p < 0.001$) [14]. However, in the PESSRI clinical trial, all women were treated sequentially with both ring and Gellhorn pessaries, and fitting success rates were high (92%) and did not differ by pessary type [9].

Many published protocols use the ring or ring with support pessary as a first choice pessary in all patients because of its ease of use and reserve other pessary types (most often Gellhorn, donut, or cube pessaries) for women unable to retain or to be comfortably fitted with a ring [10,14,22,23]. In fact, 64%–70% of POP patients can be fit successfully with a size 3, 4, or 5 ring pessary [14,22].

Iowa Pessary Protocol

Given the few published studies on pessary treatment, the literature cannot guide clinicians in choosing pessary management strategies. Therefore, much of clinical pessary practice is based on clinical experience and expert opinion. Here, we present the pessary protocol used at the University of Iowa Urogynecology Clinic.

Prior to fitting a pessary, we treat most women that demonstrate vaginal atrophy for 6 weeks with vaginal estrogen therapy, as this may increase the likelihood of a successful pessary fitting [19]. Similar to other reported protocols [10,14,22], we begin by trying to fit a ring or ring with support pessary as these are easy for providers to fit and for patients to self-manage. If unable to successfully fit a ring pessary, we next try a Gellhorn pessary. Our experience mirrors reports in the literature that >90% of women with POP can be fit with one of these two pessary types [14]. If unable to fit either a ring or Gellhorn pessary, other types (commonly a donut or cube) are tried.

An appropriately fitting pessary should fill the vagina, but allow the clinician’s finger to easily sweep between the pessary and the vaginal wall. After finding a pessary with a good fit, we instruct women to do vigorous activity in the clinic area (such as brisk walking and straining) to ensure that the pessary is retained in the vagina and is comfortable. We also ask that women attempt to void with the pessary in place before leaving the office. In postmenopausal patients without contraindications to hormonal therapy, low-dose vaginal estrogen is often prescribed. In most cases, patients are scheduled for an initial follow-up appointment within 2 weeks. Women fitted with a cube pessary are asked to return sooner (within 1 week) because of an increased risk of vaginal erosions [22], which in our experience may occur rapidly.

At each subsequent pessary appointment, patients are first examined with the pessary in place to ensure correct fit and placement in the vagina. The pessary is then removed and washed. The vagina is examined for signs of excessive discharge, irritation, or erosions. Careful inspection of all vaginal surfaces is essential to identify erosions. We recommend turning the speculum 90° to visualize the anterior and posterior surfaces carefully. After an initial 2-week and 3-month check, we examine women who manage their own pessary yearly.

In contrast to reports from some centers [14,22], we find the majority of women can be instructed to remove and replace their pessaries at home. We recommend women remove the pessary once or twice weekly, leave it out overnight, and then reinsert it in the morning. When removed, the pessary is simply washed with warm water. Women rarely encounter excessive or malodorous vaginal discharge using this approach. If women are unable or unwilling to remove the pessary at home, they are seen at regular intervals in the office for pessary removal and examination. In these patients, we gradually increase the office visit interval after the initial follow-up visit to a maximum interval of 3 months. Women who develop increasing vaginal discharge or erosions over shorter intervals will need more frequent follow-up.

Visiting nurses can be an invaluable resource for women unable to care for the pessary on their own. They are often able to visit the woman at home, remove the pessary in the evening, and return in the morning to replace it. Excessive or foul-smelling discharge, increased discomfort, or vaginal bleeding signals a need to arrange medical follow-up.

PESSARIES AND DEVICES FOR STRESS URINARY INCONTINENCE

Supportive pessaries are also used for treating SUI. Pessaries used to treat incontinence frequently have a knob that is placed under the urethra (Figure 44.3). Some of the most commonly used incontinence pessaries include the incontinence dish (with or without support) and the incontinence ring with knob (with or without support) (inset, Figure 44.3), but other types (e.g., Hodge with knob) are also available. Clinical protocols for fitting and following patients with incontinence pessaries are similar to those used in patients who use pessaries for POP (described earlier). In addition to pessaries, other vaginal and urethral devices may be used to treat SUI, including tampons, diaphragms, disposable vaginal devices, and urethral inserts.

Mechanism of Action

Small prospective studies of incontinence pessaries have demonstrated positive changes in urethral function and support measures using urodynamic tests and dynamic magnetic resonance imaging (MRI) [24–26]. In 12 women who underwent urodynamic studies with and without a Smith Hodge pessary, the pessary increased urethral functional length and static and dynamic urethral closure pressures and reduced urodynamic stress incontinence (USI) [24]. Flow rates did not decrease, and voided and postvoid volumes were unchanged with the pessary, suggesting that urethral obstruction did not occur. Maximal urethral closure pressures also increased in 33 women with SUI after placement of an incontinence dish, and urethral straining angles decreased [25].

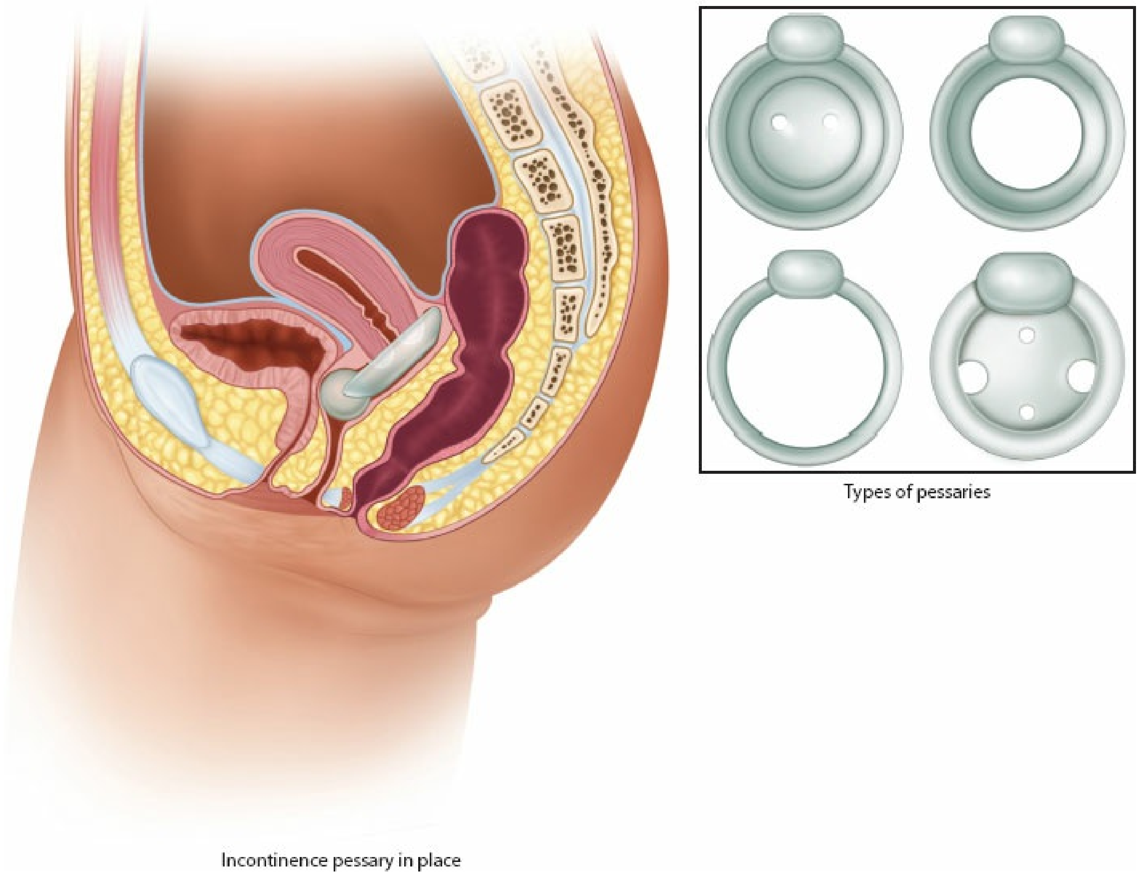

Figure 44.3 Pessary placement for the treatment of stress urinary incontinence and (inset) commonly used incontinence pessaries (clockwise from *top left*: an incontinence dish with support, an incontinence dish without support, an incontinence ring with support and knob, and an incontinence ring without support). (Figure used with permission, from Rogers RG, *N Eng J Med*, 358, 1029, 2008; Copyright © 2008 Massachusetts Medical Society. All rights reserved.)

One study used urodynamics and dynamic MRI in 15 women to assess changes associated with incontinence dish pessaries [26]. All women had USI before pessary placement, but only three had USI after placement of the dish. At urodynamics, maximal urethral closure pressures did not increase (as seen in previous studies), but functional urethral length did increase. Contrary to prior findings [24], maximal flow rates decreased and detrusor pressures increased, suggesting increased urethral resistance, although postvoid volumes were not elevated. MRI findings included greater bladder neck elevation, increased urethral length, decreased urethral funneling with cough, and smaller (more acute) posterior urethrovesical angles following pessary placement [26]. These studies together suggest pessaries may reduce SUI by stabilizing the proximal urethra and urethrovesical junction, thereby facilitating pressure transmission to the proximal urethra. Increasing urethral resistance and elevation of the bladder neck may also help restore continence.

Effectiveness

Few controlled trials have been published evaluating the use of incontinence pessaries. Nygaard et al. [27] performed a small, randomized, crossover, clinic-based study of 18 women who completed three standardized aerobics sessions, wearing either a Hodge with support pessary, a large menstrual tampon, or no device. Both devices significantly decreased urine loss (measured with a pad test) during exercise when compared to the control session. Better outcomes were seen with both devices in women who had milder urine loss [27].

The National Institutes of Health Pelvic Floor Disorders Network conducted a large, multicenter, randomized trial (the Ambulatory Treatments for Leakage Associated with Stress Incontinence [ATLAS] trial) to test mechanical devices for SUI [28]. In total, 450 participants with stress-predominant urinary incontinence were randomized to incontinence pessary, behavioral therapy with pelvic muscle training, or a combined treatment arm. After 3 months of treatment, some outcomes favored behavioral therapy over pessary therapy (bothersome SUI symptoms [33% vs. 49%, $p = 0.006$] and satisfaction [75% vs. 63%, $p = 0.03$]), but other outcomes did not differ between the groups. The combined treatment group did not have better outcomes than single therapy. At 12 months, there were no differences between the treatment groups. Using an intent-to-treat analysis at 12 months follow-up, 32% of the pessary group felt they were better or very much better, 35% reported no bothersome SUI symptoms, and 50% were satisfied with treatment. Of the original 146 women, 67 (46%) continued the use of the pessary at 12 months, and among this group, about 60% reported they were better or very much better, 60% reported no bothersome SUI symptoms, and 90% were satisfied with treatment [28].

Incontinence pessary use in practice appears quite variable. In two retrospective studies (including 100 and 190 patients), about 60% chose to undergo a pessary fitting for stress or mixed urinary incontinence, and 85%–90% were successfully fit [29,30]. Of those successfully fit with a pessary, 55%–60% continued using the pessary (median duration of follow-up 11–13 months). In contrast to these findings, in a small prospective study, only 16% of 38 women fit with an incontinence ring with support pessary chose to continue use out to 1 year [31]. In the few that continued the use, the pessary resulted in fewer leaking episodes and 9 (24%) were subjectively “dry.”

Other Stress Urinary Incontinence Devices

Fewer and typically smaller studies have tested other types of vaginal and urethral devices for treatment of SUI. The vaginal contraceptive diaphragm has been shown to decrease SUI symptoms with success rates of 40% and 75% in two small, short-term studies [32,33]. Placement of a menstrual tampon has similar moderate levels of success (57% continent during use) in treating exercise-induced incontinence [27].

In a small study (32 women), a novel bell-shaped self-positioning incontinence pessary (Uresta, EastMed, Inc., Dartmouth, Nova Scotia, Canada) was found to significantly improve urinary symptoms as well as diary-recorded leaking episodes and urinary pad weights [34]. Similar to the larger retrospective studies of traditional incontinence pessaries described earlier, 50% of women beginning the study chose to continue the use of the pessary for SUI treatment after 12 months.

Other internal vaginal devices have been developed for the treatment of SUI and have demonstrated moderate efficacy in small prospective studies. One reusable device available in Australia and Europe (Contiform International, Blacktown, New South Wales, Australia) is shaped like a large hollow tampon [35]. The device, designed to be fitted and self-managed by patients, can be reused for 30–60 days. In a small study of this device, 54% of women who completed the treatment period were dry.

Single-use, disposable vaginal devices are available for treating SUI in several countries outside the United States. The Contrelle Activgard (Codan, Kobenhavn, Denmark) is a polyurethane foam tampon.

A prospective trial of 94 women tested the Contrelle device for treatment of stress-predominant urinary incontinence, finding 48% of participants were subjectively continent and 36% improved after 5 weeks of treatment [36]. Another disposable vaginal device, consisting of a flexible resin core surrounded by a porous nylon mesh (ConTIPI Ltd., Caesarea, Israel), intends to provide urethral support similar to a tension-free suburethral sling. Used by 60 women with severe SUI, 85% had a ≥70% reduction of urine loss on daily pad weights. In the 50 women who completed the 4-week trial, 92% were subjectively continent [37].

Urethral inserts and external urethral occlusive devices function as mechanical barriers to prevent urinary leakage. These devices require highly motivated and manually dexterous patients as the devices must be removed to urinate and then replaced after each void. Studies suggest they have lower overall success rates than seen for some of the vaginal devices, partly because of higher dropout rates [38].

Urethral inserts are sterile, single-use devices placed into the urethra by the patient and held in place by an inflated balloon at the bladder neck. Such inserts are appropriate for women with no history of recurrent urinary tract infections and no serious contraindications to bacteriuria (e.g., artificial heart valves). Currently, only the FemSoft insert (Rochester Medical, Inc., Stewartville, MN) is commercially available in the United States. Multicenter studies demonstrate high rates of continence with urethral inserts in place (80%–95%) and high rates of satisfaction in women who continue use, but overall results are limited by high withdrawal rates and frequent adverse events [39,40]. While inserts remain an appropriate treatment option for many women with SUI, the need to frequently insert the device into the urethra means many patients are unwilling to try this therapy.

External urethral occlusive devices fit over the external urethral meatus and are held in place by adhesive or suction. These devices have fewer reported side effects than the urethral inserts, but reported continence rates are lower (40%–50%) [41,42]. Patient acceptability of this type of device, similar to urethral inserts, appears to be limited. Several types have been marketed in the United States in the past, but none are currently commercially available.

In summary, published studies suggest most women who are interested can be successfully fit with an incontinence pessary and about half of those women find it an acceptable and satisfactory long-term therapy for SUI. Most pessary and device studies (with the notable exception of the ALTAS trial [28]) remain limited by small sample sizes and lack of comparison groups. A 2011 Cochrane review of vaginal and urethral incontinence devices found there was still insufficient evidence to recommend any specific pessary or device or to show that mechanical devices are better than other forms of treatment for SUI [43].

ADVERSE EVENTS

Adverse events related to pessary use are uncommon and generally minor, although published data in this area are sparse. In a 5-year prospective study, 12% of pessary users experienced minor complications (including pain or discomfort, vaginal excoriation or bleeding, and constipation) [15]. Most complications occurred within the first 6 months of use. Frequent removal and care of a pessary may prevent most pessary problems [21]. Vaginal discharge, odor, and vaginal infections may also occur in pessary users, but these are infrequent reasons for discontinuing the use [22,29]. Vaginal erosions have been reported to occur in 5%–10% of women treating POP with a pessary [13,19,22], and erosions are less common in women using a pessary for SUI. In the ATLAS trial, no vaginal erosions occurred among 168 women followed to 3 months and 94 women followed to 12 months using an incontinence pessary for SUI [28]. Erosions may be more common in women with hypoestrogenic vaginal changes and in those using a cube pessary. In one case series, erosions developed in 5 of 6 women using cube pessaries, but in only 3 of 101 women using ring pessaries [22].

Vaginal erosions due to pessary use typically can be managed by removing the pessary more frequently, suspending use entirely for some period of time (e.g., 2 or more weeks), and/or with vaginal estrogen treatment. If erosions recur, a change to a different size or type of pessary may be necessary. Symptomatic vaginal discharge associated with pessary use may be treated with antibiotics and vaginal estrogen treatment or by suspending pessary use until symptoms resolve. Some clinicians routinely recommend the regular use of vaginal products for vaginal acidification or lubrication to decrease vaginal discharge or odor symptoms in pessary users, but minimal evidence exists to support or refute this practice.

More serious complications related to pessaries can also occur, such as erosion or impaction into surrounding structures or organs, but these appear to be rare and typically are seen in patients with a "neglected" pessary [44]. A 2008 literature review identified 39 cases of major complications, including 8 vesicovaginal fistulas, 5 other urological complications, 4 rectovaginal fistulas, 3 other bowel complications, and 19 impacted pessaries [44]. Sixty percent of these complications required operative management. Only 2 of the 39 occurred in women who received appropriate clinical follow-up, again supporting the importance of careful pessary management by providers and patients.

Adverse events associated with the use of disposable vaginal devices for SUI are typically mild and most often include vaginal spotting, irritation, and discomfort [36,37], and such local side effects may decrease over time as patients become more skilled at device placement. In a 4-week trial of a disposable vaginal device, 52% of patients reported adverse events (most often discomfort and spotting) in week 1 compared to 5% in week 4 of device use [37]. Vaginal infections (e.g., candidiasis), asymptomatic bacteriuria, and cystitis are infrequently reported [37].

Urethral devices, especially urethral inserts, have higher rates of adverse events than the vaginal devices. The most commonly reported complications include urinary tract infections, hematuria, and urethral and/or bladder irritation and discomfort [39,40]. These complications appear to occur most often in the first month of device use. In a long-term study of a urethral insert, symptomatic cystitis occurred in 10.5% of participants during the first month of use, but in only 2%–3% in subsequent months [40].

CONCLUSION

Pessaries and other devices are an important nonsurgical treatment option for both POP and SUI. Current research supports that most women with an interest in pessary treatment for POP or SUI can be successfully fit with a pessary, and about 50% of women who are successfully fit will continue pessary use for a year or longer. Urethral inserts and occlusive devices are also effective, but their use is limited because of more frequent adverse effects and the intensive patient effort required for use. Careful pessary and device management and follow-up is essential to minimize side effects and avoid complications. Additional clinical trials comparing pessary or device treatment with other nonsurgical and surgical treatments and long-term studies of both effectiveness and adverse events associated with pessaries and devices are needed.

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45 Catheters, Pads, and Pants

Lynette E. Franklin

INTRODUCTION

History

The history of catheterization to empty the bladder dates back to approximately 1000 BC. Records from India attest to the use of tubular objects made from iron, gold, silver, and wood and lubricated with liquid butter to drain the bladder and manage urethral strictures. Chinese records from the 100 BC time period record use of lacquered onion leaves to provide hollow instruments to empty the bladder [1]. In China in AD 30, urinary retention was managed with lead and bronze pipes. These devices were smoother, as compared to other devices, and had a more manageable size that functioned both for men and women's needs. Catheters have also been found in Pompeii, preserved in the lava from the eruption of Vesuvius [2]. The early devices were rigid and did not provide the user with a continuous drainage system. Urinary catheterization was revolutionized with the advent of rubber technology. In the mid-nineteenth century, Auguste Nelaton produced catheters that were portable, flexible, and reusable. Eventually, this flexibility allowed for indwelling catheters that could be secured with tape, an external device, or sutures. Hence, the advent of the modern indwelling urinary catheter was realized.

Urosepsis was a common almost invariably fatal problem in the early years of catheterization. The introduction of antiseptics, beginning with Lister, followed by the use of antibiotic therapies decreased mortality associated with this therapy and provided better outcomes overall. In 1966, the Stoke Mandeville National Spinal Injuries Center introduced sterile technique for catheterization, which provided more options for people requiring catheterizations [1]. Shortly after the sterile technique introduction, Lapides pioneered the clean intermittent self-catheterization (CISC) technique after one of his patients reused a catheter that had been dropped, without resterilization, without untoward consequences to the patient's urinary tract.

Catheters for bladder care continue to change and evolve while providing patients with more options for comfort, ease, and safe usage.

CATHETERS

Goals of Catheterization

Catheterization of the bladder may be indicated for either the long or short term. The goals may be quite different in different situations. When considering the selection, one must consider the overall goal of therapy. These goals may include one or more of the following [3]:

- *Temporary emptying of the bladder*: This includes the maintenance of bladder drainage during periods of acute or sudden urinary retention such as that during or following surgical procedures.
- *Long-term emptying of the bladder*: Chronic bladder dysfunction and urinary retention such as that due to bladder underactivity or bladder outlet obstruction not amenable to treatment.
- *Intravesical instillation therapy and treatment*: Instillation of medications or solutions into the bladder to treat underlying diseases such as bladder cancer, interstitial cystitis, or infection.
- *Incontinence management*: To divert urine into a containment device to reduce skin exposure to moisture for goals of wound healing, patient/caregiver respite, and palliative care.
- *Studies*: Radiographic and urodynamic studies may require intubation of the bladder to instill filling media such as radiographic contrast agents or measure bladder pressures.
- *Monitoring*: Measurement of urine output in the acutely ill or postoperative patient.
- *Testing*: Catheterization can be utilized to obtain accurate postvoid residual urine measurement or acquire an uncontaminated urine specimen for laboratory analysis.

Urethral Catheterization

Definition

Urethral catheterization is the passage of a tube through the urethral os into the bladder to drain the bladder of urine. This process may be done on an intermittent basis or as a permanent indwelling arrangement. Intermittent catheterization may be chronic or a onetime event for an acute patient care need, for example, urinary retention or drug administration. Indwelling catheterization is the passage and anchoring of a catheter for an extended period of time. The catheter is not immediately removed but is stabilized to the skin through an anchoring device such as a leg strap [1].

Designs and Materials

Catheters have evolved over the years as new materials are developed and patient needs and demands dictate changes in the market. Choice of materials and design allows the best catheter to be employed. There is not one catheter that does all, but the variety currently available permits patients and care providers the opportunity to choose the best catheter for the specific need of the patient. However, depending on the location of practice and the macroeconomic environment, third-party payers or other external forces may at times dictate the catheter used (Table 45.1).

Table 45.1 Catheter Types

Material	Definition	Pros	Cons	Best use
Silicone elastomer–coated latex	A coating of chemically bonded silicone adhered to a latex catheter.	Reduces contact of latex to the urethra in the latex-sensitive patient Reduces incidence of insertion trauma, urethritis, and encrustation Less expensive than 100% latex	More flexible than 100% silicone but less flexible than 100% latex. Elastic coating may dissolve over time exposing patient to latex. Balloons may lose fluid filling over time as compared to 100% latex.	Short-term usage Patients with latex sensitivity
Red rubber latex	A latex catheter that is soft allowing for flexibility. Latex is a natural product that is a yellowish brown in color.	Flexible allowing for easy insertion especially for short-term usage Low cost Comfort	Latex based, contraindicated in patients with latex allergies. Becomes brittle after repeated usage. Swells with absorption of fluid thereby decreasing diameter of lumen and increasing outside diameter. Some toxicity with mucosal tissue resulting in stricture and inflammation. Prone to encrustations.	Short-term usage as in CICS For patients without allergies to latex
PVC	A firm catheter made from a plastic polymer that has had plasticizer added to soften and increase flexibility.	Becomes soft and pliable at body temperature Has wide internal diameter	Limited utility as indwelling catheters, since encrustation is common with greater than 1-week usage. Has been debated as to safety with exposure to liquid over long periods of time, i.e., may break down. Uncomfortable due to stiffness. Balloon may be made of latex.	CISC Short-term use
Hydrophilic coated catheters	A plastic polymer catheter with a coating of polyvinylpyrrolidone and salt. When exposed to water, this outer coating becomes very lubricated and slippery.	Easier insertion and withdrawal resulting in a minimization of urethral trauma Safer for allergy-prone patients as no latex is present Reduction in the amount of CAUTIs [4]	Only one-time use. May be difficult for some patients to manipulate secondary to the very slick nature of the catheter. Some packaging includes water to activate, may be difficult to break seal, or may become broken early, causing problems for patient with cleanup. Expensive.	Long-term usage for CISC
Silicone	An inert product that is clear or white in color.	Inexpensive Thin-walled tube with larger lumen Catheters more compatible with lining of the urethra Latex-free	Rigid and uncomfortable—increasing risk for bypassing and bladder spasms [5]. Balloons tend to form cuffs when deflated making removal difficult. Balloon has tendency to lose fluid filling over time requiring frequent evaluation for indwelling catheter. More lumen stability with irrigation and aspiration.	Long-term usage, patients with allergies to other products
Antimicrobial	Silver ions, bactericidal and nontoxic to humans, are used to coat the catheter on the outside, inner lumen, or both. Silver phosphate. Nitrofurazone impregnated.	Some evidence that CAUTI are reduced from 3.3% to 35.5% per year Potential reduction in the rate of asymptomatic bacteriuria with short-term use Reduces bacterial load for up to 14 days	More research needed to know full extent of CAUTI reduction. Expensive. Limited studies and benefit beyond 14 days. Limited clinical studies. May contain latex.	CISC, indwelling, or SPT

Source: Wound, Ostomy, and Continence Nurses Society, *Indwelling Urinary Catheters: Best Practice for Clinicians*, New Jersey, 2009.

Size and Length

Catheters are sized in the standardized measurement developed by J.F.B. Charriere. This so-called

“French” scale is based on the metric system where the external circumference is measured in millimeters. This measurement referred to as either French gauge (Fg or Fr) or Charriere and is approximately equal to three times the external diameter. Thus, a 30 Fr catheter is 10 mm in diameter. In women, the size of catheter used most often is between 14 and 16 Fr. However, at times a larger diameter may be indicated. For an indwelling catheter, a retention balloon is located just proximal to the tip of the catheter; the balloon should be inflated properly to the correct volume. If under inflated, there can be distortion of the catheter tip, and over inflation can risk balloon rupture. Correct selection of catheter size is important to decrease pain and discomfort with insertion of the catheter. Generally, the smallest, softest catheter that is sufficient to fulfill the clinical indication for catheterization is used. At times, selection of a larger catheter may be necessary for a variety of indications including hematuria drainage.

Catheter lengths, for intermittent catheterization, are measured in the imperial or metric system. Long or male length is 42 cm or 16 in. This length is not, however, gender specific and in fact a longer catheter may be beneficial for obese women with large perineal skinfolds. Female or short length is 6 in. or 26 cm. Shorter pediatric length catheters are also available. The proper selection of catheter length should meet the needs of the patient and/or caregivers taking into consideration the patient’s habitus, preference, and dexterity. Generally, indwelling catheters are a standard long length of 42 cm.

Various catheter tips are available. Catheter tips differ in order to facilitate insertion and drainage of the bladder for a variety of clinical scenarios (see Figure 45.1).

Indwelling vs. Clean Intermittent Catheterization vs. Suprapubic

Patient Selection

Although health professionals may be very comfortable with the practice of long-term catheterization, the lay person may experience high degrees of anxiety when approached with this modality. Varying responses including fear, anxiety, and revulsion can be exhibited in the patient who is attempting to assimilate not only the diagnosis of the underlying urinary tract problem but also the prospect of caring for oneself with a foreign object.

General criteria to evaluate whether a woman should be managed with a chronic versus intermittent catheter should be reviewed with the patient and her caregivers if applicable. Evaluation should include but not be limited to the following:

- *Motivation*: This is the ability of the patient to review goals and incorporate a desired outcome into her treatment plan. Acceptable levels of self-involvement in continence care will differ between patients and an assessment of such will help develop the best treatment plan.
- *Dexterity*: This is the combination of the ability of the patient to properly position herself for catheterization and the ability to self-access her perineal area and the precision and ability of her upper arm extremities movement to separate and locate the urethral os either visually or by tactile sense. The degrees of dexterity will dictate independence with respect to urinary tract management. If a caregiver is willing to provide self-catheterization services, then he or she will need to have a similar skill set.
- *Bladder capacity*: The low-pressure storage capacity of the bladder should be adequate such that if intermittent catheterization is recommended, there can be a reasonable time interval between catheterizations so that urinary storage pressures are maintained in a safe range, urinary incontinence is minimized, and upper urinary tract integrity is maintained.
- *Adequate mental capacity*: The woman should have the cognitive capacity to independently care for herself, follow directions for self-care or alternatively, allow a caregiver to complete care with minimal stress to the patient and/or caregiver.
- *Health-care beliefs*: The choice of management is ultimately a decision made to effectively control the woman’s condition. Her understanding of the condition coupled with social, religious, personal, and economic beliefs and responsibilities should be considered as these may or may not lead to successful implementation of a given strategy.

Despite adequate planning and informed consent, problems with a catheterization method can arise after implementation has been enacted. These problems need to be identified and addressed in a time-efficient manner to decrease potential adverse outcomes. Such issues include [1] the following:

- *Psychological issues*: Implementation may require the assistance of a trained counselor or mental health expert to overcome fear, depression, and/or anger about the current situation.
- *Visual problems*: Although initially visualization of the urethral os may be assisted with the use of a mirror, the continual use of a mirror may be cumbersome and awkward especially when catheterizing away from home. Teaching patients to use manual location of the urethral opening in relation to the vagina can be beneficial to prevent this problem.
- *Dexterity changes*: Due to aging, illness, or other factors, anatomical or functional factors can change throughout the course of a woman's illness, altering her ability to continue in the mode of catheterization initially chosen. Under these circumstances, physical and occupational health services can help provide devices that may maintain or reestablish dexterity in otherwise difficult situations. These professionals are also experts with upper and lower limb aids to assist with adduction or abduction that may provide access to the urethral os. Also, these professionals may provide additional therapy that may be initiated to decrease other comorbidities that impede dexterity such as range of motion exercises for those individuals with arthritis.

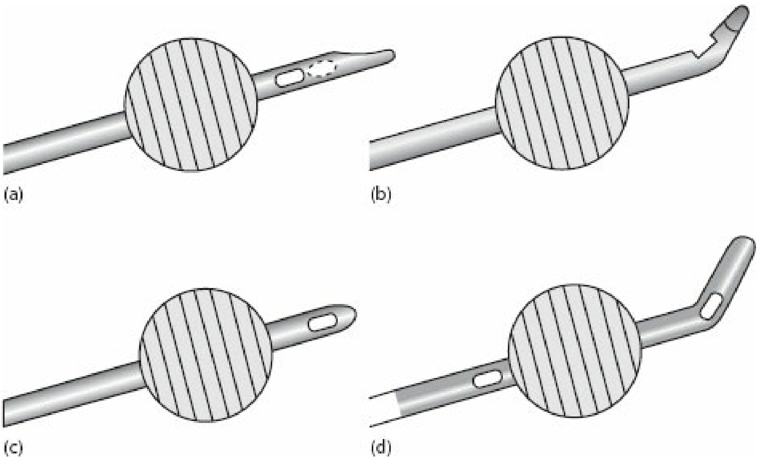

Figure 45.1 Catheter tips: (a) whistle, (b) Tiemann, (c) round, and (d) Roberts.

Technique of Clean Intermittent Self-Catheterization

The first self-catheterization will set the tone for the woman to become confident and self-sufficient in self-care. The environment should be calm, prepared, and unrushed to assist her in achieving maximum benefit from the lesson. As an adult learner, it is best that she demonstrate the catheterization as opposed to watching the health-care provider do it [6].

Many manufacturers provide written and visual material to review with patients. It is prudent to review with the patient the anatomy and physiology of the urinary tract system prior to introduction of the catheter to prevent any misconceptions of passage and potentially decrease anxiety. Written materials in the patient's native language should be given if possible to further increase knowledge acquisition.

Once the supplies are gathered, positioning the patient in a semireclining position with good lighting will aid her in seeing the urethral orifice with a mirror. Prior to attempting the initial catheterization, it is important to review her preexisting knowledge and goals and consider any limitations. These considerations will help to tailor the lesson to provide successful outcomes.

Using a touchless system with an attached drainage bag may be beneficial in the early stages of learning. This technique decreases the concerns regarding spillage of urine out of the catheter and generally decreases anxiety and embarrassment. As the woman gains mastery of CISC, her positioning may change and her ability to direct the fluid becomes easier without added appliances. Table 45.2 provides general instructions for CISC (see Figure 45.2).

Table 45.2 General Guidelines for Clean Intermittent Self-Catheterization

1. Gather supplies.
2. Wash the hands and the perineum with soap and water.

3. Separate the labia and locate the urethral os with the nondominant hand.
4. Pass the lubricated catheter into the urethra until urine passage is achieved.
5. Once the bladder is drained, slowly advance the catheter approximately 5 cm further to fully drain the bladder, and then slowly remove the catheter.

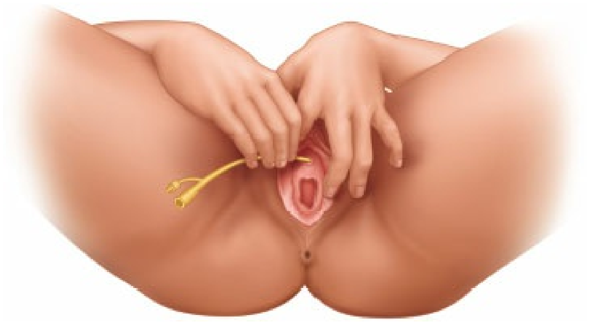

Figure 45.2 Clean intermittent self-catheterization.

Indwelling Catheters

A catheter may be placed that is retained with a fluid balloon. The catheter is placed through the urethral os into the bladder using sterile technique. The balloon is inflated with sterile water according to the manufacture's guidelines. Generally, the balloon holds between 5 and 30 cc of fluid. Saline and contrast should not be used to inflate the balloon. These fluids may crystallize in the balloon port, clogging it, and prevent balloon deflation and catheter removal. The bladder can be maintained in a decompressed state with the use of a drainage bag or may be intermittently drained with a plug. The catheter should be changed every 4–6 weeks.

Limiting unnecessary indwelling catheter usage has been identified with varying degrees of evidence from the Infectious Disease Society of America [7]. Placing and discontinuation of catheters should follow proper indications while considering the needs of the patient. The Centers for Disease Control and Prevention has outlined examples of appropriate indications for catheters including acute urinary retention or bladder outlet obstruction, accurate measurement of urine output in critically ill patients, and specific needs such as long-term diuretics, healing of open sacral and perineal wounds in incontinent patients and immobilized patients, and end-of-life care improvement [8].

Suprapubic Catheters

A suprapubic tube (SPT) is an indwelling catheter that is surgically percutaneously placed through the abdominal wall directly into the bladder. It is secured in this location using the same balloon mechanism as a urethral catheter. This type of drainage system avoids urethral catheterization. Approximately 1 month after initial placement, a well-healed epithelized tract is formed maintaining a patent opening for simplified office-based catheter changes. These tubes are indicated for patients who are unwilling or unable to manage urethral indwelling catheters or clean intermittent catheterization, for those individuals who have urethral disease precluding placement of a urethral catheter (e.g., severe urethral stricture disease), and for those who are at risk for complications such as urethral erosion and fistula formation. SPTs may be temporary, for example, in patients who have recently had pelvic surgery and maximal (when also combined with a urethral catheter) bladder decompression must be maintained temporarily postoperatively. This therapy is not optimal for the patient who is willing and able to perform CISC. As described later, indwelling tubes (urethral and suprapubic) are associated with complications that are much less likely than with CISC.

SPTs are usually placed electively in the operating room in sensate patients. Under anesthesia, a catheter is passed directly into the bladder via a stab incision through the abdomen 2–4 cm cephalad to the symphysis pubis. The catheter is exchanged in the office or in the patient's residence every 4–6 weeks. A well-epithelized tract develops through the abdomen wall into the bladder allowing for simple catheter changes. When counseling a patient about the possibility of this catheterization type, acknowledgment and discussion about altered body image are essential. Many patients will find it difficult to accept a permanent foreign body protruding from their abdomen, identifying concerns of “normal function loss,” changes in sexual practices, and leakage. Although such concerns are warranted, quality of life indicators may actually improve when patients have been converted from urethral to a suprapubic catheters especially in patients who are dependent on wheelchairs or who are sexually active [9] (see Figure 45.3).

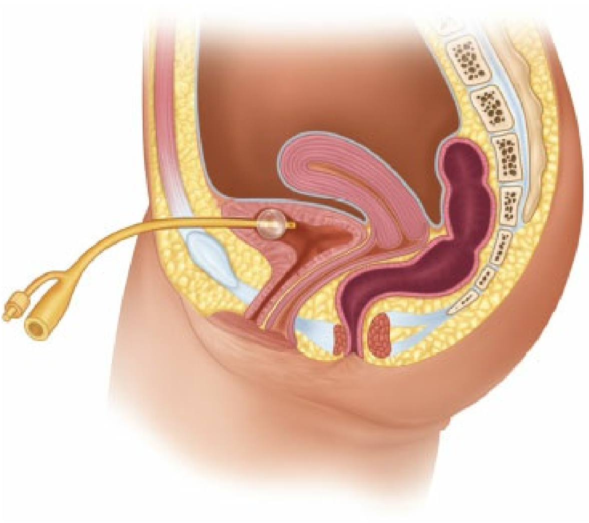

Figure 45.3 Position of suprapubic catheter.

Catheter-Associated Problems

Infection/Hematuria/Trauma

The most prevalent type of hospital-acquired infection is urinary tract infections (UTIs), with 80% of infections being associated with indwelling catheters (catheter-associated UTIs [CAUTIs]) [4]. Women are more susceptible to CAUTI as compared to men [10]. Infection is related to several potential mechanisms of entry of bacteria: insertion technique, cross-contamination with staff care, or retrograde flow from drainage bags.

UTI symptoms in patients with catheters are often atypical. Upon insertion of the catheter, bacterial biofilms will begin to develop within 24 hours. These bacterial colonies are found on the device surface, and they will not necessarily result in an infection. Patients with catheters often have bacteriuria, which is the presence of bacteria in normally sterile urine. Bacteria will be present in the bladder within 2–10 days of insertion, but not necessarily result in an infection [10]. After 30 days of an indwelling catheter, virtually all patients have bacteriuria due to colonization. This colonization of bacteria may not be eliminated with antibiotic use, and in the vast majority of cases, it is not necessary to do so. Bacteriuria or colonization is not equivalent to infection, the latter of which mandates treatment. It is important to differentiate colonization from infection. An infection is an immunological activation in response to a foreign body such as a microorganism. Colonization is a symbiotic growth of bacteria in the body that does not result in activation of the body’s immune system.

Newman [10] has outlined signs and symptoms of UTI in nursing home residents with catheters to include two of the following:

- Fever (>38°C) or chills
- New flank pain or suprapubic pain or tenderness
- Change in character of urine (smell, blood, etc.) *or* lab report of new hematuria or pyuria
- Worsening mental or functional status
- Local findings of obstruction, leakage, mucosal trauma, or hematuria

If a UTI is suspected with an indwelling catheter or in a patient who self-catheterizes, the specimen needs to be obtained from a new catheter insertion [11]. The catheter is changed and the urine is obtained from the bladder through the new tube. This prevents a sample of the catheter biofilm being collected and is more representative of the bladder flora.

Multiple other complications may result from catheter usage [12]. Long-term catheter usage may result in the formation of bladder stones. Hematuria may result from the trauma of insertion, the trauma of removal, or the trauma with sudden traction on the tube itself. Trauma from insertion or removal without deflating the balloon can cause urethra injury, tearing, or subsequent stricture. Removal of the catheter inadvertently is common among women with dementia or those prone to falls, those who strain for bowel movements, or when excessive tension is suddenly placed on the catheter [10]. Securing the catheter to the leg can aid in decreasing the movement of the catheter and friction on the perineal skin and potentially reducing bladder spasms. In addition, secure placement of the bag probably reduces intravesical trauma thus reduces gross hematuria. Devices to secure catheters are available in a variety of forms including self-adhesives, Velcro closures, latex leg straps, and abdominal belts. There has not been consensus established as to the most beneficial location for placement of the securement device, but rather to place it to provide maximum functioning for the women wearing the catheter [10]. Fistula, traumatic hypospadias, and bladder cancer are also complications associated with catheter usage.

Complications specific to suprapubic catheterization are similar to those complications listed for other types of catheters [6]. In addition, the placement of the SPT may result in bowel injury, vascular injury, and soft tissue infection. Published complications rates [13] resulting from urinary catheterization include the following:

- *Bladder stones*: approximately 1/3 in over 10 years
- *30-day complication rate*: 19%
- *Mortality rate*: 1%
- *Long-term complications including recurrent UTIs*: 1%
- *Catheter blockage*: 25%

The Joanna Briggs Institute [14] developed a best practice paper on short-term catheter removal based on a review on current research. These authors recommend for practice the following three strategies for removal of short-term indwelling urethral catheters, defined as insertion for a period from 1 to 14 days:

1. Timing of removal when appropriate should be at midnight.
2. Duration of catheterization should be as brief as possible and medically appropriate following pelvic surgery. Early catheter removal results in a reduced risk for UTI and a shorter hospital stay, but also carries with it a greater risk of subsequent short-term voiding problems.
3. Placing and removing a clamp from the tube to “retrain the bladder,” a technique known as clamping, prior to the removal of the catheter has limited degree of effectiveness in facilitating a successful voiding trial.

Leakage

Pericatheter leakage (also termed “bypassing”) should always be investigated [15]. Causes for pericatheter leakage include UTIs, stones, malignancy, bladder overactivity (“spasms”), poor drainage due to clogging, urethral erosion, and a number of other causes. A careful physical examination and history along with gentle irrigation will be able to differentiate between several of these entities. Careful assessment of the patient and the system should be conducted to evaluate for easily reversible factors such as tubing kinks and poor catheter drainage. The addition of an antimuscarinic agent may treat leakage associated with bladder spasms. Before prescribing these medications, other causes of pericatheter leakage should be considered and investigated when appropriate.

Drainage Bags

Before the advent of drainage bags, indwelling urinary catheters were drained into nonsterile open systems. Ascending bacterial infections occurred very commonly in this setting. Subsequently, closed drainage systems with nonreturn valves were developed that reduced the incidence of ascending bacteria from the bag to the person. Drainage bags range in collection volumes of 250–1000 mL. These bags can be fastened to the bed, the leg, or the abdomen. Volume selection may be changed based on the need. For example, larger systems are convenient for overnight use, and smaller leg bags may be used discreetly during the day. These can be washed and reused for several months at a time. Recommendations for bag cleaning are listed in Table 45.3. Minimal disruption of the closed system should be maintained to reduce infection risk. Strict adherence to a hand washing prior to manipulation should also be maintained.

Table 45.3 Recommendations for Bag Cleaning

1. Rinse bag with lukewarm water.
2. Vigorously agitate clean water in the collection system twice.
3. Pour a diluted solution of bleach (1:10 parts water) on drainage port, sleeve, cap, and connector. Also pour in bag and agitate for 30 seconds, drain, and allow to air-dry. The bag should always be rinsed with soap and water after using any disinfectant.

Source: Newman DK, *J Wound Ostomy Continence Nurs*, 34(6), 655, 2007.

Manufacturers have developed various systems for the ambulatory and bed-restricted patient. These bags can be maintained in a dependent position using straps, buttons, Velcro, and hooks. The goal is to keep the bag in a dependent position so that the urine will flow freely from the patient into the bag and not in the opposite direction (see Figure 45.4).

Cleaning drainage bags should be cleaned prior to reuse, for example, after changing from leg to night drainage. Methods [11] include the following steps:

1. Wash hands before and after bag cleansing with soap and water.
2. Disconnect bag from the catheter.
3. Run clear water through the system or use a soft squirt bottle to irrigate with water.
4. Irrigate with cleansing system with either a bleach solution *or* a vinegar solution.
5. *Bleach solution*: 1 part bleach to 10 parts water
6. *Vinegar solution*: 1 part vinegar to 3 parts water
7. Place solution in bag and tubing, irrigate for 30 seconds, and then drain.
8. Air-dry.

Be aware that bleach solution may discolor surfaces that it comes in contact with.

Drainage Valves

To facilitate emptying, the catheter and/or the bag, various spigots, and valves have been developed. These devices come in a variety of sizes that attach directly to the bag or may be inserted into the catheter. These systems provide a noncontinuous drainage system, which allows increased freedom for the patient to perform activities of daily living without a bag. When deciding if a valve is an appropriate adaptation for a patient, one must also consider the selection process as listed earlier: motivation, dexterity, level of mental capacity, and bladder functioning/capacity [13] (see Figure 45.5).

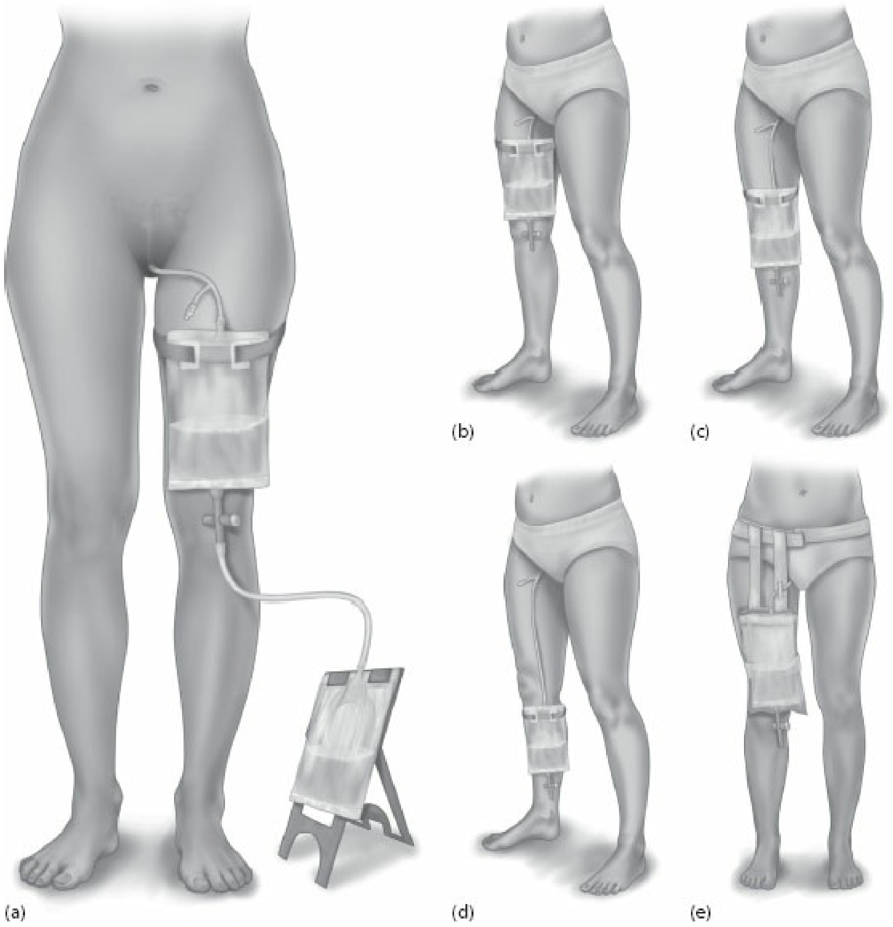

Figure 45.4 Leg bags and lengths. (a) Closed drainage system with a night bag attached to the leg bag; note the short female catheter. (b–e) Different lengths of leg bags, ranging from 350 to 750 mL in capacity, and suspensory systems: (b) short-tube bag, (c) medium-tube bag, (d) long-tube bag, and (e) alternative method of suspension.

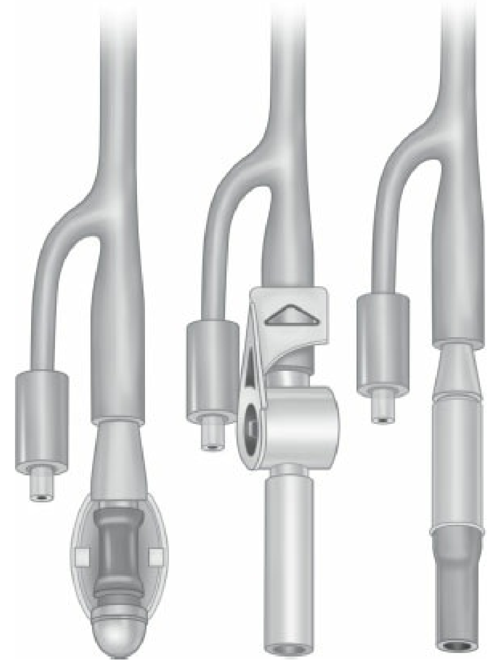

Figure 45.5 Examples of catheter valves: (a) EMS Medical, (b) Bard Flip-Flo, and (c) Sims Portex Uro-Flo.

PAD AND PANTS

Pads

Urinary incontinence can be managed by absorbent products that are known either as “body-worn” or for the protection of furniture. Body-worn systems are defined as those that are placed in undergarments. The goal of these products is to contain the urine. Other functions may include odor protection, skin protection, and avoidance of stained outer garments. Currently, pads are available in reusable/washable or single-use/disposable products. Geographic location will partially dictate the availability of different products. In some countries, pads are considered medical devices and are allocated by the government health-care system, whereas, in other countries, these products are available over the counter and consumption is consumer driven. There are very few studies, which directly compare these products with respect to efficacy, safety, or cost, and international standards do not exist.

Product design is based on numerous factors. These factors include gender and the amount of fluid to be absorbed. Female products are designed to absorb urine that drains into the middle of the undergarment. The capacity of the product’s absorption is dependent on fiber arrangement and type. Urinary incontinence pads are designed to absorb and/or contain urine and are not interchangeable with products designed to absorb menstrual waste. This is an important differentiation that should be emphasized to the patient.

Urine collection pads are designed to collect the urine from the surface of the pad and wick it away to an inner core away from the perineal skin. Currently, there is no standardization as to capacity or quality of product used in incontinence pads. Newman et al. [10] recommends some standardization for evaluation to include the following:

1. *Rewet value*: This value reflects the dryness of a product after subsequent wetting of the product when the measurement is taken at the skin level. Lower rewet values represent drier product performance.
2. *Rate of acquisition*: This is the speed at which a product is able to absorb a set volume of liquid.
3. *Total absorbent capacity*: This measurement would help delineate the differences in absorption between products that are designed for light, medium, and heavy absorbency.

   In 2012, the National Association for Continence released national (United States) standards for quality performance of disposable adult absorbent products for incontinence in the elderly, frail, and/or disabled populations [16]. These recommendations add to the three earlier for a total of eight, including the following:
4. *Sizing options*: A selection of youth and adult sizes to optimize fit and performance and reduce waste.
5. *Safety*: None of the components of the product should be deemed “unsafe” by the Federal Regulatory Agency.
6. *Presence of closure systems*: Products should incorporate a “mechanical” closure system to allow for multiple unfastening and refastening.
7. *Breathable zones*: An acceptable minimum air flow in side “wings” to release trapped body heat and gaseous body perspiration in these areas.
8. *Ability to contain fecal matter/loose stools*: Delivery of gentle, snug fit using leg and waistband elastics.

Pads are fairly uniform in their construction. Typically, there is

1. A securement layer that is an adhesive strip or strap
2. A waterproof layer to protect garments
3. A fluff layer to absorb the fluid
4. A top mesh layer to wick away the fluid from the skin

Technological advances have improved the saturation point of disposables with the addition of superabsorbent polymer (SAP). This polymer is added to the middle layer of the pad’s fluff layer, in a powder form. This hydrocolloid material changes from a powder into a gel that wicks away urine from the pad’s surface. Urine leakage outside the pad is decreased as the SAP can absorb 70 times its original weight, while maintaining a relatively small particle size of 1–2 mm.

Reusable products are made from fibers such as rayon or polyester. These options are attractive to users in that they can be used repeatedly and may provide more stability for the user. As compared to pads secured with an adhesive, these products are less likely to shift allowing for a more secure feeling of placement. The absorbent pad is fixed into the undergarment and does not lend itself to shifting from the perineal area as a disposable or removable product potentially could. They also provide the user with a more flexible quiet system without the inclusion of plastic.

Urinary leakage can be quantified per episode [10] as

- Light 0–50 mL
- Moderate 50–200 mL
- Severe greater than 300 mL

The importance of quantifying urinary leakage is that it allows the consumer to choose the smallest product for maximum benefit. It also helps health-care providers know the extent of urinary leakage per episode (Table 45.4). A Cochrane review showed that there is no strong evidence for superiority among light urinary incontinence products, disposables, or washables with respect to better skin health. There is no dominant design for cost-effectiveness although disposable pads are the most expensive. In the same review, moderate to heavy product comparison showed no single best design. Women preferred pull-ups. Washables are the least expensive [17,18].

Diaper design has been improved to include features that are specific for the female patient with incontinence needs [19]. The absorbent polymer and pulp in the front region, with a flexed convex surface in the perineal region, prevents flow toward the buttock. This design has a curled fiber–citric acid cross-linked process that helps maintain acidic skin pH, as well as air permeable side panels to minimize occlusion and results in improved incontinence-associated dermatitis (IAD) lesions [6].

Table 45.4 Pads for Undergarments

Pad type	Description	Pros	Cons
Perineal pads	Discreet options for women with light to moderate incontinence. Available in disposable and reusable products, these pads adhere to the underwear of the patient to provide body-formed protection. Generally, rectangular shaped with some differences to accommodate larger volumes, i.e., gathered edges, width changes to accommodate larger volumes.	Self-adhesive strips provide use of preexisting undergarments. Convenient: easily carried in purses to provide ease of change when out of the home environment. Pads stay in place although can be reused in the event a leakage accident does not occur. May contain built in deodorant. “Booster systems”can be used with other products to increase absorptive capacity.	Expensive May be difficult for manually dexterity-challenged patient to position
Undergarments	Form-fitting pads that are attached with elasticized, Velcro, or button fasteners.	Provides protection moderate to severe protection from urine leakage.	Often bulky and cumbersome May not be as discreet when applied under

		Available in various shapes that accommodates application in supine, sitting, and standing positioning. Soft external backing provides comfort and air exchange.	form-fitting clothing Requires large area for storage of multiple garments, more inconvenient to transport when travelling
Protective underwear	Disposable product that is pulled on, as with the cloth counterpart, but can be ripped off at the side to provide ease of removal.	Moderate to severe leakage protection. Option to provide security especially with women who may attempt to remove device when disoriented or demented. Available in systems that provide active patients to continue activities such as swimming.	Bulky, difficult to change with patient who has limited mobility or who is bed bound
Adult brief	Disposable product similar to the child's diaper provides protection with self-adhesive tabs that can be refastened and repositioned.	Moderate to severe urinary incontinence containment. Positioning ease especially with the patient who is bed bound.	Expensive Bulky Can become disheveled with frequent position changes and transfers
Pad and pant systems	Combination products using mesh or knit pants with disposable inserts for moderate incontinence.	Allows for self-toileting between changes without removal of all clothing, option for ambulatory patient. Adaptations for lingerie and nightgown options provide for apparel during intimate moments.	Inconvenience while travelling, as inserts can be bulky and nondiscreet

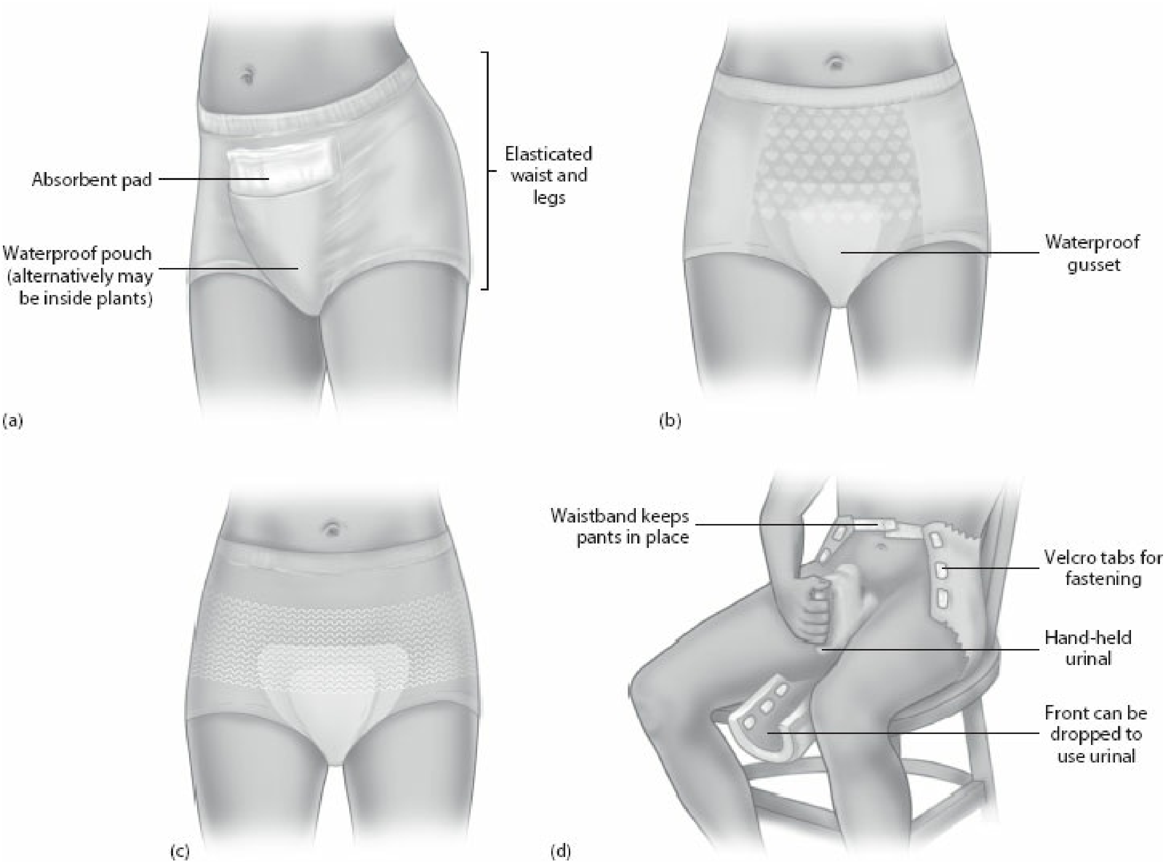
Absorbent pad
Waterproof pouch (alternatively may be inside plants)
Elasticated waist and legs
(a)
Waterproof gusset
(b)
(c)
Waistband keeps pants in place
Velcro tabs for fastening
Hand-held urinal
Front can be dropped to use urinal
(d)

Figure 45.6 Pouch pads and pants: (a) pouch pants, (b) stretch pants with waterproof gusset, (c) stretch pants for use with plastic-backed pad, and (d) drop-front pants.

Generally, when choosing a pad product, the woman and/or caregiver should evaluate the goals of treatment. Reviewing leakage quantity, type (urine, feces, menses), and timing may dictate changes in the padding system throughout the day and night. Typically, discreet protection coupled with ease of use while maintaining a reasonable cost will provide a product that is beneficial to meet identified goals (see Figure 45.6).

Pads for Beds and Chairs

Designed similarly to undergarment pads, these pads can be placed on furniture to provide protection. Many of these products have a nonslip backing to maintain positioning under the patient. Disposable products have lost favor to the reusable products (see Figure 45.7).

Economical and Environmental Issues

In recent years, global knowledge about the so-called “green” choices has influenced consumers on their choice of products. The reusable pad is often thought of as a more environmentally friendly alternative but considerations must be given to the by-product wastes of reuse including energy expenditures and cleaning product runoff. The downsides of disposable products include biodegradability, landfill versus incineration disposal, waste by-products, and manufacturing expenditures. Economically, both types of products have their advantages and disadvantages. The initial cost for the reusable product is usually higher, and then one must consider the cost of maintaining this product with washing, drying, and convenience for the patient and the caregiver. Ultimately, the decision for the product used will be dependent on resources available to the patient.

Skin Care

The skin is the largest organ in the human body and it has multiple functions to perform. It does these functions best when it is healthy and intact. Prevention of skin breakdown, especially in the patient with incontinence, will minimize future problems such as pain, infection, and nonhealing wounds. Inflammation of the skin from chronic exposure to urine and feces is defined as incontinence associated dermatitis (IAD). IAD presents as reddened skin with or without evidence of blisters and skin erosions. Areas involved include the skin in the perianal area, buttocks, thighs, lower abdomen, scrotum (men), labia and vulva (women), and anus. Multifactorial in origin, the study of IAD is an emerging science. Epidemiology of IAD in long-term care centers may be as high as 46% for urinary incontinence, 50% for community-dwelling adults, and 42% of hospitalized adult patients [13].

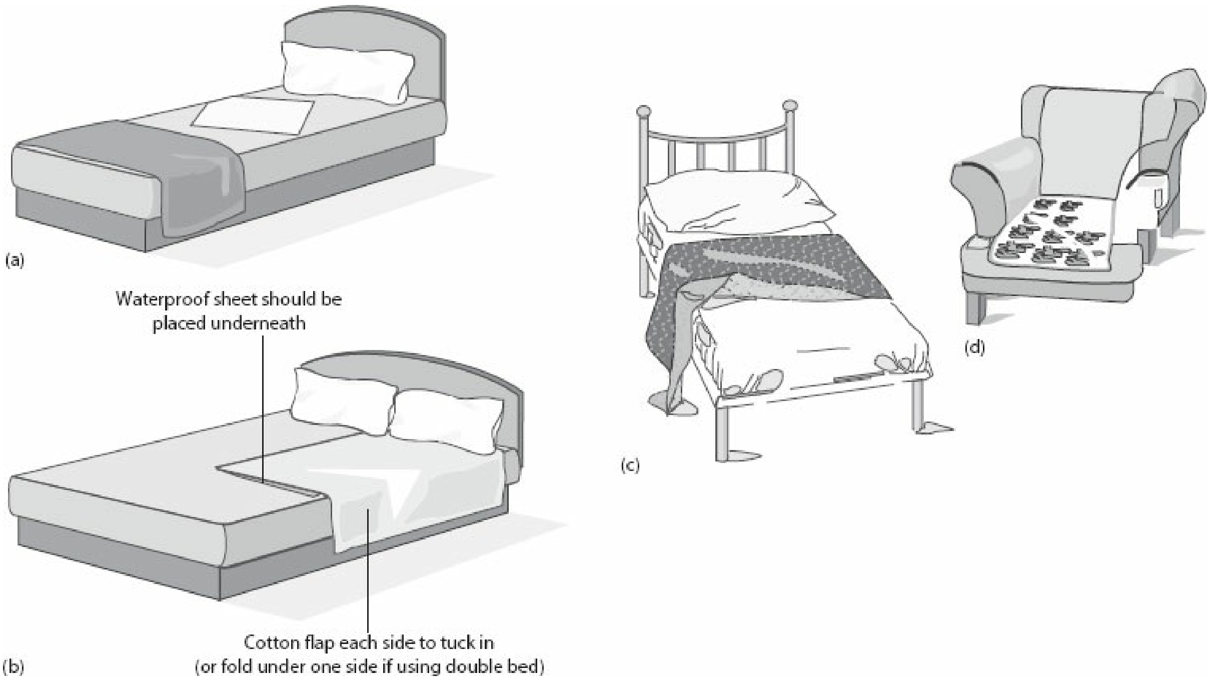
(a)
Waterproof sheet should be placed underneath
(b)
Cotton flap each side to tuck in (or fold under one side if using double bed)
(c)
(d)

Figure 45.7 Bed pad products. Disposable and washable types of bed protection: (a) disposable bed pad and (b) washable bed sheet. Reusable bed and chair protection: (c) reusable bed pad and (d) reusable chair pad.

Skin pH

The skin has a natural acid mantle, which is a protective layer and usually maintains a pH between 4.3 and 5.9. When this pH is maintained, the integrity of the skin is maximized thus decreasing the risk of infection, breakdown, and problems associated with these maladies. When a patient is incontinent, the chronic exposure to urine and or cleaning products can change the pH to a more alkaline environment that promotes transepidermal water loss and barrier breakdown. Many commercially available cleansers are now produced that remove the incontinence debris from the perineal skin, while maintaining the normal pH. Traditionally, commercially available soaps do not offer this option and actually will slowly raise the pH of the skin with repeated usage. It is therefore recommended that patients requiring frequent cleaning during the day invest in pH-balanced cleansers. These are typically more expensive initially, but the long-term benefits will promote skin health. This point is especially sensitive for patients with dual fecal and urinary incontinence. When mixed, these substances produce urea, which further increases the alkalinity. In the presence of an alkaline environment, digestive enzymes that have not been activated will become activated outside of the gastrointestinal tract, thereby prompting further skin breakdown [20].

Skin Barriers vs. Treatments

Many commercially available products are now available for protection of the perineal skin. Prevention prior to breakdown is by far the easiest way to keep the skin intact and decrease further complications such as infection, pain, and pressure damage. Urine barriers include dimethicone, petrolatum, and skin barrier products (for example, Cavilon Spray, 3M, St. Paul, MN). These products when used prophylactically provide a physical barrier between the skin and the effluence. This barrier repels the fluid away from the skin, thus maintaining the acid mantle and decreasing maceration changes and breakdown in the epidermal layer of the skin. In the presence of stool, a zinc oxide–based barrier provides additional protection as it has the properties to repel stool effluence and maintain skin integrity. Once applied, these products do not need to be removed from the skin but cleansed and reapplied after each incontinent episode to maintain sufficient barrier protection.

Cutaneous candidiasis is also common in the patient with incontinence. Typically, candidiasis is not a microorganism that is found in the perineal skin area but can easily be deposited to this area from the gastrointestinal tract. When provided with the right environment (a moist, dark, location in an immunocompromised host), candidiasis can rapidly reproduce causing a topical cutaneous candidiasis. Treatment topically may include miconazole or clotrimazole in ointment, powder, or cream form. Treatment is usually initiated with empirical therapy when identification by observation is made. Cutaneous candidiasis is identified as a reddened rash with a confluent erythema with satellite lesions around the border. There may also be evidence of tiny fluid-filled vesicles or macules that have been opened as a result of friction from shear of clothing and pads [20].

AIDS AND APPLIANCES

Toileting Aids

Commodes

To provide access to a toilet, when a lavatory is not available or easily accessible, many freestanding commodes are available. These have such features as raised seats, adjustable legs, and chemical-emptying devices. This provides women with options to facilitate access and support independent toileting (see Figure 45.8).

Urinals for Females

Although available, these products are not used frequently. They do have some function in providing a urination receptacle for the continent patient who is not a candidate for catheter management, yet does not want pads, or many not be able to get to the toilet, such as a woman in rehabilitation for hip surgery (see Figure 45.9).

Odor Control

A good hygiene program includes adequate skin protection and control of odor. Women with incontinence tend to shower more and use additional perfumes, creams, and deodorants to conceal leakage [21]. Many women will use scented laundry detergents, which in fact may contribute to dermatitis problems as these perfumes can cause an allergic dermatitis.

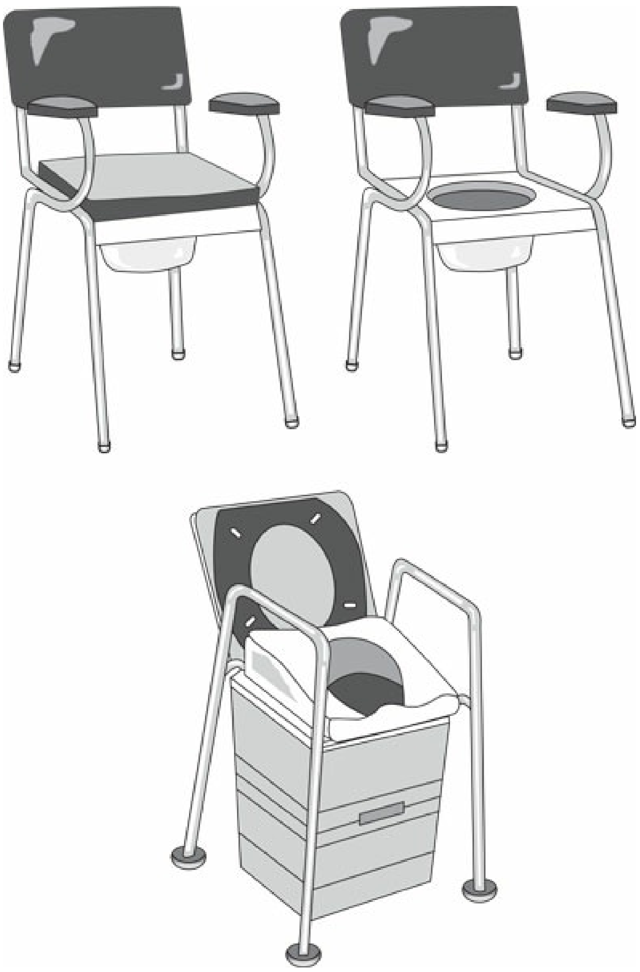

Figure 45.8 Toilet aids.

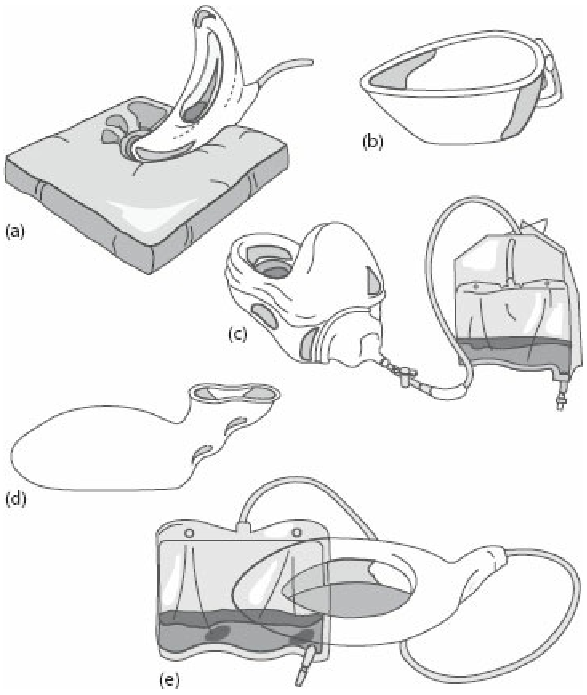

Figure 45.9 Female urinals: (a) bridge urinal with U-shaped cushion, (b) St Peter’s boat, (c) female urinal connected to drainage bag, (d) swan-neck urinal, and (e) pan-type urinal connected to drainage bag.

Assessment to control odor should include [21]

- History of devices used and current hygiene practices
- Difficulties maintaining hygiene and odor control
- Perineal assessment (skin, prolapsed, hemorrhoids, dermatitis)
- Allergies

Odor control can be accomplished by removal of the offending fluid. Also keeping the urine in an acidic state through fluid intake, the urine smell will be decreased. Various sprays are commercially available to mask the odor, without harming the skin.

RESOURCES

International Agencies

The Internet provides multiple profit and not-for-profit resources for patients, caregivers, and professionals to address the unique management needs of incontinence. The Continence Product Advisor (http://www.continenceproductadviosor.org) is an independently reviewed and written resource that uses evidence-based information on generic products, and brand name when necessary, with international links for access to products use dependent on local availability, guidelines, and regulations. The National Association for Continence provides a link on their website that is a marketplace with the latest product information (http://www.nafc.org/find-a-product/). The International Continence Society offers extensive lists on their webpage, www.icsoffice.org, about international agencies. Many of these agencies provide information on incontinence and resources to professional and lay persons about available products and guidelines for use within the said country's health-care system.

Continence Organizations

Australia
Continence Foundation of Australia Ltd.
Website: www.contfound.org.au/

Austria
Medizinische Gesellschaft für lnkontinenzhilfe Österreich
Website: www.inkontinenz.at

Belgium
U-Control vzw (Belgian Association for Incontinence)
Website: www.sosincontinence.org

Canada
The Canadian Continence Foundation
Website: www.continence-fdn.ca/

Czech Republic
Inco Forum
Website: www.inco-forum.cz

Denmark
Kontinensforeningen (The Danish Association of Incontinent People)
Website: www.kontinens.dk/

France
Association d'Aide aux Personnes Incontinentes
Website: www.aapi.asso.fr

Femmes Pour Toujours
Website: www.femsante.com

Germany
Deutsche Kontinenz Gesellschaft e.V.
Website: www.gih.de
Women's Health Coalition
Website: http://www.w-h-c.de

Hong Kong
Hong Kong Continence Society
Email: emfleung@ha.org.hk

Hungary
Inko Forum
Website: www.inkoforum.hu

India
Indian Continence Foundation
Website: www.indiancontinencefoundation.org/

Indonesia
Indonesian Continence Society
Email: urogyn@centrin.net.id

Israel
The National Centre for Continence
Website: welcome.to/continence

Italy
Fondazione Italiana Continenza
(The Italian Continence Foundation)
Website: http://www.continenza-italia.org/
Associazione Italiana Donne Medico (AIDM)
Website: www.donnemedico.org
The Federazione Italiana Incontinenti (FINCO)
Website: www.finco.org

Japan
Japan Continence Action Society
Website: www.jcas.or.jp

Korea
Korea Continence Foundation
Website: www.kocon.or.kr

Malaysia
Continence Foundation (Malaysia)
Email: lohcs@medicine.med.um.edu.my

Mexico
Asociacion de Enfermedades Uroginecologicas
Website: www.asenug.org

Netherlands

Pelvic Floor Netherlands
Website: www.pelvicfloor.nl
Pelvic Floor Patients Foundation (SBP) (Netherlands)
Website: www.bekkenbodem.net
Vereniging Nederlandse lncontinentie, Verpleegkundigen (V N I V)
Website: www.vniv.nl/

New Zealand

New Zealand Continence Association, lnc.
Website: www.continence.org.nz/

Norway

NOFUS (Norwegian Society for Patients with Urologic Diseases)
Website: www.nofus.no

Philippines

Continence Foundation of the Philippines
Email: dtbolong@pacific.net

Poland

NTM "Incontinence—To live a Normal Life"
(The Polish Continence Organisation)
Website: www.ntm.pl

Singapore

Society for Continence (Singapore)
Website: http://sfcs.org.sg

Slovakia

Slovakia Inco Forum
Website: www.incoforum.sk

Spain

Associacion Nacional de Ostomizados e Incontinentes (ANOI)
Website: www.coalicion.org

Sweden

Sinoba—Föreningen för kunskap om urininkontinens och blåsproblem
Website: www.sinoba.se
Swedish Urotherapists
Tel: (46) 31 50 26 39

Switzerland

Schweizerische Gesellschaft für Blasenschwäche
Website: www.inkontinex.ch

Taiwan

Taiwan Continence Society
Website: www.tcs.org.tw

Thailand

Email: ravkc@mahidol.ac.th

United Kingdom
Association for Continence Advice (ACA)
Website: www.aca.uk.com/
The Continence Foundation
Website: www.continence-foundation.org.uk
Enuresis Resource and Information Centre (ERIC)
Website: www.eric.org.uk/
InconTact
Website: www.incontact.org/
Royal College of Nursing Continence Care Forum
Tel: (44) 020 7409 3333

United States of America
The Simon Foundation for Continence
Website: www.simonfoundation.org/
National Association for Continence
Website: www.nafc.org/
International Foundation for Functional Gastrointestinal Disorders
Website: www.iffgd.org/ and www.aboutincontinence.org
Society of Urologic Nurses and Associates (SUNA)
Website: www.suna.org
Wound Ostomy and Continence Nurses
Website: www.wocn.org

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46 Drug Treatment of Lower Urinary Tract Dysfunction in Women

Ariana L. Smith, Alan J. Wein

INTRODUCTION

The lower urinary tract (LUT) has two basic functions: storage of urine and emptying of urine. These functions are achieved in two discrete phases of micturition [1].

Phase one involves filling and storage of urine in the bladder and is accomplished through the following:

1. Accommodation of increasing volumes of urine at low intravesical pressure
2. Appropriate sensation of bladder filling without allodynia
3. A bladder outlet that *is closed at rest* remains closed despite increases in intra-abdominal pressure
4. The absence of involuntary detrusor contractions (IVCs) secondary to neurogenic or nonneurogenic detrusor overactivity (DO)

Phase two involves voiding and emptying of the bladder and is accomplished through the following:

1. Coordinated contraction of the bladder smooth muscle with adequate magnitude and duration
2. Concomitant lowering of resistance at the level of the smooth and striated urethral sphincter
3. The absence of anatomic obstruction

Voiding dysfunction is a broad term that results from disruption of any one of the factors listed earlier, essentially, a failure store, a failure to empty, *or any combination of these factors*. Likewise, all treatments of voiding dysfunction can be classified under the categories of facilitating urinary storage or facilitating urinary emptying. These actions are achieved pharmacologically primarily by acting selectively or nonselectively on bladder smooth muscle or bladder outlet smooth or striated muscle. As a result of advances in the fields of neuropharmacology and neurophysiology of the LUT, effective pharmacological therapy now exists for the management of many categories of voiding dysfunction. In fact, in some categories, so many drug therapies are available for use with varying quality and quantity of research performed on them, and the International Consultation on Incontinence has assessed and made recommendations on many of the available agents (Tables 46.1 [updated] and 46.2 [updated]). The clinical drug recommendations are based on evaluations made using a modification of the Oxford system (Table 46.3).

CLINICAL UROPHARMACOLOGY OF THE LOWER URINARY TRACT

LUT uropharmacology addresses the innervations and receptor contents of the bladder, urethra, and pelvic floor. The targets of pharmacological intervention include not only these structures but also the peripheral nerves and ganglia that supply these tissues and the central nervous system (CNS), including the spinal cord and supraspinal areas. Specifically, pharmacological targets include nerve terminals that alter the release of neurotransmitters, receptor subtypes, cellular second messenger systems, and ion channels. The autonomic nervous system assumes primary control over the two functions of the LUT; however, due to its lack of specificity and ubiquitous nature of its receptors, there are no pharmacological agents that are purely selective for the LUT. Consequently, side effects of the treatment are common and are the result of collateral effects on organ systems that share some of the same neurophysiological or pharmacological characteristics as the bladder and urethra.

Our approach to pharmacological management is to start with the simplest and least perilous form of treatment first. After appropriate dose escalation, other, potentially more toxic, therapeutic options can be offered. Alternatively, a combination of agents or drugs can be used, ideally with synergistic mechanisms of action and nonsynergistic side effects. In our experience, although great improvement can occur with rational pharmacological therapy, a perfect result, i.e., the restoration to normal function, is seldom achieved.

FACILITATION OF URINE STORAGE

Failure of the LUT to adequately fill and store urine may be secondary to pathology in the bladder, the outlet, or both [2]. The most common etiology in women is DO that manifests symptomatically as overactive bladder (OAB), a syndrome of urgency, with or without urge urinary incontinence (UUI), which may be associated with frequency and nocturia [3]. DO includes IVCs of the bladder, discrete or phasic, and decreased compliance. IVCs are commonly associated with neurological disease, inflammatory processes of the bladder, bladder outlet obstruction (BOO), and aging, can be stress induced, or may be idiopathic. Decreased compliance is usually the sequelae of neurological disease but may also result from any process that destroys the elastic or viscoelastic properties of the bladder wall. The treatment for these conditions is aimed at decreasing bladder activity or increasing bladder capacity.

Heightened or altered sensation of the bladder may manifest as urgency with or without DO or as painful bladder syndrome. This may result from inflammatory, infectious, neurological, or psychological factors, or it may be idiopathic. Therapy is aimed at increasing bladder capacity or decreasing sensory (afferent) input. The various therapeutic options for painful bladder syndrome will be dealt with in a separate chapter.

Table 46.1 Drugs Used in the Treatment of Overactive Bladder/Detrusor Overactivity

	Level of evidence	**Grade of recommendation**
Antimuscarinic drugs		
Atropine, hyoscyamine	3	C
Darifenacin	1	A
Fesoterodine	1	A
Imidafenacin	1	B
Propantheline	2	B
Solifenacin	1	A
Tolterodine	1	A
Trospium	1	A
Drugs with mixed actions		
Dicyclomine	3	C
Flavoxate	2	D
Oxybutynin	1	A
Propiverine	1	A
Drugs acting on membrane channels		
Calcium antagonists	2	D
K-channel openers	2	D
Antidepressants		
Duloxetine	2	C
Imipramine	3	C
Alpha-AR antagonists		
Alfuzosin	3	C
Doxazosin	3	C
Prazosin	3	C
Terazosin	3	C
Tamsulosin	3	C
Silodosin	3	C
Naftopidil	3	C
Beta-AR antagonists		

Mirabegron (beta 3)	1	B
Terbutaline (beta 2)	3	C
Salbutamol (beta 2)	3	C
PDE-5 inhibitors[a] (sildenafil, tadalafil, vardenafil)	1	B
COX inhibitors		
Indomethacin	2	C
Flurbiprofen	2	C
Toxins		
Botulinum toxin (neurogenic)[b]	1	A
Botulinum toxin (idiopathic)[b]	1	B
Capsaicin (neurogenic)[c]	2	C
Resiniferatoxin (neurogenic)[c]	2	C
Other drugs		
Baclofen[d]	3	C
Hormones		
Estrogen	2	C
Desmopressine[e]	1	A

Source: Andersson K-E et al., Pharmacological treatment of urinary incontinence, in: Abrams P et al., eds., *Incontinence, 5th International Consultation on Incontinence*, ICUD-EAU, 2013, pp. 623–728. With permission.

Note: Assessments according to the Oxford system (modified).

[a] Male LUTS/OAB.

[b] Bladder wall.

[c] Intravesical.

[d] Intrathecal.

[e] Nocturia (nocturnal polyuria), caution hyponatremia especially in the elderly.

Table 46.2 Drugs Used in the Treatment of Stress Urinary Incontinence

Drug	**Level of evidence**	**Grade of recommendation**
Clenbuterol	3	C
Duloxetine	1	B
Ephedrine	3	D
Estrogen	2	D
Imipramine	3	D
Methoxamine	2	D
Midodrine	2	C
Phenylpropanolamine	3	D

Source: Andersson K-E et al., Pharmacological treatment of urinary incontinence, in: Abrams P et al., eds., *Incontinence, 5th International Consultation on Incontinence*, ICUD-EAU, 2013, pp. 623–728. With permission.

Note:Assessments according to the Oxford system (modified).

Table 46.3 International Consultation on Incontinence (ICI) Assessments 2008: Oxford Guidelines (Modified)

Levels of evidence

Level 1: Systematic reviews, meta-analyses, good-quality RCTs

Level 2: RCTs, good-quality prospective cohort studies

Level 3: Case-control studies, case series

Level 4: Expert opinion

Grades of recommendation

Grade A: Based on level 1 evidence (highly recommended).

Grade B: Consistent level 2 or 3 evidence (recommended).

Grade C: Level 4 studies or “majority evidence” (optional).

Grade D: Evidence is inconsistent/inconclusive (no recommendation possible) or the evidence indicates that the drug should not be recommended.

Source: Andersson K-E et al., Pharmacological treatment of urinary incontinence, in: Abrams P et al., eds., *Incontinence, 5th International Consultation on Incontinence*, ICUD-EAU, 2013, pp. 623–728. With permission.

Decreased outlet resistance may manifest from damage to the smooth or striated sphincter secondary to surgical, obstetric, or other mechanical trauma or degeneration of innervation with the loss of neuronal mass secondary to neurological disease, aging, or trauma [4]. In addition, in women, it may result from decreased pelvic floor support of the bladder outlet. Clinically, this manifests as an effort related or stress urinary incontinence (SUI) or, when severe, as complete gravitational incontinence. Treatment is aimed at increasing outlet resistance.

Disruption in the filling and storing function of the bladder can, in theory, be improved by agents that decrease detrusor activity, increase bladder capacity, decrease sensory input, or increase outlet resistance [2].

Decreasing Bladder Contractility

Antimuscarinic Agents

Physiological bladder contractions are thought to be primarily triggered by acetylcholine (ACh)-induced stimulation of postganglionic parasympathetic muscarinic cholinergic receptor sites on bladder smooth muscle [1,5]. Atropine and other antagonists of ACh that bind these receptor sites will depress normal bladder contractions and IVCs of any cause [5,6]. In addition, these agents increase the volume to first IVC and the total bladder capacity and decrease the amplitude of the contraction [7]. The commonly held belief regarding antimuscarinic drugs is that they bind receptors on the detrusor that are stimulated by ACh, thereby decreasing the ability of the bladder to contract. However, during bladder filling and storage, there is no sacral parasympathetic outflow [8], which raises the following question: “Why do antimuscarinics affect the filling/storage phase of the micturition cycle, increasing, in patients with OAB and without DO, bladder capacity and decreasing urgency?” Muscarinic receptors are also present in the bladder urothelium and suburothelium [9], and there is a basal ACh release in human detrusor muscle that may be produced, at least partly, by the urothelium and suburothelium [10]. This suggests that detrusor tone may be affected by ongoing ACh-mediated stimulation. There is now good direct experimental evidence that the antimuscarinics decrease activity in both C- and A-delta afferent nerve fibers from the bladder during filling/storage [11,12].

ACh acts on two classes of receptors, nicotinic and muscarinic. Signal transduction between parasympathetic nerves and smooth muscle of the detrusor involves muscarinic receptors [13]. At least five different muscarinic receptor subtypes exist, which are designated M_1–M_5. Although it appears that the majority of the muscarinic receptors in human smooth muscle are of the M_2 subtype, in vitro data indicate that most smooth muscle contraction, including that of the bladder, is mediated by the M_3 receptor subtype. The muscarinic receptors are found not only on smooth muscle cells of the bladder but also on urothelial cells, on suburothelial nerves, and on suburothelial structures such as interstitial cells with a M_2 and M_3 preponderance [9]. Based on the work in animals, the M_2 receptors have been implicated in the contraction of diseased bladders (denervated, hypertrophied rat bladders) [11].

Antimuscarinics can be divided into tertiary and quaternary amines, which differ in molecular size, molecular charge, and lipophilicity [13]. Small molecular size with little charge and greater lipophilicity increase the passage through the blood–brain barrier with the theoretical potential of greater CNS side effects. Tertiary compounds have higher lipophilicity and less molecular charge than quaternary agents. Quaternary compounds have greater molecular charge and less lipophilicity resulting in limited passage into the CNS and a low incidence of CNS side effects [14].

A meta-analysis on antimuscarinic agents found that these agents are more effective than placebo in improving continent days, mean voided volume, urgency episodes, and micturition frequency [15]. The vast majority of agents studied provided improvement in health-related quality of life (HRQL). Across large patient samples, all of the currently available antimuscarinics appear to have comparable efficacy but do show some measurable differences in tolerability [16]. Since the profiles of each drug and the dosing schedules differ, these things along with medical comorbidities and concomitant medications should be considered when individualizing treatment for patients.

The currently available antimuscarinic drugs lack selectivity for the bladder and as a result produce side effects on other organ systems (Figure 46.1). The most common adverse effects include dry mouth, blurred vision, pruritus, tachycardia, somnolence, impaired cognition, and headache. Constipation is reported as the most burdensome side effect [15]. This class of drug is contraindicated in patients with urinary retention, gastric retention, and other severe decreased gastrointestinal motility conditions and uncontrolled narrow-angle glaucoma. The concomitant use with other anticholinergic agents may increase the frequency and/or severity of these effects. Specific patient populations including those with renal or liver impairment and those with genetic heterogeneity in drug-metabolizing enzymes may experience increased side effects due to altered pharmacokinetic behavior of a given drug [16]. Many of these drugs should not be used with potent cytochrome P450 (CYP) 3A4 inhibitors including ritonavir, ketoconazole, itraconazole, verapamil, and cyclosporine [17–20].

It is estimated that about one-third of all patients with OAB have at least one risk factor for altered drug metabolism [16]. While relative muscarinic receptor selectivity exists for some agents, there is no uroselective option that avoids unpleasant systemic side effects. As a result, patient compliance is extremely low and the search for uroselectivity continues. Intravesical administration, in the absence of systemic absorption, would greatly diminish the antimuscarinic side effects; however, this is practical only in patients who perform clean intermittent catheterization (CIC).

Antimuscarinic agents are considered first-line pharmacotherapy for OAB [21]. Specific antimuscarinic drugs are listed as follows with available data on efficacy and comparative efficacy with other drugs in class.

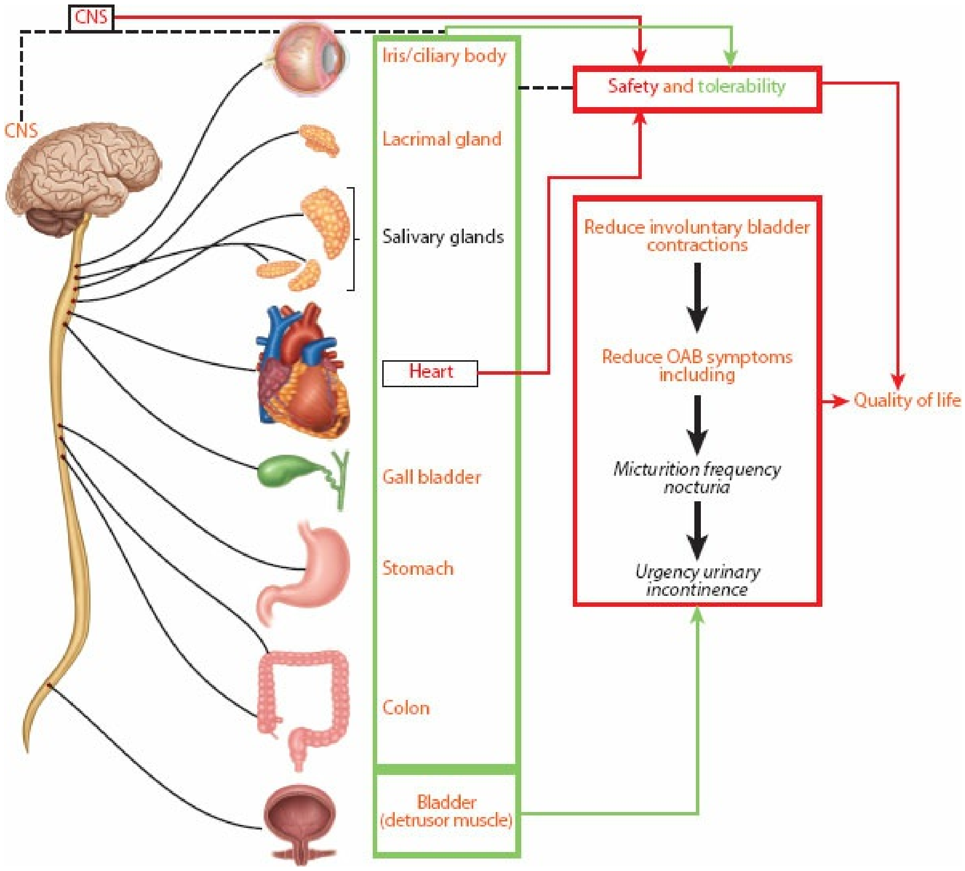
CNS
CNS
Iris/ciliary body
Safety and tolerability
Lacrimal gland
Salivary glands
Reduce involuntary bladder contractions
Heart
Reduce OAB symptoms including
Quality of life
Micturition frequency nocturia
Gall bladder
Stomach
Urgency urinary incontinence
Colon
Bladder (detrusor muscle)

Figure 46.1 Important sites of action of antimuscarinics. Abbreviations: CNS, central nervous system; OAB, overactive bladder. (Adapted from Andersson K-E et al., Pharmacological treatment of urinary incontinence, in: Abrams P et al., eds., *Incontinence, 5th International Consultation on Incontinence*, ICUD-EAU, 2013, pp. 623–728.)

Atropine

Atropine, along with hyoscyamine and scopolamine, is active belladonna alkaloids, derived from the toxic belladonna plant with anticholinergic properties [12]. Atropine has significant systemic side effects including ventricular fibrillation, tachycardia, dizziness, nausea, blurred vision, loss of balance, dilated pupils, photophobia, extreme confusion, and dissociative hallucinations, which limit its oral use for the treatment of OAB. Intravesical atropine at a dose of 6 mg four times per day was shown to be as effective as intravesical oxybutynin (OXY) for increasing bladder capacity with minimal systemic side effects in patients with multiple sclerosis in a double-blind, randomized placebo-controlled trial (RCT) with crossover design [22]. Its mention in this chapter is more of a historic one.

Darifenacin

Darifenacin is a tertiary amine with moderate lipophilicity and is a relatively selective M_3 receptor antagonist. At least theoretically, darifenacin's advantage is the ability to relatively selectively block the M_3 receptor that although less prevalent than the M_2 receptor appears to be more important in bladder contraction. This selectivity is expected to increase efficacy in patients with OAB while reducing the adverse events related to the blockade of other muscarinic subtypes [23]. Darifenacin has been developed as a controlled release formulation to allow daily dosing and is available at 7.5 and 15 mg/day. Several RCTs have documented the clinical effectiveness of the drug. Haab et al. performed a multicenter, double-blind RCT comparing darifenacin 3.75, 7.5, 15 mg and placebo once daily for 12 weeks [24]. The study enrolled 561 patients (85% female) age 19–88 years with OAB symptoms for at least 6 months and included patients with prior exposure to antimuscarinic therapy. The 7.5 and 15 mg doses of darifenacin had rapid onset of effect with significant improvement in symptoms over placebo at 2-week follow-up. The clinical parameters in which the treatment arm was significantly better than placebo included micturition frequency, bladder capacity, frequency of urgency, severity of urgency, and number of incontinence episodes. No significant change in nocturia was seen. The most common side effects were mild to moderate dry mouth and constipation. The CNS and cardiac safety profiles were similar to placebo. Discontinuation was rare.

A review of the pooled data from three phase III, multicenter, double-blind RCTs was performed by Chapple et al. in 2005 [25]. A total of 1059 patients (85% female) with urgency, UUI, and frequency were treated with darifenacin 7.5, 15 mg or placebo daily for 12 weeks. Significant dose-related improvements in number of incontinence episodes per week were seen: 8.8 less episodes per week with the 7.5 mg dose and 10.6 less episodes per week with the 15 mg dose. Improvements in micturition frequency, bladder capacity, and severity of urgency were also seen. The most common side effects were dry mouth and constipation resulting in few discontinuations.

The ability to postpone urination is one of the most noticeable clinical effects of antimuscarinic therapy. Often, measured as "warning time," which is defined as the time from first sensation of urgency to the time of voluntary micturition or incontinence, the ability to postpone a few extra minutes can be the difference between wet and dry. Cardozo and Dixon performed a multicenter, double-blind RCT looking at the effects of darifenacin on warning time [26]. Overall, 47% of the darifenacin group compared to 20% of the placebo group achieved a >30% increase in mean warning time. The patients in this study received a 30 mg dose of darifenacin, which is higher than the clinically recommended dose. These results have not been replicated using the 15 mg dose.

Darifenacin has been shown to improve HRQL sustained at 2 years of treatment [310].

The effects of darifenacin on cognitive function in elderly volunteers were tested in a randomized, double-blind, three-period crossover study with 129 patients 65 years of age or older [27]. After 2 weeks of treatment, no effect on cognitive function compared with baseline was found. The authors hypothesized that this was related to its M_3 receptor selectivity. Further studies on the blood–brain barrier by Chancellor et al. indicate that darifenacin, along with trospium and fesoterodine, is actively transported away from the brain as the result of a protein-mediated transport system [303]. Darifenacin has not been found to have any effect on QT/QTc intervals or heart rate compared to placebo [334,341].

Fesoterodine

Fesoterodine is a newer antimuscarinic drug that is metabolized rapidly and extensively to 5-hydroxymethyl tolterodine (5-HMT), the same active metabolite of tolterodine (TOLT) [28]. Fesoterodine relies on nonspecific esterases that produce a rapid and complete conversion to 5-HMT with little pharmacokinetic variability. 5-HMT is further metabolized in the liver, but a modest percentage of 5-HMT undergoes renal excretion without additional metabolism, raising the possibility that 5-HMT could also work from the luminal side of the bladder [29]. Whether this contributes to clinical efficacy in human remains unknown at this time. Like TOLT, this compound is a nonsubtype selective muscarinic receptor antagonist [30]. The 4 mg/day dose can be used in patients with moderately impaired renal or hepatic function since there is dual metabolism of 5-HMT by both organ systems [307,320].

Fesoterodine is indicated for the treatment of DO at doses of 4 and 8 mg daily. In a multicenter, double-blind, double-dummy RCT with TOLT extended release (ER), 1132 patients were enrolled and received treatment [28]. The trial showed that both the 4 and 8 mg doses of fesoterodine were effective in improving the symptoms of OAB with the 8 mg dose having greater effect at the expense of a higher rate of dry mouth. Only one subject from the fesoterodine 8 mg group and one subject from the TOLT ER 4 mg group withdrew from the study due to dry mouth. The dose–response relationship was confirmed in another study that pooled data from two phase III RCTs [31]. Fesoterodine 8 mg performed better than the 4 mg dose in improving urgency and UUI as recorded by 3-day bladder diary, offering the possibility of dose titration. A study on the effect of fesoterodine on HRQL in patients with OAB confirmed improvement for both the 4 and 8 mg dose of the drug [32]. A head-to-head placebo-controlled trial comparing fesoterodine 8 mg to TOLT ER 4 mg (n = 1590) showed greater improvements in urgency incontinence episodes, completely dry rates, voided volume, and patient perception of improvement with fesoterodine [315]. No difference was noted in frequency of micturition and urgency episodes. Significantly, greater side effects (dry mouth, headache, constipation, and discontinuation) were reported with fesoterodine. This study suggests that fesoterodine 8 mg can provide improved symptom control over TOLT ER. In a large double-blind, double-dummy, phase III study (n = 2417), fesoterodine 8 mg showed greater improvement in urgency incontinence episodes, frequency of micturition, urgency episodes, and patient perception of improvement than TOLT ER 4 mg or placebo [323]. No difference in voided volume or nocturia was noted. Dry mouth, constipation, and discontinuation rates were greater with fesoterodine 8 mg. Fesoterodine has not been found to prolong QT/QTc or produce other cardiac abnormalities [321].

Hyoscyamine

Hyoscyamine is a pharmacologically active antimuscarinic component of atropine that is reported to have similar actions and side effects [12]. Few clinical studies are available to evaluate efficacy in the treatment of DO [33]. A sublingual formulation of hyoscyamine sulfate is available.

Imidafenacin

Imidafenacin is a muscarinic antagonist with greater affinity for the M_3 and M_1 receptors than the M_2 receptor [326]. The oral administration of imidafenacin in rats showed longer-lasting and more selective binding to muscarinic receptors in the bladder than other tissues, with little binding in the brain [352]. Whether this translates to its pharmacological effects on humans remains unknown. The drug is primarily metabolized in the liver by cytochrome P450 enzyme CYP3A4 [322]. The drug is also excreted in the urine; however, the pharmacological importance of this has not yet been elucidated.

Clinical studies have primarily been performed in Japan and the drug is not available in Western countries. A randomized, double-blind, placebo-controlled phase II study (n = 401) showed a dose-dependent reduction in urgency incontinence episodes that was significant over placebo [318]. In addition, frequency of micturition, urgency episodes, and voided volume were significantly improved. In a larger study, the same authors performed a placebo- and propiverine-controlled trial (n = 781) that demonstrated noninferiority of imidafenacin compared to propiverine for the reduction of urgency incontinence episodes [317]. The incidence of side effects was significantly lower with imidafenacin than propiverine. A long-term 52-week study by the same authors (n = 376) demonstrated a persistent improvement in voiding symptoms with the most common adverse event being dry mouth in 40.2% [316]. Imidafenacin has not been found to prolong QT/QTc or alter vital signs, laboratory values, or postvoid residual (PVR) measures.

Propantheline Bromide

The classic oral agent for antimuscarinic effects on the LUT was propantheline bromide, a nonselective quaternary ammonium compound that is poorly absorbed after oral administration [12]. It has a short plasma half-life of <2 hours and varying biological availability requiring individual titration. It is initially prescribed at 15–30 mg four times daily, but larger doses are often required [34]. Despite having antimuscarinic binding potential quite similar to atropine, there is a lack of convincing data on the effectiveness for the treatment of OAB/DO. Contradictory studies are available that show complete response in 25/26 patients [35] and no difference from placebo in 154 and 23 patients, respectively [36,37]. By today's standards, the effect of propantheline on DO has not been well documented in RCTs; however, with its long history of use, it can be considered effective and may, in individually titrated doses, be clinically useful.

Scopolamine

Scopolamine, a belladonna alkaloid, has greater penetration through the blood–brain barrier than atropine and as a result produces more prominent central depressive effects even at low doses [12]. Transdermal scopolamine has been used for treating DO at a continuous dose of 0.5 mg for 3 days [38]. A double-blind RCT was performed in 20 patients with DO. After 14 days, patients in the treatment group showed significant improvements in frequency, nocturia, urgency, and UUI over the placebo group. Side effects included dizziness, ataxia, blurred vision, dry mouth, and skin irritation at patch site. No patients discontinued use during the study period [33].

Solifenacin

Solifenacin is a tertiary amine with modest selectivity for the M_3 receptor over the M_2 and marginal selectivity over the M_1 receptors [13,39]. Solifenacin is metabolized in the liver utilizing the cytochrome P450 enzyme system (CYP3A4), but a modest percentage undergoes renal excretion without additional metabolism raising the possibility that solifenacin could also work from the luminal side of the bladder. Whether this contributes to clinical efficacy in humans remains unknown at this time. Studies have demonstrated that solifenacin increases maximum bladder capacity and area under the bladder volume sensation curve [327,344]. It is a once-daily antimuscarinic that is being marketed at the 5 and 10 mg doses. There have been several large trials examining the effects of solifenacin. A large, phase II, multinational RCT was performed comparing solifenacin 2.5, 5, 10, and 20 mg daily to TOLT immediate release (IR) 2 mg twice daily and placebo [40]. A total of 225 patients with urodynamically confirmed DO were enrolled, treated for 4 weeks, and followed for two additional weeks. There was a significant decrease in micturition frequency, incontinence episodes, and urgency episodes, and an increase in volume voided in the 5, 10, and 20 mg solifenacin groups compared to placebo. The mean effects with TOLT were generally smaller as compared to solifenacin. The 5 and 10 mg doses of solifenacin had a lower dry mouth rate than TOLT. Discontinuation rates were highest for solifenacin 20 mg.

Cardozo and colleagues performed a multinational RCT comparing solifenacin 5 and 10 mg daily to placebo in 857 patients [41]. Both doses significantly improved micturition frequency, urgency, volume voided, and incontinence episodes compared to placebo as determined by the 3-day micturition diaries. Of patients who reported any incontinence at baseline, 50% achieved continence after treatment with solifenacin compared with 27.9% after placebo. Dry mouth was reported in 7.7% of patients taking solifenacin 5 mg, 23.1% in solifenacin 10 mg, and 2.3% in the placebo arm. Only a small percentage of patients (2%–4%) did not complete the study due to adverse events and this was comparable in all groups.

The solifenacin and TOLT as an active comparator in a randomized trial was a prospective double-blind, parallel group 12-week study comparing solifenacin 5 and 10 mg once daily to TOLT ER 4 mg once daily [42]. After 4 weeks of treatment, patients were given the option to increase medication dosage. However, only those on solifenacin actually received the dose increase. The results showed noninferiority of solifenacin's flexible dosing regimen compared to TOLT ER for voiding frequency. Solifenacin showed increased efficacy in decreasing urgency episodes, incontinence, and pad usage compared with TOLT ER. Additionally, more solifenacin patients achieved dryness, as documented by 3-day voiding diary, by the end of the study (59% vs. 49%). However, these symptomatic improvements were accompanied by an increase in adverse events with dry mouth and constipation occurring in 30% and 6.4% of the solifenacin group, respectively, versus 23% and 2.5% in the TOLT group. The discontinuation rate was comparably low in both groups.

A systematic review and meta-analysis of 9 RCTs concluded that solifenacin provides significant improvement in voiding symptoms compared to placebo or TOLT [329]. Solifenacin 10 mg was better than 5 mg in reducing frequency of micturition. Constipation and blurred vision were greater with solifenacin as compared to TOLT.

The efficacy in mixed urinary incontinence [43], the elderly [44], and in multiple sclerosis patients [348] has been shown, as has an improvement in HRQL [45].

Data on solifenacin treatment in children are limited. An open-label study including 72 children of which 27 had neurogenic bladder demonstrated improved urodynamic capacity and improved continence [299].

Solifenacin has shown QT interval prolongation and torsade de pointes in an 81-year-old female [297]. In a large open-label postmarketing study (n = 4450) including patients with cardiovascular comorbidities and comedication, solifenacin did not demonstrate any clinically relevant alteration in blood pressure or heart rate [332].

Tolterodine

TOLT is a tertiary amine with a major active metabolite, 5-HMT, which significantly contributes to the therapeutic effect of the drug [46]. Both TOLT and its metabolite have plasma half-lives of 2–3 hours, but their effects on the bladder seem to be more long lasting. Whether this could be the result of urinary excretion of the drug with direct bladder mucosal effects remains unknown. TOLT does not have muscarinic subtype selectivity but there is evidence in some experimental models that it has functional selectivity for the bladder over the salivary glands [47]. This has been shown in the guinea pig where the binding affinity of TOLT and OXY to muscarinic receptors in the bladder were very similar, but the affinity of TOLT for muscarinic receptors in the parotid gland was eight times lower than that of OXY [48]. TOLT is available in two formulations: an IR form prescribed as 2 mg twice daily and an ER form prescribed as 2 or 4 mg once daily. There appears to be advantages in both efficacy and tolerability with the ER form [49]. There appears to be a very low incidence of cognitive side effects with TOLT, which is likely due to the low lipophilicity of the drug and its metabolite, minimizing penetration into the CNS [50]. A notable subset of patients, up to 10% of whites and up to 19% of blacks, lack the specific CYP enzyme, 2D6, that metabolizes TOLT to 5-HMT [51]. In these patients, a higher side-effect profile, specifically including sleep disturbance, is seen [52]. Drugs that do not require CYP2D6 metabolism have the potential for less pharmacokinetic variability.

The efficacy of TOLT has been documented by several double-blind RCT on patients with DO. The Overactive Bladder: Judging Effective Control and Treatment (OBJECT) trial compared TOLT IR 2 mg twice daily to OXY ER 10 mg daily [53]. This was a double-blind, parallel group RCT, which included 378 patients with OAB treated for 12 weeks. The study showed OXY ER to be significantly more effective than TOLT in reducing UUI episodes, total incontinence, and micturition frequency. The most common adverse event, dry mouth, was reported in 28% of those taking OXY ER and 33% of those taking TOLT IR. The rates of other adverse events including CNS effects were generally low and comparable between the groups.

The Overactive Bladder: Performance of Extended Release Agents (OPERA) trial compared TOLT ER 4 mg daily to OXY ER 10 mg daily in 790 women with OAB symptoms [54]. This was a double-blind RCT with duration of 12 weeks. Improvements in UUI episodes were similar between the two groups but cure of UUI was greater in the OXY ER group (23.0% vs. 16.8%). OXY ER was also more effective in reducing micturition frequency at the price of increased rates of dry mouth. Adverse events were mild and occurred at low rates, with both groups having similar rates of discontinuation of treatment.

The antimuscarinic clinical effectiveness trial was an open-label study of 1289 patients with OAB comparing TOLT ER 2 or 4 mg daily to OXY 5 or 10 mg daily [55]. After 8 weeks, 70% of patients taking TOLT ER 4 mg perceived an improved bladder condition compared to 60% in the TOLT ER 2 mg group, 59% in the OXY ER 5 mg group, and 60% in the OXY ER 10 mg group. Dry mouth was dose dependent with both drugs; however, patients treated with TOLT ER 4 mg reported a significantly lower severity of dry mouth compared with OXY ER 10 mg. Fewer patients withdrew from the TOLT ER 4 mg group (12%) than either the OXY ER 5 mg group (19%) or the OXY ER 10 mg group (21%).

Although the findings suggest that TOLT ER 4 mg may have improved clinical efficacy and tolerability to OXY ER 10 mg, the open-label design of this study makes for a less convincing conclusion.

In the Improvement in Patients: Assessing Symptomatic Control with TOLT ER study, the efficacy of TOLT in improving patients' most bothersome symptoms was assessed [56]. It found significant reduction in bothersome symptoms whether it be incontinence, urgency episodes, or micturition frequency. Dry mouth occurred in 10% of patients and constipation in 4%.

Conflicting data exist on the concomitant use of TOLT and pelvic floor muscle training. In a prospective, open study of 139 women with OAB who were randomized to TOLT, bladder training or both, combination therapy was found to be most effective [57]. Similarly, a multicenter, single-blind study of 505 patients comparing TOLT alone to TOLT plus bladder training concluded that the effectiveness of TOLT can be augmented with the addition of a bladder training regimen [58]. However, a similar multinational RCT including 480 patients concluded that no additional benefit was seen with the addition of pelvic floor muscle exercises to TOLT [59].

TOLT ER has shown a significant increase in the heart rate in a proportion of subjects, and this effect was not seen with darifenacin or placebo [334]. In a study of solifenacin versus TOLT ER, similar therapeutic and urodynamic effects were noted but TOLT had a greater effect on increasing heart rate [319].

Trospium

Trospium is a hydrophilic, quaternary amine with limited ability to cross the blood–brain barrier. This should result in minimal cognitive-related dysfunction [60] and has demonstrated undetectable levels in the cerebral spinal fluid on day 10 of use [343]. Trospium does not have muscarinic subtype selectivity and, unlike the previous antimuscarinics mentioned, is not metabolized by the CYP enzyme system. It is mainly eliminated unchanged in the urine by renal tubular secretion, and as a result, may affect the urothelial mucosal signaling system as has been shown in the rat [61]. Whether this contributes to clinical efficacy in humans remains unknown at this time. In a multicenter, double-blind RCT, the effect of trospium on urodynamic parameters was studied in patients with neurogenic DO secondary to spinal cord injury (SCI) [62]. A 20 mg dose was given twice daily for 3 weeks. An increase in maximum cystometric capacity and compliance and a decrease in maximal detrusor pressure were seen in the treatment group. A similar study compared the use of trospium and OXY in the treatment of neurogenic DO [63]. Both medications appeared to have equal effect, but the patients on trospium had fewer side effects. The effectiveness of trospium in the treatment of nonneurogenic DO has also been well documented. Allousi et al. performed a double-blind RCT comparing trospium 20 mg twice daily to placebo in 309 patients [64]. At 3 weeks, urodynamic studies revealed an increase in maximum bladder capacity and volume at first IVC in the trospium group. In a study comparing the efficacy of trospium 20 mg twice daily with TOLT 2 mg twice daily and placebo in 232 patients with DO or mixed urinary incontinence, Jünemann and Al-Shukri found trospium to be significantly more effective in decreasing the frequency of micturition than either TOLT or placebo [65]. Additionally, trospium caused a greater reduction in incontinence episodes with a similar rate of dry mouth as TOLT.

A long-term tolerability and efficacy study comparing trospium 20 mg twice daily and OXY 5 mg twice daily in 358 patients with DO undergoing treatment for 52 weeks was performed [66]. Urodynamics and patient-recorded voiding diaries were performed at baseline, 26 weeks, and 52 weeks. Mean maximum cystometric capacity increased in the trospium group by 92 mL at 26 weeks and by 115 mL at 52 weeks. No other significant urodynamic differences were seen between the groups. The micturition diaries indicated a reduction in micturition frequency, incontinence frequency, and urgency episodes in both treatment groups. At least one adverse event occurred in the majority of patients: 64.8% in the trospium group and 76.6% in the OXY group. The most common side effect in both groups was dry mouth. Overall, both drugs were comparable in the efficacy in improving urinary symptoms, but trospium had a better benefit/risk ratio than OXY due to better tolerability.

An ER formulation of trospium, 60 mg once daily, has been shown in RCTs to have similar efficacy and side effects as the twice daily preparation [67]. An analysis of patients 75 years of age and older (n = 143) showed improvement in all voiding diary parameters and quality of life in patients on trospium ER compared to controls [339]. No CNS adverse effects were reported during the 12-week study; however, during the 9-month open-label follow-up, one patient reported dizziness and one reported vertigo thought to be possibly related to trospium ER.

Intravesical installation of trospium was studied with a single-center, single-blind RCT with 84 patients [68]. Since intravesical trospium does not seem to be absorbed, an opportunity exists for treatment with minimal systemic antimuscarinic effects [69]. Compared to placebo, intravesical trospium produced a significant increase in maximum bladder capacity and a decrease in detrusor pressure. No improvement in uninhibited bladder contractions was seen. No adverse events were reported, but an increase in residual urine was noted. Trospium has not been reported to result in cognitive dysfunction.

Dual Musculotropic Relaxants: Antimuscarinic Agents

Some agents have been identified that have dual mechanisms of action. They have antimuscarinic activity and direct musculotropic relaxant effects on the bladder smooth muscle at a site metabolically distal to the antimuscarinic receptor. It is felt that the clinical effects of these drugs are primarily explained by an antimuscarinic action.

Flavoxate

Flavoxate also has direct inhibitory action on smooth muscle along with very weak anticholinergic properties [70]. The drug has also been found to possess moderate calcium antagonistic activity, exhibit local anesthetic properties, and have the ability to inhibit phosphodiesterase (PDE) [71]. In rats and in cats, there is some evidence that flavoxate may also have central effects on the inhibition of the micturition reflex [72,73].

Clinical studies addressing the efficacy of flavoxate in the treatment of OAB/DO have been mixed. In a double-blind crossover study comparing flavoxate 1200 mg daily with OXY 15 mg daily in 41 women with idiopathic DO, both drugs had similar efficacy with flavoxate having fewer and milder side effects [74]. A very small study in the elderly population with nonneurogenic DO showed flavoxate had essentially no effect on cystometric capacity and incontinence [75]. Chapple et al. also suggest no beneficial effect of flavoxate in the treatment of idiopathic DO [76]. In general, few side effects were reported during treatment. No recent RCTs addressing the efficacy of this drug have been performed.

Oxybutynin

OXY is a moderately potent antimuscarinic agent that has strong independent musculotropic relaxant activity as well as local anesthetic activity (that is likely only important during intravesical administration). It is a tertiary amine that is metabolized primarily by the CYP system into its primary metabolite, *N*-desethyloxybutynin (DEO) [77]. The recommended oral adult dose for the IR formulation is 5 mg three or four times daily. An ER once-daily oral formulation as well as a transdermal delivery system (TDS) with twice weekly dosing and a transdermal gel with once-daily dosing is available. Side effects are secondary to nonspecific muscarinic receptor binding.

Initial reports documented success in depressing neurogenic DO [78], and subsequent reports documented success in inhibiting idiopathic DO as well [79]. A meta-analysis summarizing 15 RCTs ($n = 476$) reported a 52% mean reduction in incontinence episodes, a 33% mean reduction in micturition frequency, and a 74% mean overall improvement rate. This came at the expense of a 70% of patients experiencing an adverse event [80].

Holmes and associates compared the results of OXY and propantheline in a small group of women with DO [37]. The experimental design was a randomized crossover trial with a patient-regulated variable dose regimen. This kind of dose titration study allows the patient to increase the drug dose to whatever is perceived to be the optimum ratio between clinical improvement and side effects. Of the 23 women in the trial, 14 reported subjective improvement with OXY as opposed to 11 with propantheline. Both drugs significantly increased the maximum cystometric capacity and reduced the maximum detrusor pressure on filling. The only significant objective difference was a greater increase in the maximum cystometric capacity with OXY. The mean total daily dose of OXY tolerated was 15 mg (range 7.5–30 mg) and that of propantheline was 90 mg (range 45–145 mg).

The therapeutic effect of OXY IR is associated with a high incidence of side effects, which are often dose limiting [81]. The ER form of OXY uses an osmotic system to release the active compound at a controlled rate over a period of 24 hours. As a result, there is less absorption in the proximal portion of the gastrointestinal tract and less first-pass metabolism. By decreasing the liver metabolite DEO, it was thought that fewer side effects, especially dry mouth, would occur, thus improving patient compliance

[82]. Studies looking at salivary output showed markedly diminished production following administration of OXY IR or TOLT IR with gradual return to normal. In OXY ER group, salivary output was maintained at predose levels throughout the day [83]. OXY IR and ER have been compared in a multicenter, double-blind RCT of 106 patients, all of whom had previously responded to IR OXY [84]. Similar efficacy and similar side effect profiles were noted for both formulations.

As noted earlier in the OBJECT study, OXY 10 mg ER proved superior to TOLT 2 mg IR twice daily with respect to weekly UUI episodes, total incontinence, and frequency [53]. The two drugs were equally well tolerated. The follow-up OPERA study compared OXY 10 mg ER to TOLT 4 mg ER and found no significant difference in efficacy between the two drugs [54]. The incidence of dry mouth was statistically lower in the TOLT group. One general consensus following this study was that IR formulations of one drug should not be compared to ER formulations of another drug.

Three difference doses of OXY (5, 10, and 15 mg) were compared in a RCT, and a significant dose–response relationship for both UUI episodes and dry mouth was found. The greatest patient satisfaction was with the 15 mg dose [85].

Transdermal administration of OXY (OXY-TDS) alters the metabolism of the drug further reducing the production of DEO compared to OXY ER. The 3.9 mg daily dose patch decreased both micturition frequency and incontinence episodes, while increasing mean voided volume [86]. Dry mouth rate was similar to placebo. In a study comparing OXY-TDS to OXY IR, similar reductions in incontinence episodes were found, but significantly less dry mouth was seen with OXY-TDS (38% vs. 94% with OXY IR) [87]. In a third study, OXY-TDS was compared to placebo and TOLT ER [88]. Both drugs had similarly significant reduced daily incontinence episodes and increased voided volume, but TOLT ER was associated with a higher rate of adverse events. The major side effect for OXY-TDS was pruritus at the application site in 14% and erythema in 8.3%. The pharmacokinetics of OXY-TDS was studied using the blood and saliva samples in a two-way crossover RCT with OXY ER [89]. The TDS route of administration resulted in greater systemic availability of drug with minimal metabolism to DEO. As a result, patients had greater salivary output and less dry mouth than when taking OXY ER. However, in a review by Cartwright and Cardozo on the published and presented data, they concluded that the good balance between efficacy and tolerability with OXY-TDS was offset by the rate of local skin reaction [90]. In a study assessing the achievement of patient-selected goals of therapy, OXY-TDS demonstrated a significant improvement in daily urgency episodes with no difference in the achievement of patients' own goals for therapy or HRQL compared to placebo [302]. Intravesical administration of OXY is a conceptually attractive form of drug delivery, especially for patients who already perform CIC. A specific intravesical formulation of the drug is not available and currently the oral formulation, either liquid or crushed tablet in solution, is delivered by periodic insertion through a catheter. Several nonrandomized, unblinded, and nonplacebo-controlled studies have demonstrated efficacy of this therapy in a variety of patients with neurogenic bladders showing significant improvements in cystometric capacity, volume at first IVC, bladder compliance, and overall continence [91,92]. In a study looking at the pharmacokinetics of intravesical OXY versus oral, it was found that plasma OXY levels following oral administration rose to 7.3 mg/mL within 2 hours then precipitously dropped to <2 mg/mL at 4 hours [93]. In the intravesical group, plasma levels rose gradually to a peak of 6.2 mg/mL at 3.5 hours and remained between 3 and 4 mg/mL at 9 hours. From these data, it is unclear whether the intravesically applied drug acted locally or systemically.

In a double-blind RCT in 52 women with DO, patients received once-daily intravesical OXY (20 mg in 40 mL sterile water) or placebo for 12 days [94]. The results revealed significant differences in first desire to void (from 95 mL pretreatment to 150 mL posttreatment), cystometric capacity (205–310 mL), maximum pressure during filling (16–9 cmH_2O), daytime frequency (7.5–4), and nocturia (5.1–1.8). Side effects were similar in the treated and placebo groups. For unexplained reasons, 19/23 patients in the treated group continued to have symptomatic relief after termination of the study.

OXY topical gel is a transdermal formulation, which is applied once daily to the abdomen, thigh, shoulder, or upper arm area [95]. The 1 g application dose delivers approximately 4 mg of drug to the circulation with stable plasma concentrations. In a multicenter RCT, 789 patients (89% women) with urge predominant urinary incontinence were assigned to OXY gel or placebo once daily for 12 weeks. The mean number of UUI episodes, as recorded on a 3-day voiding diary, was reduced by 3.0 episodes/day versus 2.5 in the placebo arm ($p < 0.0001$). Urinary frequency was decreased by 2.7 episodes/day and voided volume was increased by 21 mL (vs. 2.0 episodes, $p = 0.0017$ and 3.8 mL, $p =$

0.0018 in the placebo group, respectively). Dry mouth was reported in 6.9% of the treatment group versus 2.8% of the placebo group. Skin reaction at the application site was reported in 5.4% of the treatment group versus 1.0% in the placebo arm. It is felt that improved skin tolerability of the gel over the OXY TDS delivery system is secondary to lack of adhesive and skin occlusion. The gel dries rapidly upon application and leaves no residue; person-to-person transference via skin contact is largely eliminated if clothing is worn over the application site. In a phase III study of 704 with urgency predominant urinary incontinence, OXY topical gel resulted in improvement in daily incontinence episodes, frequency of micturition, voided volume, and HRQL [338]. Dry mouth occurred in 7.4% vs. 2.8% of the placebo group ($p = 0.006$).

Propiverine

Propiverine is a musculotropic smooth muscle relaxant with nonselective antimuscarinic activity. Calcium antagonistic properties have also been found, but the importance of this component for the drug's clinical effects has not been established [96]. In an analysis of nine RCTs using propiverine in a total of 230 patients, a 17% reduction in micturition frequency was seen. Additionally, there was a 64 mL mean increase in bladder capacity and a 77% subjective improvement rate. Side effects were found in 14% [97]. In a study on patients with neurogenic DO, propiverine was found to increase bladder capacity and decrease maximum detrusor contractions compared to placebo [98]. Several comparative studies have confirmed the efficacy of propiverine and suggested that the drug may be equally efficacious in increasing bladder capacity and lowering bladder pressure with fewer side effects than OXY [99,100]. A study comparing propiverine 15 mg twice daily to TOLT IR 2 mg twice daily showed comparable efficacy, tolerability, and improvement in HRQL [101]. In 2006, Abrams and colleagues presented data that refuted these prior studies [102]. In a double-blind, placebo-controlled crossover study comparing propiverine 20 mg daily, propiverine 15 mg three times daily, OXY 5 mg three times daily, and placebo, propiverine 20 mg daily was inferior to OXY in reducing IVCs. Additionally, propiverine had a more pronounced effect on gastrointestinal, cardiovascular, and visual function.

A large Japanese study of 1584 patients randomized patients to solifenacin 5 or 10 mg, propiverine 20 mg, or placebo [103]. All active treatments showed superiority to placebo in reducing voiding frequency, increasing voided volume, and improving HRQL. Solifenacin 10 mg showed greater reduction in nocturia episodes and urgency episodes and increased volume voided compared to propiverine 20 mg. Side effects were also greater for the solifenacin 10 mg group with more dry mouth and constipation.

Antimuscarinic drugs are proven efficacious and safe and are the mainstays of treatment for OAB [15]. The continuous evolution and development of newer agents stems from the fact that the ideal agent has yet to be found—one that is LUT selective, easily administered, and relatively inexpensive. This search continues and therapies with different mechanisms of action are currently being studied with great promise. Until then, the lessons we have learned from comprehensive systematic review of the literature include the following [15]:

1. Older drugs such as OXY have high withdrawal rates due to side effects, while TOLT ER has consistently favorable tolerability.
2. Newer agents such as darifenacin, solifenacin, and fesoterodine provide dose flexibility to allow individual titration for maximal efficacy versus tolerability.
3. Once-daily dosing appears to be better tolerated and potentially more efficacious in improving symptoms and HRQL.

However, head-to-head studies comparing all of these agents are limited.

Three specific areas of concern with antimuscarinic medication deserve special mention: urinary retention, cognitive impairment, and glaucoma.

In the past, there was a universal concern regarding the risk of urinary retention when prescribing antimuscarinic drugs. However, as Andersson and Wein [11] and Andersson et al. [12] propose, these drugs are usually competitive antagonists that imply that when there is massive release of ACh during voiding, the effect of the drug should be diminished. If this did not occur, urinary retention would result from inability of the bladder to contract. And in fact, at high doses, urinary retention can occur but this is uncommon at the doses typically prescribed for DO [11]. Figure 46.2 illustrates our current understanding regarding the dose range used for beneficial effects in OAB/DO, and those needed to produce a significant reduction in the voiding contraction. Monitoring PVRs in patients with prostatic enlargement or incomplete bladder emptying is still recommended; however, these diagnoses should not be considered as absolute contraindications to the use of antimuscarinics.

More recently, a concern over the association of anticholinergics and cognitive impairment has prompted several studies evaluating reaction time, memory, confusion, and other cognitive decrements. In a longitudinal cohort study involving 372 adults age >60 years without dementia at recruitment, the effects of continuous anticholinergic drug use on cognition were assessed [104]. In this study, 80% of anticholinergic users were classified as having mild cognitive impairment compared with only 35% of nonusers. There was no difference between users and nonusers in the risk of developing dementia after 8 years of follow-up. Other studies in continent elderly volunteers have shown no significant effects on cognition [27].

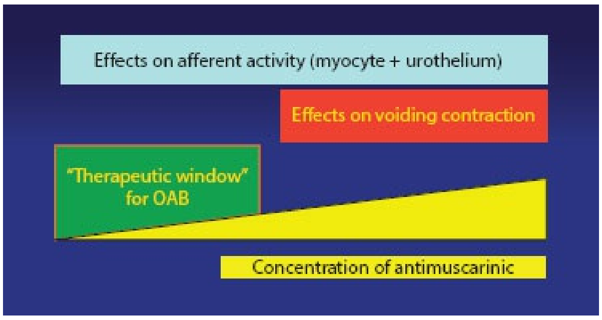
Effects on afferent activity (myocyte + urothelium)
Effects on voiding contraction
"Therapeutic window" for OAB
Concentration of antimuscarinic

Figure 46.2 Rationale for the use of antimuscarinics for treatment of OAB/DO. Blockade of muscarinic receptors at both detrusor and nondetrusor sites may prevent OAB symptoms and DO without depressing the contraction during voiding. Abbreviations: OAB, overactive bladder; DO, detrusor overactivity. (Adapted from Andersson K-E et al., Pharmacological treatment of urinary incontinence, in: Abrams P et al., eds., *Incontinence, 5th International Consultation on Incontinence*, ICUD-EAU, 2013, pp. 623–728.)

There are few data available on the cognitive consequences of anticholinergics in patients with dementia. However, cholinesterase inhibitors that are often used to improve cognition in Alzheimer's disease have been shown to precipitate urinary incontinence [105].

Patients with OAB and glaucoma present another therapeutic dilemma for urologists. Both conditions increase in prevalence with age, and it has been estimated that the conditions coexist in approximately 11.6% of female patients (in Japan) [106]. The distinction between open-angle and narrow-angle glaucoma is an important one, and when the answer is unknown, referral to an ophthalmologist is imperative. A Japanese study reported that in approximately 75% of the patients with glaucoma and OAB, the glaucoma is open angle, and this was felt to confer no additional risk to therapeutic intervention with anticholinergic medication. In the remaining 25% with narrow-angle glaucoma, the risk was felt to be elevated only if iridotomy has not been performed or has not successfully controlled the disease, reducing the true contraindication rate to approximately 8.3% of the patients with OAB. Interestingly, the same study found that 33% of the patients did not report glaucoma on their medical intake form. Underestimating the risk of glaucoma can result in blindness, albeit rarely, while overestimating (which often occurs out of fear) can result in denial of the most effective oral agents for the treatment of OAB. Complaints of eye pain, headache, or visual loss following initiation of anticholinergic therapy should be taken seriously and prompt medical advice should be sought [107].

Calcium Antagonists

Calcium channels and free intracellular calcium play a large role in excitation–contraction coupling in striated, cardiac, and smooth muscle [108]. Inhibitors of calcium channels have repeatedly been shown to inhibit bladder contraction in vitro [109], suggesting a possible role in the treatment of DO and incontinence; however, only limited clinical studies are available. Common side effects include headache, dizziness, flushing, and peripheral edema. These drugs are contraindicated in patients with poor cardiac conduction and those taking β-blockers [110].

Nifedipine

Nifedipine has been shown to be effective in inhibiting contraction in human and guinea pig bladder muscle [111]. It has also been shown to completely block the noncholinergic portion of contraction in the rabbit bladder [112]. These data suggest a potential role for nifedipine in controlling “atropine resistant” contractions, possibly in combination with an antimuscarinic agent. No clinical data are available to support this view.

Nimodipine

A double-blind, crossover RCT of 30 mg of nimodipine versus placebo in 86 patients with DO was performed [113]. There was no significant difference in the number of incontinent episodes or scores on validated questionnaires in those patients on treatment versus placebo.

Verapamil

Intravesical verapamil was compared to intravesical OXY, intravesical trospium, and placebo in 84 patients with urgency or UUI [114]. While OXY and trospium both significantly increased bladder capacity, decreased detrusor pressure, and decreased IVCs, verapamil did not.

There is no agent that will specifically block intracellular calcium release only in the bladder smooth muscle cells. Presently, there is no clinical evidence to support the use of calcium-channel inhibitors in the treatment of bladder dysfunction.

Potassium-Channel Openers

Similar to calcium channels, potassium channels also contribute to the membrane potential of smooth muscle cells and as a result affect smooth muscle tone. Potassium-channel openers relax various types of smooth muscle, including the detrusor, by increasing potassium efflux [79]. Several types of potassium-channel openers exist and at least two types, ATP dependant and big calcium activated, have been shown to induce bladder smooth muscle relaxation and reduce spontaneous contractions in human and other mammalian detrusor muscle [115]. Potassium-channel openers are not specific for the bladder, however, and are more potent in relaxing other tissues. In particular, potassium channels are expressed in vascular smooth muscle producing side effects on cardiovascular function, with potentially significant lowering of blood pressure [116]. Common side effects of this class of drug include headaches, flushing, reflex tachycardia, edema, angina, and hypertrichosis [117].

Cromakalim and Levcromakalim

Cromakalim was evaluated in 16 patients with refractory DO or neurogenic DO who had stopped other drug therapy due to intolerable side effects [118]. Of the 16 patients, 6 (38%) of them showed a decrease in micturition frequency and an increase in volume voided. Long-term observation was not possible because the drug was withdrawn from the market owing to reported adverse effects of high doses in animal toxicology studies.

Levcromakalim was administered intravenously to six patients with SCI and neurogenic DO [119]. An increase in the duration of detrusor contraction was seen but no other effects on urodynamic parameters were appreciated. A significant drop in blood pressure was seen precluding studies at a higher dose.

Pinacidil

Pinacidil is a potassium-channel opener that inhibits spontaneous myogenic contractions as well as contractile responses induced by electrical field stimulation and carbachol in isolated human detrusor [120]. A double-blind, crossover study in nine patients with DO and BOO failed to show any effects of pinacidil 25 mg daily on symptoms [121]. A significant decrease in standing blood pressure with stable heart rate was reported.

ZD0947

A double-blind, placebo-controlled, phase II study evaluated the efficacy and safety of ZD0947 at a dose of 25 mg daily for 12 weeks [122]. The results showed no improvement in voided volume, micturition frequency, or incontinence episodes.

Despite the promising preclinical efficacy data, presently potassium-channel openers are not a therapeutic option due to a lack of selectivity for the bladder over the cardiovascular tissues.

Prostaglandin and Cyclooxygenase Inhibitors

Prostaglandins (PGs) can be synthesized from the human bladder and released in response to different types of trauma [123]. They appear to cause contraction of the bladder muscle but it is unclear if PGs contribute to the pathogenesis of DO. Possible sensitization of sensory afferent nerves by PGs has been suggested by Andersson [79]. This would essentially increase the afferent input produced by a given degree of bladder filling contributing to the triggering of IVCs at a small bladder volume. Provided this theory is correct, PG synthesis inhibitors should decrease bladder contractility in response to various stimuli. However, clinical evidence for this is scant. Common side effects include hypertension, headache, diarrhea, dyspepsia, nausea, gastroesophageal reflux, and arthralgias. These drugs are contraindicated in renal impairment, advanced liver disease, and congestive heart failure and in the perioperative setting following coronary artery bypass surgery [124].

Flurbiprofen

Flurbiprofen is a PG synthesis inhibitor. A double-blind RCT evaluated the effects of flurbiprofen 50 mg three times daily in women with DO [125]. The results showed a favorable effect of the drug on delaying the intravesical pressure rise to a larger volume but did not abolish IVCs. There was a 43% incidence of side effects, primarily nausea, vomiting, headache, and gastrointestinal symptoms.

Indomethacin

A single-blind, crossover RCT in 32 patients with neurogenic DO compared indomethacin 50–100 mg daily to bromocriptine. Results showed symptomatic relief in daytime micturition frequency and nocturia in the indomethacin group. There were no urodynamic data reported. The incidence of side effects was high, occurring in 19 of 32 patients; no patients withdrew from the study.

Numerous PG synthesis inhibitors exist, most of which belong to the category of nonsteroidal anti-inflammatory drugs, but few have been studied in the treatment of DO. Despite the recent rage over cyclooxygenase inhibitors in many fields of medicine, no new RCTs in patients with DO have been published in the last decade.

β-Adrenergic Agonists

We have yet to prove whether the sympathetic nervous system plays an active role in filling/storage of the bladder in humans; however, the presence of β-adrenoceptors (AR) in human bladder muscle prompted many attempts to increase bladder capacity with β-adrenergic stimulation. Such stimulation can cause significant increases in the capacity of animal bladders that contain a moderate density of β-AR (1). In vitro studies show a strong dose-related relaxant effect of β_2-agonists on the bladder body of rabbits but little effect on the bladder base or proximal urethra. Receptor-binding studies suggest that the β-AR of the human detrusor is primarily of the β_2-subtype and favorable effects have been reported in patients with DO with the use of selective β_2-agonists [108,126]. More recently, the attention has turned to β_3-AR agonists after the real-time reverse transcriptase polymerase chain reaction data revealed a predominant expression of β_3-AR mRNA in human detrusor muscle [127]. In isolated human detrusor muscle, the selective β_3-agonists solabegron and mirabegron were both found to mediate muscle relaxation [130,131]. Facilitation of bladder storage with these agents is thought to be the result of both direct inhibition on the detrusor muscle and inhibition of sensory afferents from the bladder. β_3-AR agonists increase bladder capacity without altering voiding pressure or PVR urine volume [320]. Reported side effects include tachycardia, hypertension, headache, gastrointestinal effects, nervousness, palpitations, elevated serum glucose and lactate, and decreased serum potassium and calcium. These drugs are contraindicated in patients with uncontrolled hypertension and cardiac arrhythmias associated with tachycardia [128]. Overall, the side-effect profile is considered favorable compared to antimuscarinics and as a result has become a notable alternative agent for the treatment of OAB since its approval in the United States in June 2012.

Clenbuterol

Clenbuterol is a selective β_2-agonist. A double-blind, controlled study in women with UUI showed clenbuterol 0.01 mg three times daily had good therapeutic effect in 15 of the 20 patients [129]. This drug is not available in the United States.

Mirabegron

Mirabegron, a selective β_3-agonist, has been evaluated in human clinical trials and was approved in the United States in June 2012 for the treatment of OAB. The drug is rapidly absorbed after oral administration and 55% is excreted unchanged in the urine and 34% excreted unchanged in the feces. It is metabolized by the liver primarily by CYP3A4 and to a lesser degree by CYP2D6 [312]. Moderate renal impairment and mild hepatic impairment have little impact on drug metabolism and are not clinically important [308].

Mirabegron was evaluated in 262 patients with OAB in a phase IIA RCT versus TOLT 4 mg and placebo [132]. The treatment groups received either 100 or 150 mg twice daily and experienced a significant reduction in micturition frequency, incontinence episodes, and urgency symptoms, as well as an increase in volume voided. The drug was well tolerated in this study with the most common side effects being headache and gastrointestinal effects. A 5 beats per minute increase in pulse was noted in the 150 mg twice daily group. A phase IIB dose–response double-blind RCT was conducted using an ER form of mirabegron ranging from 25 to 200 mg once daily compared to TOLT 4 mg and placebo [304]. Dose-dependent improvements in micturition frequency and volume voided were noted. Discontinuation rates were very low ranging from 2.4% to 5.3%. The mean pulse rate increases in the 100 and 200 mg daily groups by 1.6 and 4.1 beats per minute, respectively. There was no increase in cardiovascular adverse events.

In a phase III, multicenter, double-blind RCT (n = 1328), patients with OAB were randomized to mirabegron 50 or 100 mg daily or placebo. After 12 weeks, both treatment groups demonstrated a statistically significant decrease in micturition frequency and incontinence episodes compared to placebo. The drug was well tolerated with similar rates of adverse events in the treatment and placebo groups.

In a similar European–Australian phase III study (n = 1978), patients with OAB were randomized to mirabegron 50 or 100 mg, TOLT 4 mg, or placebo [324]. Both doses of mirabegron achieved statistically significant improvement in urgency incontinence episodes and micturition frequency over placebo. The study was not appropriately powered to detect a statistical difference from TOLT but a numerical difference was noted. The incidence of hypertension and urinary tract infection (UTI) was identical in the two mirabegron and the placebo arm. The TOLT group has an increased incidence of dry mouth compared with placebo, and this was not observed with mirabegron. Post hoc subgroup analysis of this cohort was performed to assess the response to mirabegron in patients who had tried prior antimuscarinic agents [325]. Similar treatment benefit was noted in treatment-naïve patients and those who had discontinued prior antimuscarinic agents due to poor efficacy.

The safety and efficacy of mirabegron in the older population (age ≥65 and ≥75 years) were assessed with a prospective subanalysis of three phase III trials [351]. This study demonstrated that mirabegron 25 and 50 mg were effective in reducing urgency incontinence episodes and micturition frequency in this population and were well tolerated. A 1-year safety trial in this population demonstrated a sixfold higher incidence of dry mouth in the TOLT group than the mirabegron groups. Hypertension and UTI were the most common adverse effects of mirabegron. The drug was available in Japan several years before obtaining approval in the United States; the Japanese label contains a warning advising against the use of the drug in patients of reproductive age.

Terbutaline

Terbutaline, a β_2-agonist, has been reported to have a beneficial clinical effect at an oral dose of 5 mg three times a day [126]. In 15 patients evaluated, 12 became subjectively continent. Of the eight patients with documented urodynamic DO, six had stabilization of the detrusor on repeat evaluation. In nine patients, transient side effects including palpitations, tachycardia, or hand tremor occurred.

Antidepressants

Several antidepressants have been found to have beneficial effects in patients with OAB (1). These effects include facilitating urine storage by decreasing bladder contractility and increasing outlet resistance. In general, these agents have two major pharmacological actions. They have anticholinergic effects both centrally and peripherally, and they block the reuptake of serotonin and noradrenaline [133]. The most common side effect includes nausea, followed by dry mouth, dizziness, constipation, insomnia, and fatigue. Tricyclic antidepressants (TCAs) can have cardiotoxic side effects, as well as CNS effects including weakness, parkinsonian effects, fine tremor, manic or schizophrenic picture, and sedation [133]. The use of TCAs in conjunction with monoamine oxidase inhibitors is contraindicated. In general, the doses given for the treatment of DO are much lower than those prescribed for depression. Whether the same toxicity profile exists for these drugs at the lower dose remains to be seen.

Doxepin

Doxepin is a TCA that has been found to be more potent than other tricyclic compounds with respect to antimuscarinic and musculotropic relaxant activity [134]. In a double-blind, crossover RCT of women with IVCs and frequency, urgency, or UUI, it was found that this agent caused a significant decrease in nighttime frequency and incontinence episodes [135]. There was a near significant decrease in urine loss measured by pad weight and in cystometric parameters of first sensation and maximum bladder capacity. Doxepin treatment was preferred by 14 of the 19 patients, while 2 preferred placebo and 3 had no preference. During the treatment, 12 patients claimed they became continent.

Duloxetine

Duloxetine is a combined serotonin–norepinephrine reuptake inhibitor (SNRI), which has been shown to increase both bladder capacity and sphincteric muscle activity during filling and storage in the cat [136]. The data to support its role in increasing outlet resistance will be presented later. A RCT on 306 women with OAB looked at the effects of duloxetine 80 mg daily for 4 weeks, followed by 120 mg daily for 8 weeks [137]. The duloxetine group showed significant improvement in number of voids and incontinence episodes, voiding interval, and HRQL. No urodynamic indices showed improvement. The product information for this drug contains a black box warning due to increased suicidal thinking and behavior in those taking the drug for psychiatric disorders. Furthermore, the high withdrawal rate affecting 20%–40% of patients using the drug in short-term studies and up to 90% in long-term studies limits the potential clinical utility of this drug for the treatment of OAB [296].

Imipramine

Imipramine is a TCA that has been widely used clinically to treat DO despite a lack of good RCTs to document its effects. Imipramine has prominent systemic anticholinergic effects but only a weak antimuscarinic effect on bladder smooth muscle [138]. The effect of imipramine on noradrenaline reuptake is nonselective, and direct evidence suggesting it occurs in the LUT as well as the brain has been provided [139].

Clinically, imipramine seems to be effective in decreasing bladder contractility and increasing outlet resistance. In a study of elderly patients with DO, imipramine 25 mg nightly was given and increased by 25 mg every 3 days until either the patient was continent, the patient had side effects, or a dose of 150 mg was reached [140]. Of 10 patients, 6 became continent. In those patients who underwent repeated cystometry, bladder capacity increased by a mean of 105 mL and bladder pressure at capacity decreased by a mean of 18 cmH_2O. In our experience, the effects of imipramine on the LUT are often additive to those of antimuscarinic agents; however, it should be noted that the anticholinergic side effects may also be additive. A combination of low-dose imipramine and an antimuscarinic or an antispasmodic has been reported as useful for decreasing bladder contractility and detrusor pressure in some neurogenic patients [141]. However, serious toxic side effects can occur with therapeutic doses of imipramine, including orthostatic hypotension, ventricular arrhythmias, and prolongation of the QT interval. A proper risk–benefit analysis of imipramine in a good-quality clinical trial has not been performed.

Phosphodiesterase Inhibitors

PDE inhibitors were initially prescribed for the treatment of erectile dysfunction (ED) and found incidentally to improve LUT symptoms (LUTSs) in men [142]. LUT smooth muscle undergoes relaxation in the presence of cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP) [143]. PDE inhibitors block the degradation of cAMP and cGMP resulting in greater intracellular concentrations. Side effects include headache, flushing, dyspepsia, vision changes, and myalgias. This class of drug is contraindicated in patients taking nitrates [34]. Tadalafil is the only PDE inhibitor approved for the treatment of LUTS and is specifically indicated in men with benign prostatic obstruction.

Sildenafil

A RCT evaluated the effects of sildenafil on ED and LUTSs in 189 men. Significant improvements in the International Prostate Symptom Score (IPSS) and HRQL were seen [144]. In the first RCT looking at sildenafil and voiding dysfunction in women, no significant differences were seen in patients with complete retention, partial retention, or obstructed voiding [145].

Tadalafil

A RCT comparing tadalafil to placebo in 281 men with ED and LUTSs produced clinically meaningful and significant symptomatic improvement in LUTS [146]. The drug was well tolerated with mild side effects.

Vardenafil

In another RCT, vardenafil 10 mg twice daily in men with ED and LUTS showed a significant improvement in IPSS and HRQL [147].

Vinpocetine

The PDE-1 inhibitor vinpocetine was evaluated in a multicenter, double-blind RCT in patients with urgency and UUI with urodynamically documented DO who failed the anticholinergic therapy [148]. The patients received either vinpocetine 20 mg three times daily or placebo. The results showed a significant reduction in micturition frequency in men; however, the remainder of assessed outcomes showed a trend toward improvement without reaching significance. The lack of side effects indicates that the dose delivered may have been too low. While large-scale studies in women using PDE inhibitors for DO have yet to be done, the early data in men suggest a possible role in the treatment of the bladder diseases. The mechanism of action to produce this beneficial effect in OAB remains unknown at this time. Few data are available regarding the use in women.

Botulinum Toxin

Botulinum toxin (BTX) is a neurotoxin produced by *Clostridium botulinum* and is a potent presynaptic inhibitor of ACh release at the neuromuscular junction of the muscle. In the bladder, cholinergic nerves play an important role in detrusor contraction and blockade of Ach is felt to play an essential role in decreasing DO in patients with OAB [321]. In addition to its effects on efferent pathways, BTX decreases the afferent sensory response of the bladder via inhibition of glutamate, substance P, and other neuropeptide release in the spinal cord [328]. Additional mechanisms of the effect of BTX on OAB symptoms may be explained by its ability to decrease expression of neurotrophic factors including nerve growth factor (NGF) and brain-derived neurotrophic factor in the bladder [335]. BTX is applied directly by cystoscopic injection into the detrusor muscle or suburothelial space producing a chemical denervation, which is reversible after approximately 6 months. Intravesical administration allows for high concentrations of the agent to reach the bladder tissue without systemic administration and resultant unsuitable levels in other organs. BTX does not cross the urothelium if instilled into the bladder and as a result injection cannot be avoided at this time [305]. BTX is considered second-line therapy in patients who are refractory to conventional oral antimuscarinic therapy or who do not tolerate it due to systemic side effects.

There are seven subtypes of BTX with subtype A (BTX-A) being the most relevant clinically. BTX-A is available under at least four different trade names, Botox® (onabotulinum toxin A), Dysport® (abobotulinum toxin A), Xeomin® (incobotulinum toxin A), and Prosigne®, and it has been found that these formulations are not equivalent. The vast majority of intravesical experience has been with

Botox®, with no bladder experience reported for Xeomin®. Botox® appears to be approximately three times more potent than Dysport® [149].

The dose and injection protocol for BTX has not been universally agreed upon and several variations exist. In the initial description, 300 units (U) of BTX-A was diluted in normal saline to a concentration of 10 U/mL. Under direct cystoscopic visualization using a 6F injection needle, 30 injections of 1 mL each were administered to the bladder wall in 30 different locations above the trigone [150]. Since that description, several other authors have described varying doses, dilutions, number of sites, and locations (trigone, suburothelial space) [151]. BTX has been approved for use in the United States at a dose of 200 U for the treatment of neurogenic DO and 100 U for the treatment of idiopathic OAB. This dose reduction was felt to appropriately balance the efficacy of treatment with risk of incomplete bladder emptying or urinary retention. There remains quite a bit of variability in dilution volume, injection volume, and number and location of injection sites.

Two phase III studies have been completed documenting the efficacy of 200 and 300 U of BTX on patients with neurogenic DO [306,314].

Cruz et al. reported a significant improvement in urinary incontinence episodes, quality of life, and urodynamic parameters in patients with multiple sclerosis (n = 154) and SCI (n = 121) treated with either 200 or 300 U of BTX compared to placebo [306]. There was no clinically relevant difference in the efficacy or duration of effect between 200 and 300 U, and the treatment was equally efficacious in patients with MS and SCI. The most frequent adverse effects reported were UTI and urinary retention, which were dose related. In patients who were not on CIC prior to BTX treatment, 30% of the 200 U groups and 42% of the 300 U group required initiation of CIC after treatment compared to 12% of the placebo group. The time to retreatment request was similar in both treatment groups (median 42.1 weeks).

Ginsberg et al. also reported a significant improvement in urinary incontinence episodes, quality of life, and urodynamic parameters in patients with multiple sclerosis (n = 227) and SCI (n = 189) treated with either 200 or 300 U of BTX compared to placebo [314]. This study also showed no clinically relevant difference in the efficacy or duration of effect between 200 and 300 U. In patients who were not on CIC prior to treatment, 35% of the 200 U group and 42% of the 300 U group required initiation of CIC after BTX treatment compared to 10% of the placebo group. Median time to retreatment request was similar for both treatment groups (36.4 weeks). Further studies are needed to assess the efficacy of 100 U in the neurogenic OAB population that voids spontaneously. Maintaining volitional voiding in the post-BTX injection phase may decrease the rate of postinjection UTI, although this is yet to be proven.

The onset of BTX-A effects is seen within the first 2 weeks after injection [152]. Urgency, nocturia, and frequency have been shown to improve as early as 2 days after BTX-A injection in neurogenic DO patients [153]. The reported duration of BTX-A following the first injection was 6–9 months [152] and duration of effect along with beneficial clinical effect after subsequent injections is maintained [154].

As clinicians and investigators gained experience and enthusiasm for BTX in neurogenic patients, the use for idiopathic OAB refractory to antimuscarinics was launched. In a double-blind RCT including 34 patients with idiopathic DO refractory to antimuscarinics, 200 U of BTX-A was studied [155]. Significant improvements in maximum cystometric capacity, frequency, and incontinence episodes were seen at 4 and 12 weeks. Despite clinical improvement, six patients (37.5%) required CIC to empty the bladder. In another RCT, 28 women with refractory idiopathic DO received BTX-A 200 U and 15 received placebo [156]. Approximately, 60% of the women who received BTX-A reported a clinical response with a mean duration of response of 373 days (compared to 62 days or less for placebo). PVR urine was increased in 43% of women in the treatment group and UTIs occurred in 75% of these women. The duration of retention following the first injection was approximately 2 months; however, following repeat injection, this duration increased to 5 months. In the largest study to date for idiopathic refractory OAB (n = 240 women), a double-blind, placebo-controlled trial of 200 U BTX versus placebo was conducted [347]. In this study, the 200 U of BTX was diluted in 20 mL of saline and injected in 1 mL aliquots in 20 bladder wall locations above the trigone. Significant reductions in voiding frequency (8.3 vs. 9.67, $p < 0.0001$), urgency episodes (3.83 vs. 6.33, $p < 0.0001$), leakage episodes (1.67 vs. 6.0, $p < 0.0001$), and incontinence rates (88% vs. 69%, $p = 0.002$) were noted at 6 months. UTI and initiation of CIC were more common after BTX injection, 31% vs. 11% and 16% vs. 4% ($p < 0.003$), respectively.

Given the degree of voiding dysfunction seen after BTX injection in patients with idiopathic DO, dose reduction studies looking at 100 U have been done. In a prospective, nonrandomized study including 100 men and women, 100 U of BTX-A was injected in 30 locations [157]. At 4 and 12 weeks follow-up, 88% of patients showed significant improvement in bladder function in regard to subjective symptoms, urodynamic parameters, and HRQL. There were four cases of urinary retention. Dmochowski et al. performed a large phase II, multicenter, dose-escalating RCT ($n = 313$) with BTX doses ranging from 50 to 300 U [309]. Doses of 100 U and greater were found to demonstrate durable efficacy with doses greater than 150 U contributing minimal additional benefit. Dose-dependent increases in PVR and the need for CIC were demonstrated. This study concluded that 100 U was the ideal dose to balance symptom relief and safety concerns for the treatment of refractory idiopathic OAB. Subanalysis of this study concluded that the presence of DO on baseline urodynamics was not necessary for successful treatment [337]. It was noted that clinical improvements and improvements in urodynamic parameters generally trended together.

BTX has also been compared to antimuscarinics in patients with nonrefractory idiopathic OAB [350]. This double-blind, placebo-controlled trial randomized women ($n = 249$) with urgency incontinence to anticholinergic therapy (solifenacin 5 mg, dose escalation to 10 mg or change to trospium XR 60 mg as needed) plus intradetrusor injection of saline or 100 U of intradetrusor BTX plus oral placebo. No difference was detected in reduction of urgency incontinence episodes between the two groups. Complete resolution of incontinence was significantly better in the BTX group (27% vs. 13%, $p = 0.003$). The anticholinergic group had a higher rate of dry mouth (46% vs. 31%, $p = 0.002$) but lower rates of catheter use (0% vs. 5%, $p = 0.01$) and less UTIs (13% vs. 33%, $p < 0.001$).

BTX in the elderly has been reported in 21 patients with a mean age of 81.2 years (range 75–92). One month after treatment with 200 U, 76% of patients reported greater than 50% improvement in symptoms. Mean duration of effect was 7.1 months. No treatment-related complications were reported.

Side effects of intravesical BTX include elevated PVR, urinary retention, and UTI [158].

BTX appears to be an effective addition to the armamentarium of therapies for the treatment of neurogenic and idiopathic OAB. Further studies are needed to determine optimum dosage, location, and methods of injection. The case for usage in patients with neurogenic OAB on CIC who leak between catheterizations seems clearer than in patients with idiopathic OAB or neurogenic OAB not on CIC, in whom the PVR issue has yet to be clarified.

Polysynaptic Inhibitors

Baclofen

Baclofen depresses synaptic excitation of motor neurons in the spinal cord and normalizes interneuron activity [159]. It has been found useful for the treatment of skeletal spasticity due to a variety of causes, and oral baclofen was tried in patients with idiopathic DO; however, its efficacy was poor likely due to the fact that it does not cross the blood–brain barrier [160]. Intrathecal baclofen has been shown to be useful in some patients with spasticity and bladder dysfunction [161]. All patients reported marked symptomatic improvement. Increases in bladder compliance and capacity were seen. Side effects of baclofen include drowsiness, vertigo, insomnia, weakness, ataxia, slurred speech, and psychiatric disturbances [162].

Other Potential Agents

Estrogen

The hormonally sensitive tissues of the bladder, urethra, and pelvic floor may play a role in voiding mechanisms. Noteworthy scientific work has been done looking at the effects of estrogen and its receptors on the LUT. Two types of estrogen receptors (α and β) have been identified in the trigone of the bladder, urethra, vagina, levator ani muscles, pelvic fascia, and the supporting ligaments [163]. In fact, all four layers of the urethra (epithelium, vasculature, connective tissue, and muscle) are estrogen sensitive and thought to play a role in maintaining positive urethral pressure. Menopause causes marked decline in the presence and expression of both α- and β-receptor subtypes. Epidemiological studies have implicated estrogen deficiency, as a result of menopause, in the etiology of voiding symptoms that occur as women age. However, the role of estrogen replacement for the treatment of LUTSs remains controversial.

It has been recognized that estrogen therapy has little effect in the management of SUI (this topic will be addressed further later) [164]. Estrogen may be of benefit in the treatment of irritative voiding symptoms including urgency, frequency, and UUI. It is unclear whether this is the effect of the drug on the reversal of urogenital atrophy or direct action on the LUT. One difficulty in interpreting the available conflicting data on the topic is the use of several difference estrogen preparations, doses, routes of administration and the inconsistent use of concomitant progesterone. There is good evidence that urogenital atrophy, both the symptoms and cytological changes, can be reversed by treatment with low-dose vaginal estrogen.

Estrogen is hypothesized to be able to affect LUTSs by several potential mechanisms including increasing urethral resistance, raising the sensory threshold of the bladder [165], and promoting relaxation of the bladder via the β_3-AR [166]. In the ovariectomized rabbit, estrogen replacement has been shown to decrease muscarinic receptor density thereby diminishing contractile response [167]. Estradiol has also been found to reduce the frequency and amplitude of rabbit spontaneous rhythmic detrusor contractions [168].

In the human clinical literature, conflicting data on the efficacy sustained release 17β-estradiol vaginal tablets for urgency and UUI exists. Cardozo et al. performed a RCT in 110 women with urgency, frequency, and UUI [169]. After 3 months of treatment, they were unable to show objective evidence of a reduction in urinary frequency or urgency. In a subset of patients with pretreatment urodynamic urgency without DO, visual analog scales posttreatment showed a reduction in urgency symptoms. The authors hypothesized that the symptomatic improvement in this group was likely related to the treatment of their urogenital atrophy. They concluded that “improvement in LUT pathology can not be expected unless it is due to estrogen deficiency.” A further RCT on 154 women using the same estrogen preparation showed a significant improvement in subjective frequency, urgency, and urge and SUI. No urodynamic assessment was performed in this study [170].

A systematic review of the effects of estrogen on OAB was performed by Cardozo et al. and identified 11 RCTs with 236 women receiving estrogen and 230 placebo controls [171]. Statistically, significant improvements in urinary frequency, urgency, number of incontinence episodes, first sensation to void, and bladder capacity were found for patients taking estrogen therapy. Separate analysis for systemic and locally applied estrogen revealed that local therapy, but not systemic, had a significant beneficial effect on all outcome variables. Systemic estrogen did have a beneficial impact on incontinence episodes and first sensation to void.

Major concerns about the use of estrogen must be addressed. Common adverse effects include anxiety, insomnia, irritability, mood disturbances, melasma, rash, pruritus, breast enlargement, breast pain, increase in high-density lipoprotein cholesterol and triglycerides, glucose intolerance, hot flashes, change in libido, dysmenorrhea, vaginal discharge, and arthralgias. Estrogen is contraindicated in women with hepatic dysfunction. Results of the Women’s Health Initiative (WHI) study clearly established a small but significant increase in the risk of breast cancer in estrogen–progestin combination therapy given for >3 years [172]. Unopposed estrogen in postmenopausal women increases the risk of endometrial carcinoma by 5–15-fold. However, coadministration with progestin eliminates this risk [172]. The Heart and Estrogen Replacement Study (HERS) together with the results of WHI unequivocally establish that the combination estrogen–progestin does not protect against coronary heart disease [172]. The risk of thromboembolic disease is clearly elevated in women taking oral estrogens with a history of preexisting cardiovascular disease [172].

The female LUT is greatly influenced by estrogen throughout life. The LUTSs that temporally coincide with menopause may or may not be the result of estrogen deficiency. Regardless, estrogen replacement has produced conflicting results in improving symptoms. Most authors believe that urogenital atrophy is the result of estrogen deficiency and responds well to estrogen replacement, especially locally. In some cases, irritative urological symptoms (usually in combination with vaginal symptoms) may result from atrophy and may respond to estrogen therapy [173]. At the current time, there is little evidence to support the primary use of estrogen therapy alone for the treatment of OAB symptoms. Further studies are needed to define its role as an adjuvant therapy in the treatment of OAB and perhaps provide a strong argument for primary use. Of great interest would be a study looking at the role of prophylactic estrogen versus that of therapeutic estrogen on LUTS development and progression.

Gabapentin

Gabapentin was originally designed as an anticonvulsant, but now has expanded indications for neuropathic pain, anxiety, and sleep disorders [174]. In a study of 16 patients with neurogenic DO, the efficacy of gabapentin was explored [175]. Results showed significant improvement in urodynamic parameters, particularly IVCs, and a reduction in irritative voiding symptoms. No adverse events were recorded. The authors hypothesized that DO may be controlled by modulating the afferent input from the bladder and the excitability of the sacral reflex center. In a second study of 31 patients with refractory OAB, 14 patients reported subjective improvement of their frequency [176]. Of these patients, 8 were still on the drug 1 year later with persistent efficacy. Adverse effects of gabapentin include somnolence, dizziness, ataxia, fatigue, diarrhea, tremor, and nystagmus [177]. Further studies that include a clarification of the recommended dosages are needed.

NK1-Receptor Antagonists (Aprepitant)

Tachykinins are a class of neuropeptides that includes substance P, neurokinin A, and neurokinin B, which function as sensory neurotransmitters. Their respective receptors, NK1, NK2, and NK3, are found in various areas of the brain and spinal cord and may play a role in DO [178]. NK1- and NK2-receptor antagonists were administered to rats undergoing awake cystometry and both a dose-dependent decrease in detrusor pressure and an increase in bladder capacity were seen [179]. A combination of the two drugs caused an additive effect. In animals with BOO, the antagonists produced urinary retention at a high rate. The authors concluded that NK1 and NK2 receptors may be involved in micturition control.

Aprepitant, an NK1-receptor antagonist used to treat nausea and vomiting in patients on chemotherapy, was found to improve OAB symptoms in a double-blind RCT of 125 postmenopausal women [180]. The drug significantly decreased micturition frequency and number of urgency episodes as reported on a 4–10-day voiding diary. Despite statistical significance, the clinical significance of these findings is questionable. With respect to micturition frequency, a reduction of 1.3 episodes/day was seen in the treatment group compared to 0.4 episodes/day in the placebo group. Urgency episodes were reduced by 1.8/day in the treatment group and 0.5/day in the placebo group. The mean number of UUI episodes and total urinary incontinence were also reduced in the treatment group (−1.5 vs. −1.1 and −1.5 vs. −1.2, respectively), although not significantly. Aprepitant was well tolerated in this study.

In a multicenter, double-blind RCT, 476 patients with OAB were randomized to the NK-1 receptor antagonist serlopitant (0.25, 1, or 4 mg/daily), TOLT 4 mg daily, or placebo [313]. Mean reduction in micturition episodes was significant for serlopitant 0.25 (−1.1) and 4 mg daily (−1.1), and for TOLT (−1.5) compared to placebo (−0.5), but not for serlopitant 1 mg (−0.8). A dose–response relationship was not demonstrated for serlopitant. TOLT was superior for most endpoints studied. Dry mouth was reported in 3.3% of those on serlopitant, 4.6% on placebo, and 8.8% on TOLT. The drug was well tolerated.

Side effects include fatigue, nausea, constipation, diarrhea, weakness, hiccups, hypotension, dizziness, dyspepsia, neutropenia, leucopenia, and proteinuria [181].

Tramadol

Tramadol is a widely prescribed analgesic that is centrally acting and has dual mechanisms of action [182]. The drug is a weak opioid receptor agonist but its metabolites are nearly as effective as morphine at the opioid receptor. Additionally, the drug and its metabolites inhibit serotonin and noradrenaline reuptake. This drug profile may be particularly useful in the treatment of DO as shown in a RCT with duloxetine [137]. Animal studies have shown that tramadol abolishes experimentally induced DO [183]. In a double-blind RCT of 76 patients with idiopathic DO, tramadol 100 mg twice daily caused significant reduction in frequency and number of incontinence episodes [184]. Urodynamic parameters also showed improvement. Side effects of this drug include flushing, dizziness, headache, insomnia, somnolence, pruritus, constipation, nausea, vomiting, dyspepsia, hot flashes, diaphoresis, and weakness [185].

Increasing Bladder Capacity/Decreasing Sensory Input

Vanilloids

Relatively recently, the concept of blocking afferent nerves as a mechanism for controlling the micturition reflex has gained momentum as a potential therapeutic target in the treatment of OAB.

Afferent blockade would, at least in theory, be more desirable since it would block the micturition reflex rather than blocking the contraction of the detrusor.

There appears to be an upregulation of C-fiber afferent neurons in the bladders of patients with SCI [186] and chronic BOO [187] and those with idiopathic DO [188]. It has also been found that these upregulated C-fibers, in the bladders of patients with neurogenic DO, have increased expression of the vanilloid receptor, transient receptor potential vanilloid-1 (TRPV1) [189]. This receptor naturally responds to noxious stimuli including acidic pH, high temperatures, and spicy peppers [190]. A number of vanilloids, most notably capsaicin and resiniferatoxin (RTX), can also bind to this receptor creating an inhibitory effect. Side effects of these drugs tend to be local in nature and may include transient burning and stinging, elevated PVR, urinary retention, and UTIs.

BTX

As mentioned earlier, BTX produces a muscular paralysis in the bladder that improves DO. Additionally, BTX-A may decrease levels of neurotrophic agents in the bladder decreasing visceral afferent nerve transmission. NGF, one of these agents, is important in sensory nerve growth, maintenance, and plasticity. Generally, patients with neurogenic DO are found to produce greater levels of NGF in the bladder than controls. A significant decrease in NGF can be detected after intravesical administration of BTX pointing to another possible mechanism whereby BTX acts on the bladder [191].

Capsaicin

Capsaicin binds to TRPV1 and causes depolarization and excitation of sensory nerve fibers followed by a refractory period. Repeated or high-dose exposure causes desensitization, inactivating the nerve terminal. Systemic and topical capsaicin produce a reversible antinociceptive and anti-inflammatory action after an initially undesirable analgesic effect [192]. In a noncontrolled study of six patients, intravesical instillation of capsaicin (0.1–10 μM) produced a dose-related reduction in first desire to void, bladder capacity, and voiding pressure [193]. Five patients reported marked attenuation of symptoms beginning 2–3 days after instillation and lasting for 4–16 days; after that time, the symptoms gradually reappeared but were no worse. During instillation, patients reported a warm burning sensation in the suprapubic area that was felt in the urethra during voiding. Fowler and colleagues [194] reported considerably higher doses (1 or 2 mmol/L) in 12 patients with SCI and intractable urinary incontinence and two patients with idiopathic DO. Nine patients showed improvement in bladder function lasting for between 3 weeks and 6 months. Urodynamics revealed an increase in bladder capacity and a decrease in maximum detrusor pressure. There were no reported complications. In a larger study on 79 patients with 5-year follow-up, De Ridder and colleagues found intravesical administration of 1–2 mmol/L of capsaicin produced, complete continence in 44% of patients, satisfactory improvement in 36%, and failure in 20% [195]. Clinical benefit from single instillation lasted 3–6 months. Other studies have shown no beneficial effects of capsaicin with marked reactive changes of the urothelium [196]. Only one RCT has compared capsaicin to 30% ethanol, the vehicle solution [197]. The 10 patients randomized to capsaicin had significant decreases in voiding frequency, urinary leakage, and maximum detrusor pressure and significant increase in cystometric capacity. These changes were not seen in the control group who received the vehicle, 30% ethanol. Side effects consisted primarily of instillation triggered suprapubic pain, urgency, hematuria, and autonomic dysreflexia and were seen in seven patients from each group. The authors concluded that the side effects of capsaicin are attributable to the vehicle. Further studies by the same group showed that 1 mmol/L capsaicin diluted in glucidic solvent produced favorable and similar results as RTX 100 nMol/L diluted in 10% ethanol [198]. Neither group experienced significant side effects and the tolerance of the new capsaicin solvent was excellent.

Resiniferatoxin

RTX is an analog of capsaicin that is approximately 1000 times more potent for desensitization, but much less potent for excitation [199]. Several small, open-label studies showed beneficial effects of RTX with reduction in micturition frequency and incontinence episodes [198]. In a double-blind, placebo- controlled trial of RTX in 28 patients with neurogenic DO, a significant decrease in micturition frequency and incontinence episodes and an increase in bladder capacity were seen [200]. In a study comparing RTX to BTX-A in patients with neurogenic DO, both neurotoxins improved bladder capacity and reduced the number of incontinence episodes [201]. BTX-A, however, was considered more effective. In 54 patients with idiopathic DO, a RCT showed RTX is effective in improving incontinence [202]. Rios and colleagues, however, were unable to replicate those results in their RCT of 58 patients with idiopathic DO [203]. They showed no significant difference between a single dose of RTX 50 nM and placebo. The variability in clinical results may stem from the fact that different origins of RTX and different preparation techniques may cause substantial differences in the amount of drug actually delivered.

Overall, intravesical capsaicin and RTX may be promising therapy for DO and possibly sensory dysfunction of the LUT; however, many problems exist. Optimal dosage, method, and timing of delivery, as well as delivery vehicle, remain unclear. TRPV1 antagonists that block rather than desensitize the receptor are entering preliminary clinical trials.

Increasing Outlet Resistance

As mentioned earlier, decreased outlet resistance may manifest from damage to the smooth or striated sphincter secondary to surgical, obstetric, or other mechanical trauma, or degeneration of innervation with loss of neuronal mass secondary to neurological disease, aging, or trauma [4]. In addition, in women it may result from decreased pelvic floor support of the bladder outlet. Clinically, this manifests as effort related or SUI or, when severe, as complete gravitational incontinence. Treatment is aimed at increasing outlet resistance. Outlet resistance, at least as reflected by urethral pressure measurements, does not seem to be clinically affected by anticholinergic therapy.

Alpha-Adrenergic Agonists

The bladder neck and proximal urethra contain a preponderance of α-adrenergic receptor sites, which, when stimulated, produce smooth muscle contraction and an increase in maximal urethral pressure (MUP) and maximal urethral closure pressure (MUCP) [1]. The urethral rhabdosphincter, which is made up of striated muscle, is innervated by Onuf's nucleus and responds to noradrenaline via α1-AR receptor-dependent depolarization [353]. α-Adrenergic stimulation generally increase outlet resistance to a variable degree but are most often limited by their potential side effects including blood pressure elevation, anxiety, insomnia, headache, tremor, weakness, palpitations, cardiac arrhythmia, and respiratory difficulties. These agents should be used with caution in patients with hypertension, cardiovascular disease, and hyperthyroidism [204].

Ephedrine

The use of ephedrine to treat SUI was mentioned as early as 1948 [204]. This is a noncatecholamine sympathomimetic agent that enhances release of noradrenaline from sympathetic neurons and directly stimulates both α- and β-ARs. The oral adult dosage is 25–50 mg four times daily [205]. In 38 patients with sphincteric incontinence treated with ephedrine sulfate, 27 reported "good-to-excellent" results. The beneficial effects were most often achieved in those with minimal to moderate incontinence symptoms; little benefit was achieved in patients with severe SUI [205].

Midodrine

Midodrine is a long-acting α-adrenergic agonist reported to be useful in the treatment of seminal emission and ejaculation disorders following retroperitoneal lymphadenectomy. Treatment with 5 mg twice a day for 4 weeks in 20 patients with SUI produced a cure in 1 and improvement in 14. The MUCP rose by 8.3% and the planometric index of the continence area on profilometry increased by 9% [206].

Norfenefrine

Norfenefrine is an α-agonist given as a slow-release tablet. In a study on 20 women with SUI treated with norfenefrine, 19 reported reduced urinary leakage with 10 reporting resolution of their incontinence [207]. MUCP increased in 16 patients during treatment, the mean rise being 53–64 cmH_2O. Another study randomized 44 patients with SUI to treatment with norfenefrine (15–30 mg three times daily) or placebo for 6 weeks duration. Subjective improvement was reported in 12/23 (52%) of the treatment group versus 7/21 (33%) of the placebo group; this difference was not statistically significant. Judged by a stress test, seven patients in each group became continent with

11/23 (48%) of the treatment group improving both subjectively and objectively compared to 5/21 (24%) of the placebo group ($p = 0.09$).

Phenylpropanolamine

Phenylpropanolamine (PPA) shares the pharmacological properties of ephedrine and is approximately equal in peripheral potency while causing less central stimulation. It was available in 25 or 50 mg tablets and 75 mg timed-release capsules and was a component of numerous proprietary mixtures marketed for the treatment of nasal and sinus congestion and appetite suppression [208]. After a report that the risk of hemorrhagic stroke was 16 times greater in women <50 years of age who had been taking PPA as an appetite suppressant and three times higher in women who had been taking the drug for <24 hours as a cold remedy, PPA was removed from the market in the United States [209].

Pseudoephedrine

Pseudoephedrine, a stereoisomer of ephedrine, is used for similar indications and carries similar precautions. The adult dosage is 30–60 mg four times a day, and the 30 mg dose is available in the United States without prescription.

A recent Cochrane review evaluated randomized and quasi-RCTs in adults with SUI treated in at least one arm of the trial with an adrenergic agonist drug [210]. The number of eligible trials that were identified involving 1099 women is 22 (there were no controlled trials reporting on the use of these drugs in men). The authors concluded, “there was weak evidence to suggest that use of an adrenergic agonist was better than placebo treatment.” They also reported a similar adverse events profile for adrenergic agonists and placebo.

α_2-*AR Antagonists*

Early data in rats following spinal cord transaction suggest a potential role for α_2-antagonists in the treatment of SUI [211]. Potential mechanisms of action include CNS inhibition of the release of glutamate, an excitatory neurotransmitter released at nerve terminals to modulate the continence reflex in response to increases in intra-abdominal pressure. Essentially, α_2-antagonists may add to striated sphincter activity by inhibiting an inhibitory action on Onuf’s nucleus.

β-*Adrenergic Antagonists and Agonists*

Theoretically, β-adrenergic antagonists might be expected to “unmask” or potentiate α-adrenergic effect, thereby increasing urethral resistance. The opposite effect may be expected with β-adrenergic agonists with a decrease in urethral pressure, but β-agonists have been reported to increase the contractility of fast-contracting striated muscle fibers and suppress slow-contracting fibers [212].

Clenbuterol

Clenbuterol, a selective β_2-agonist, has been reported to potentiate field stimulation–induced contraction of periurethral muscle from the rabbit. This study led to speculation on the drugs ability to treat sphincteric incontinence and in fact, increased urethral pressures were seen with the clinical use of clenbuterol [213]. In a RCT comparing clenbuterol to pelvic floor exercises or combined therapy in 61 patients with SUI, the efficacy from the drug alone was 76.9% versus 52.6% in the exercise group and 89.5% in the combined group [214]. Further work is needed to adequately assess the effects of this drug on SUI. This drug is not available in the United States. Side effects include headache, muscle tremor, insomnia, sweating, increased appetite, palpitations, hypertension, anxiety, and hyperglycemia [215].

Propranolol

Propranolol, a β-antagonist, has been reported to have beneficial effects in the treatment of SUI; however, no RCTs have been performed for this indication. In one study, a dose of 10 mg four times daily (a relatively small dose) was found to be effective, but these results became manifest only after 4–10 weeks of treatment [216]. This is a difficult phenomenon to explain as cardiac effects of the drug occur rather promptly. Potential side effects, including heart failure and increased airway resistance, have limited its acceptance as a therapeutic agent for SUI. Side effects include bradycardia, hypotension, confusion, depression, dizziness, fatigue, lethargy, insomnia, bronchospasm, constipation, and diarrhea. Propranolol is contraindicated in patients with uncompensated congestive heart failure, severe heart block, and severe asthma or chronic obstructive pulmonary disease [217].

Antidepressants

Duloxetine

Duloxetine, as mentioned earlier, is a combined SNRI FDA approved in the United States for depression, diabetic neuropathic pain, and generalized anxiety disorder and licensed in the European Union for the treatment of SUI. It has been shown to increase sphincteric muscle activity during the filling/storage phase of micturition with no effect on sphincter function during voiding in a cat model of irritated bladder [218]. Duloxetine exerts its effects on serotonin and norepinephrine nerve terminals by prevention of reuptake [346]. These nerve terminals are dense in spinal areas associated with LUT function (pudendal nerve and Onuf's nucleus) and activation leads to rhabdosphincter contraction. The innervation of the rhabdosphincter is felt to be distinct from the innervation of the surrounding levator ani muscles [345]. It has also been noted that duloxetine increased bladder capacity, as noted earlier, probably through a CNS effect. The effects on the sphincter were reversed by α_1-adrenergic and $5HT_2$-serotonergic antagonism, while the effects on the bladder were provoked by serotonin and noradrenaline in the synaptic cleft. Duloxetine is lipophilic, well absorbed, and extensively metabolized [219].

There have been several RCTs documenting the effects of duloxetine in the treatment of SUI. Dmochowski and colleagues enrolled 683 patients in a double-blind RCT comparing duloxetine 40 mg twice daily to placebo [220]. There was a 50% decrease in incontinence episodes in the duloxetine group compared to 27% in the placebo group; a significant improvement in HRQL was also seen in the duloxetine group. The improvements with duloxetine were associated with significant increases in the voiding interval (20 min vs. 2 min) compared to placebo. The discontinuation rate was higher in the duloxetine group (24%) than placebo (4%), most frequently due to nausea, which was usually transient.

A Cochrane review of the effects of duloxetine on SUI summarizes data from nine RCTs totaling 3060 women [221]. Cure rate in the duloxetine 40 mg twice daily group was higher than in the placebo group (10.8% vs. 7.7%, $p = 0.04$). Significant reductions in incontinence episodes and improvement in HRQL and patient global impression of improvement were seen. However, no data were available on sustainability of treatment. The estimated absolute size of effect showed that for every 100 patients treated, three patients were cured. Only one trial reported objective cure data and showed no clear difference between drug and placebo. Adverse events were common (71% vs. 59% in placebo) but were not considered serious. Nausea was the most common complaint and the incidence ranged from 23% to 25% and was the main reason for discontinuation. Other side effects reported were vomiting, constipation, dry mouth, fatigue, dizziness, and insomnia. Across these six trials, 17% in the drug group withdrew versus 4% in the placebo arm. The authors conclude that more research is needed to determine whether duloxetine is clinically effective and cost effective compared to the other minimally invasive or more invasive treatment options available.

More recently, Bent et al. evaluated the effect of duloxetine 40 mg twice daily versus placebo in 588 women with mixed urinary incontinence [298]. They found a significant reduction in both urgency incontinence episodes (58% vs. 40%, $p < 0.001$) and stress incontinence episodes (59% vs. 43%, $p < 0.001$) compared to placebo. Significant improvements were also reported in quality-of-life scores and patient impression of improvement. Nausea (18% vs. 4.5%), dry mouth (12% vs. 2.8%), dizziness (9.7% vs. 2.4%), constipation (8.3% vs. 4.2%), and fatigue (6.7% vs. 2.8%) were the primary adverse effects.

Schagen van Leeuwen et al. evaluated the safety and efficacy of duloxetine in a RCT involving 265 elderly women (≥65 years) with SUI or stress predominant mixed incontinence [340]. They found a significantly greater reduction in incontinence episodes compared to placebo (−52.47% vs. 36.7%, $p < 0.001$). Secondary outcomes including pad use, mean time between voids, quality of life, and global impressions of improvement were all significantly improved compared to placebo. Adverse drug effects include dry mouth, fatigue, constipation, and hyperhidrosis were significantly more common in women taking duloxetine.

Persistence on therapy was studied and found to be quite low with only 31% of the originally 228 patients enrolled still on therapy beyond 4 weeks [349]. At 6 months, only 10% remained on therapy, which remained stable at 9% at 1 year. More than half of participants reported side effects as the reason for discontinuation and 33% reported lack of efficacy. One year after enrollment, 82% of the original cohort elected to undergo a midurethral sling procedure for treatment of their stress incontinence. In a study assessing the maintenance of efficacy of duloxetine, Bump et al. reported persistence on therapy at 1 year to be 42.5% of a cohort of 1424 [301]. Of those who continued, >80% reported they were at least "better since starting treatment" based on the Patient Global Impression of Improvement measure. In the same manuscript, a separate cohort of 2758 patients reported a median reduction in incontinence episodes of 50%–77% and a Patient Global Impression of Improvement of at least "better" in 70%–88%, both of which remained stable over 72 weeks of therapy.

Where duloxetine fits in the treatment algorithm for SUI is likely as a second-line agent for women unable or unwilling to undergo surgery as suggested by Shaban [342] and Robinson [336].

There is a "black box" warning of "increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants for major depressive disorder and other psychiatric disorders" [311]. Other warnings include risk for hepatotoxicity in patients with substantial alcohol use or chronic liver disease, orthostatic hypotension, serotonin syndrome, withdrawal symptoms with abrupt discontinuation, and increase concentration of drug with inhibitors of CYP1A2 and CYP2D6. The most common adverse effects compared to placebo are nausea (24% vs. 8%), dry mouth (13% vs. 5%), fatigue (10% vs. 5%), somnolence (10% vs. 3%), insomnia (10% vs. 6%), constipation (10% vs. 4%), and dizziness (10% vs. 5%) [311,342].

Imipramine

The actions of imipramine have been discussed in further detail earlier. On a theoretical basis, an increase in urethral resistance might be expected if an enhanced α-adrenergic effect at this level resulted from an inhibition of noradrenaline reuptake. However, imipramine also causes α-adrenergic blocking effects, at least in vascular smooth muscle. Many clinicians have noted improvement in patients treated with imipramine primarily for DO but who had in addition some component of sphincteric incontinence. In a study of 30 women with SUI who were treated with imipramine 75 mg daily for 4 weeks, 21 women reported continence; the mean MUCP for the group increased from 34.06 to 48.23 cmH_2O [222]. There are no RCTs on the use of imipramine for SUI. The safety issues (see pp. 428–429) are potentially significant. Adverse effects are listed in pp. 428–429.

Estrogens

Although estrogens have been recommended for the treatment of incontinence for many years, there remains considerable controversy over the risk/benefit ratio for this purpose. Numerous clinical studies exist; however, little consistency in the methodology or delivered drug makes interpretation of the available data problematic. As mentioned in the section earlier on estrogen treatment for OAB, menopause causes marked decline in the presence and expression of both α- and β-estrogen receptor subtypes. After menopause, urethral pressure parameters normally decrease slightly, and although this change is generally conceded to be related in some way to decreased estrogen levels, it is still largely a matter of speculation whether the actual changes occur in the smooth muscle, blood circulation, supporting tissues, or mucosal seal mechanism [223].

Two meta-analyses have shed some light on the use of estrogen therapy in the treatment of SUI. The Hormones and Urogenital Therapy Committee reviewed 166 articles containing 6 controlled and 17 uncontrolled trials [165]. They were able to show subjective improvement in urinary continence, but when objective urine loss was measured, there was no significant change. Only one study showed an increase in MUCP. In the second meta-analysis, the authors concluded that "published trials do not support estrogen replacement as efficacious therapy for SUI" [224].

In an open comparative crossover RCT in 20 postmenopausal women with SUI, both vaginal estriol suppositories 1 mg daily and oral PPA 50 mg twice daily increased the MUCP and the continence area on profilometry [225]. PPA was clinically more effective than estriol but not sufficiently so to obtain complete continence. With combined therapy, eight patients became completely continent, nine were considerably improved, and only one remained unchanged. Two patients dropped out of the study because of side effects. PPA is no longer on the market, but this study suggests estrogen may have a role in combination therapy with α-agonists.

Secondary analysis of 1525 participants of HERS who were randomly assigned to hormone therapy (n = 768) or placebo (n = 757) revealed greater worsening of incontinence symptoms in the treatment group (39% vs. 27%, $p < 0.001$). Review of the data from the WHI study on 23,296 postmenopausal women revealed that after 1 year of use hormone therapy increased all types of urinary incontinence, with SUI being the most common [226].

These women were randomized based on hysterectomy status to estrogen alone, estrogen plus progesterone, or placebo. Estrogen alone, or in combination with progesterone, was shown to increase the risk of incontinence among continent women and worsen incontinence in mildly symptomatic women.

A review article by Cardozo concluded that there is no convincing evidence that estrogen improves SUI; however, there is a suggestion that vaginal estrogen alleviates urgency, UUI, frequency, nocturia, and dysuria [227]. Vaginal estrogen is thought to exert this positive effect via improvement in cytological changes secondary to urogenital atrophy [228].

The debate over the use of estrogen runs much deeper than its potential effects on the urinary tract. Impact on cardiovascular disease, osteoporosis, vasomotor symptoms, breast cancer, and other conditions must factor into the risk–benefit analysis. Adverse effects are listed in pp. 430–431.

FACILITATION OF BLADDER EMPTYING

Absolute or relative failure to empty the bladder results from decreased bladder contractility, increased outlet resistance, or both [2]. Failure of adequate bladder contractility may result from temporary or permanent alterations in any one of the neuromuscular mechanisms necessary for initiating and maintaining a normal detrusor contraction. In a neurologically normal individual, inhibition of the micturition reflex may be secondary to painful stimuli, especially stimuli from the pelvic and perineal areas, or it may be psychogenic. Some drug therapies may inhibit bladder contractility through neurological or myogenic mechanisms. Bladder smooth muscle function may be impaired from over distension, severe infection, or fibrosis. Increased outlet resistance is generally secondary to anatomic obstruction but may be secondary to a failure of coordination of smooth or striated sphincter during bladder contraction. The treatment of failure to empty consists of attempts to increase intravesical pressure, to facilitate the micturition reflex, or to decrease outlet resistance—or some combination of the aforementioned treatment.

Facilitating Bladder Contraction

Parasympathomimetic Agents

Because a major portion of the final common pathway in physiological bladder contraction is the stimulation of parasympathetic postganglionic muscarinic cholinergic receptor sites, agents that imitate the actions of ACh might be expected to be effective in treating patients who cannot empty their bladder because of inadequate bladder contractility. ACh itself cannot be used for therapeutic purposes because of its actions at central and ganglionic levels and because of its rapid hydrolysis by acetylcholinesterases and butyrylcholinesterases [229].

Bethanechol Chloride

Many ACh-like drugs exist, but only bethanechol chloride (BC) has a relatively selective action in vitro on the urinary bladder and gut, with little or no nicotinic action [230]. In vitro, BC causes a contraction of smooth muscle from all areas of the bladder [231]. For more than 60 years, BC has been recommended for the treatment of the atonic or hypotonic bladder and it has been reported to be effective in achieving "rehabilitation" or the chronically atonic or hypotonic detrusor [232]. When so used, it is recommended that the drug be initially administered subcutaneously in a dose of 5–10 mg every 4–6 hours, along with an intermittent bladder decompression regimen. The patient is asked to try to void 20–30 minutes after each dose. When the residual urine volume has decreased to an acceptable level, the dose is gradually decreased and ultimately changed to an oral dose of 50 mg four times daily. In cases of partial bladder emptying, a therapeutic trial with an oral dose of 25–100 mg four times daily may be utilized in conjunction with attempted voiding every 4 hours. BC has also been used to stimulate or facilitate the development of reflex bladder contractions in patients with spinal shock secondary to suprasacral SCI [233].

Although anecdotal success in using BC in patients with voiding dysfunction is reported, there is little or no evidence to support its success in facilitating bladder emptying in series of patients in which the drug was the only variable [234]. Short-term studies in which the drug was the only variable have generally failed to demonstrate significant efficacy in terms of urine flow and PVR [235]. In a double-blind RCT that looked at the effects of two catheter-management protocols and the effect of BC on postoperative urinary retention following gynecological urinary incontinence surgery, BC was not at all helpful [236]. In a 2010 Cochrane systematic review, no statistically significant association between successful outcome and use of cholinergic agents was reported in the setting of postoperative retention [300]. When cholinergic agents were combined with sedatives, an improved likelihood of spontaneous voiding was noted compared to placebo (RR 1.39, 95% CI 1.07–1.82).

Although BC is capable of eliciting an increase in bladder smooth muscle tension, as would be expected from studies in vitro, its ability to stimulate or facilitate a coordinated and sustained physiological bladder contraction in patients with voiding dysfunction has been unimpressive [234]. Furthermore, it has been shown that bethanechol exerts its effects on intact smooth muscle cells only and therefore idiopathic detrusor atony is poorly responsive to therapy [297,300,333]. However, due to the paucity of pharmacotherapy to improve bladder emptying, many clinicians continue to use BC in the hope of improving emptying as long as the medication is tolerated without adverse effects by the patient or is contraindicated. The potential side effects of cholinomimetic drugs include flushing, nausea, vomiting, diarrhea, gastrointestinal cramps, bronchospasm, headache, salivation, sweating, and difficulty with visual accommodation [230]. Intramuscular and intravenous use can precipitate acute and severe side effects, resulting in acute circulatory failure and cardiac arrest, and is therefore prohibited.

PGs

The reported use of PGs to facilitate emptying is based on the hypothesis that these substances contribute to the maintenance of bladder tone and bladder contractile activity [108]. PGE_2 and $PGF_2\alpha$ cause bladder contractile responses in vitro and in vivo. PGE_2 seems to cause a net decrease in urethral smooth muscle tone; $PGF_2\alpha$ causes an increase. The most common side effect reported with PG therapy is diarrhea [237].

PGE_2

Instillation of 0.5 mg PGE_2 into the bladders of 22 women with varying degrees of urinary retention resulted in acute emptying and an improvement in long-term emptying over several months in two-thirds of the patients studied [238]. In general, a decrease in the volume at which voiding was initiated, an increase in bladder pressure, and a decrease in PVR were seen. Another studied looked at the intravesical use of 1.5 mg of PGE_2 (diluted with 20 mL 0.2% neomycin solution) in patients whose bladder exhibited no contractile activity or in whom bladder contractility was relatively impaired [239]. Of 36 patients, 20 showed a strongly positive response and six showed a weakly positive response; 14 patients were reported to show prolonged beneficial effects. The authors noted that the effects of PGE_2 appeared to be additive or synergistic with cholinergic stimulation in some patients. Other studies have reported no effect of PGE_2 on urinary retention [240], with other suggesting instigation of urinary urgency, reduced bladder capacity, and bladder instability with intravesical PGE_2 [241].

$PGF_2\alpha$

Intravesical instillation of 7.5 mg $PGF_2\alpha$ produced reflex voiding in some patients with incomplete suprasacral SCI [242].

The favorable response to a single dose of drug, when present, lasted from 1 to 2.5 months. In women undergoing hysterectomy, 16 mg of $PGF_2\alpha$ in 40 mL of saline given intravesically reduced the frequency of urinary retention compared to saline instillation alone [243]. The same treatment protocol given to women undergoing other vaginal procedures did not yield these results. Daily intravesical doses of $PGF_2\alpha$ and intravaginal PGE_2 reduced the number of days required for catheterization after SUI surgery compared with a control group receiving intravesical saline [244]. Other investigators, however, have reported conflicting or negative results [240].

PGs have a relatively short half-life, and it is difficult to understand how any effects after a single application can last as long as several months. If such an effect does occur, it must be the result of a "triggering effect" on some as yet unknown physiological or metabolic mechanism. Because of the number of conflicting positive and negative reports with various intravesical preparations, double-blind RCTs would be helpful to determine whether there are circumstances in which PG usage can reproducibly facilitate emptying or treat postoperative retention. In a 2010 Cochrane systematic review, intravesical PG was noted to significantly improve spontaneous voiding in the setting of postoperative urinary retention (RR 3.07, 95% CI 1.22–7.72) [300].

α-Adrenergic Blockers

Studies in cats have demonstrated a sympathetic reflex during bladder filling that promotes urine storage partly by exerting an α-adrenergic inhibitory effect on pelvic parasympathetic ganglionic transmission [245]. Some investigators have suggested that α-adrenergic blockage, in addition to decreasing outlet resistance, may facilitate transmission through these ganglia and thereby enhance bladder contractility. Although such an effect may be due solely to an α-adrenergic effect on the outlet, it may be that α-adrenergic blockade can, under certain circumstances, facilitate the detrusor reflex, through either a direct effect on parasympathetic ganglia or an indirect one.

Opioid Antagonists

Recent advances in neuropeptide physiology and pharmacology have provided new insights into LUT function and its potential pharmacological alteration. It has been hypothesized that endogenous opioids may exert a tonic inhibitory effect on the micturition reflex at various levels, and agents such as narcotic antagonists may, therefore, offer possibilities for stimulating reflex bladder activity [1].

Naloxone

In one study on 15 patients with SCI, no significant cystometric changes following intravenous naloxone were noted [246]. Interestingly, 11 of these patients showed decreased perineal electromyographic (EMG) activity but no associated change in dyssynergia pattern was seen. Although this issue is intriguing, it is of little practical use at present. Side effects of naloxone include precipitating withdrawal in patients addicted to opioids and sedation [247].

Decreasing Outlet Resistance at the Level of the Smooth Sphincter

α-Adrenergic Antagonists

Whether or not one believes that there is significant innervation of the bladder and proximal urethral smooth musculature by postganglionic fibers of the sympathetic nervous system, one must acknowledge the existence of α- and β-AR sites in these areas [1]. The smooth muscle of the bladder base and proximal urethral contains predominantly α-ARs. The bladder body contains both types, with the β-type being more common.

The implication that α-adrenergic blockade could be useful in certain patients who cannot empty the bladder was first made by Kleeman in 1970 [248]. Krane and Olsson were among the first to endorse the concept of a physiological internal sphincter that is partially controlled by sympathetic stimulation of contractile α-ARs in the smooth musculature of the bladder neck and proximal urethra [249]. Furthermore, they hypothesized that some obstructions that occur at this level during detrusor contraction result from an inadequate opening of the bladder neck or an inadequate decrease in resistance in the area of the proximal urethra. They also theorized and presented evidence that α-adrenergic blockade could be useful in promoting bladder emptying in such a patient, one with an adequate detrusor contraction but without anatomic obstruction or detrusor external sphincter dyssynergia (DESD). Many others have subsequently confirmed the utility of α-blockade in the treatment of what is now usually referred to as smooth sphincter or bladder neck dyssynergia or dysfunction. Successful results, usually defined as an increase in flow rate, a decrease in PVR, and an improvement in the upper urinary tract appearance, can often be correlated with an objective decrease in MUCP.

One would expect such success with α-blockade in treating emptying failure to be least evident in patients with DESD, as reported by Hachen [250]. Although most would agree that α-blockers exert their favorable effects on voiding dysfunction primarily by affecting the smooth muscle of the bladder neck and proximal urethra, some information suggests that they may decrease striated sphincter tone as well. Much of the confusion about whether α-blockers have a direct, as opposed to indirect, inhibitory effect on the striated sphincter relates to the interpretation of observations of their effect on urethral pressure and periurethral striated muscle EMG activity in the region of the urogenital diaphragm. It is impossible to tell from pressure tracings alone whether a decrease in resistance in one area of the urethra is secondary to a decrease in smooth or striated muscle activity.

α-Adrenergic blocking agents have also been used to treat both the bladder and outlet abnormalities in patients with the so-called autonomous bladders [251]. These include those with myelodysplasia, sacral or infrasacral SCI, and voiding dysfunction following radical pelvic surgery. Parasympathetic decentralization has been reported to lead to a marked increase in adrenergic innervation of the bladder, resulting in conversion of the usual β-(relaxant) bladder response to sympathetic stimulation to an α-(contractile) response [252]. Although the alterations in innervation have been disputed, the alterations in receptor function have not. Koyanagi [253] demonstrated urethral supersensitivity to α-adrenergic stimulation in a group of patients with autonomous neurogenic bladders, implying that a change had occurred in adrenergic receptor function in the urethra following parasympathetic decentralization. Parsons and Turton [254] observed the same phenomenon but ascribed the cause to adrenergic supersensitivity of the urethral smooth muscle caused by parasympathetic decentralization. Nordling and colleagues [255] described a similar occurrence in women who had undergone radical hysterectomy and ascribed this change to damage to the sympathetic innervation.

The most common adverse effects reported with this class of drugs are orthostatic hypotension, abnormal or retrograde ejaculation, dizziness, diarrhea, thirst, nasal congestion, and headache. Rarely, intraoperative floppy iris syndrome can occur and cause complications of cataract surgery. There are insufficient data to conclude whether there are additive hypotensive effects with concomitant PDE-5 inhibitor use for all α-antagonists. α-Blockers are metabolized primarily by the liver, predominantly via CYP3A4 [256].

Phenoxybenzamine

Phenoxybenzamine (POB) was the α-adrenolytic agent originally used for the treatment of voiding dysfunction; it has blocking properties at both α_1- and α_2-receptor sites. Nordling and colleagues [257] demonstrated that POB and clonidine, both of which pass the blood–brain barrier, decreased urethral pressure in the striated sphincteric area but had no effect on EMG activity. They concluded that the effect of clonidine and possibly POB was elicited mostly through centrally induced changes in striated urethral sphincter tonus, and that these agents also had an effect on the smooth muscle component of urethral pressure. POB is capable of increasing bladder compliance thereby increasing storage and decreasing urethral resistance thus facilitating emptying. The initial adult dosage of this agent is 10 mg daily, and the usually daily dose for voiding dysfunction is 10–20 mg. After the drug has been discontinued, the effects may persist for days because the drug irreversibly inactivates α-receptors, and the duration of effect depends on the rate of receptor synthesis [258]. Side effects include orthostatic hypotension, reflex tachycardia, nasal congestion, diarrhea, miosis, sedation, nausea, and vomiting.

McGuire and Savastano [259] reported that POB decreased filling cystometric pressure in the decentralized primate bladder. None of these drugs, however, affected the reflex rise in either urethral pressure or EMG activity that was seen during bladder filling, and none decreased the urethral pressure or EMG activity response to voluntary contraction of the pelvic floor striated musculature.

Prazosin

In the cat, Gajewski and colleagues [260] concluded that α-blockers do not influence the pudendal nerve-dependent urethral response through a peripheral action, but prazosin, at least, can significantly inhibit this response at a central level. In 10 healthy female volunteers, Thind and coworkers [261] reported on the effects of prazosin on static urethral sphincter function. They found that the function was diminished, predominantly in the midurethral area, and hypothesized that this response was due to a decrease in both smooth and striated sphincter muscle tone, the latter as a result of a reduced somatomotor output from the CNS. α-Adrenergic blockade can also decrease bladder contractility as Jensen [262] reported, with an increase in the “α-adrenergic effect” in the bladders characterized as “uninhibited.” Short- and long-term prazosin administration increased bladder capacity and decreased the amplitude of contractions. Prazosin is a potent selective α_1-antagonist [258], with a duration of action of 4–6 hours. Therapy is generally begun in daily divided doses of 2–3 mg and can be gradually increased to a maximum daily dose of 20 mg. Side effects are similar to those listed earlier for POB. Prazosin is contraindicated in patients taking PDE-5 inhibitors.

Terazosin and Doxazosin

Terazosin and doxazosin are two selective postsynaptic α_1-blocking drugs. They have a long plasma half-life enabling their activity to be maintained over 24 hours following a single dose [263]. These drugs are most often used for the treatment of benign prostatic hyperplasia (BPH) in men due to the high α_1-receptor content of the prostate stroma and capsule. Daily doses range from 1 to 10 mg and is generally given at bedtime. Terazosin is said to have the same affinity for α_1-receptors in genitourinary as in vascular tissue and a fourfold greater selectivity for α_1-receptors than doxazosin.

Swierzewski and colleagues [264] prospectively studied the effects of terazosin on 12 patients with SCI and decreased compliance. All patients were refractory to medical therapy and on CIC. Urodynamic studies were conducted before, during, and at the conclusion of 4 weeks of therapy with 5 mg of terazosin daily. The authors found statistically significant improvements in the bladder compliance, “safe bladder volume,” and bladder pressure in all patients, with the additional benefits of decreased episodes of both urinary incontinence and autonomic dysreflexia. They speculated that the improvement was due either to a direct effect on the α-receptors of the detrusor or to a central effect but not to any effects on outlet resistance. Terazosin is contraindicated in patients taking PDE-5 inhibitors.

Tamsulosin and Alfuzosin

Tamsulosin is an α_1-blocking agent that is selective for the α_{1a}- and α_{1d}-receptor subtypes over the α_{1b}-subtype [265]. It appears to have no significant drug-related adverse effects over placebo and has less effect on blood pressure than alfuzosin. The effects of tamsulosin on resting tone and contractile behavior of the urethra in 11 healthy females were studied using urethral pressure profilometry [266]. The drug significantly reduced the mean and MUP in the proximal, middle, and distal thirds of the urethra without any effect on systemic blood pressure. In a study on the functional bladder neck obstruction diagnosed by video urodynamics, 18 women were treated with tamsulosin 0.4 mg daily for at least 30 days [267]. Repeats of video urodynamics were performed with 56% of patients showing improvement in maximum flow, PVR, and symptoms. Tamsulosin 0.2 mg daily was studied in 97 women with chronic voiding symptoms and subnormal uroflow rates [268]. After 6 weeks of treatment, all patients experienced significant improvements in symptoms score, flow rate, and PVR, with 35.1% of the women achieving a >50% reduction in voiding symptom score and >30% increase in maximal flow rate. Only one patient in this study discontinued therapy due to intolerable dizziness. Tamsulosin was also studied in a RCT involving 364 women with OAB [269]. No difference was seen in primary or secondary outcome variables. Tamsulosin was well tolerated with 4.7% of women discontinuing treatment due to adverse events. Further, well designed, RCTs are needed to document tamsulosin’s effect on the LUT in women.

Recent molecular characterization of the α_1-receptor has led to the recognition, classification, and cloning of a number of α_1-receptor subtypes. In the human prostate, there appears to be some tissue specificity in that the majority of the stromal α_1-receptors are of the α_{1a}-subtype [270]. A drug selective to the α_{1a}-subtype would be expected to cause fewer undesired effects than the less selective drugs while maintaining clinical efficacy.

Alfuzosin is a new agent that is reported to be a selective and competitive antagonist of α_1-mediated contraction of the bladder base, proximal urethral smooth muscle, and prostate capsule (in men), with efficacy similar to that of prazosin [271]. It is said to be more specific for receptors in the genitourinary tract than in the vasculature, raising the possibility that voiding may be facilitated by doses that have minimal vasodilatory effects, thus minimizing postural hypotension. A sustained release form of the drug, which allows for once-daily dosing, is available. In a placebo-controlled study [272], it was shown to have no significant incidence of adverse effects above those of placebo. In addition, effects on blood pressure (orthostatic hypotension) were minimal, supporting its selectivity of the LUT over the vasculature.

Silodosin

Silodosin is a very selective α_{1a}-antagonist with minimal α_{1b} binding and therefore minimal cardiovascular side effects. The drug has encouraging phase III data for the treatment of LUTSs in men. There are no data available in women.

Agents with α-adrenergic blocking properties have been used in patients with various types of voiding dysfunction including functional outlet obstruction, urinary retention, decreased compliance, and neurogenic and idiopathic DO. Although there remains a paucity of data regarding the use of α-blockers in women, our experience suggests that a trial of such an agent is certainly worthwhile because its effect or noneffect should become obvious in a matter of days and the pharmacological side effects are reversible. However, our results with such therapy for non-BPH-related dysfunction have not been spectacular.

Decreasing Outlet Resistance at the Level of the Striated Sphincter

No class of pharmacological agents selectively relaxes the striated musculature of the pelvic floor. Three different types of drug, all generally characterized as antispasticity drugs, have been used to treat voiding dysfunction secondary to outlet obstruction at the level of the striated sphincter: benzodiazepines (diazepam), baclofen, and dantrolene. Diazepam and baclofen act predominantly within the CNS, whereas dantrolene acts directly on skeletal muscle. Although these drugs are capable of providing variable relief in specific circumstances, their efficacy is far from complete, and troublesome muscle weakness, adverse effects on gait, and other side effects limit their overall usefulness. Benzodiazepines and baclofen are thought to exert their effects on the LUT through interactions with inhibitory neurotransmitters in the CNS, γ-aminobutyric acid (GABA), and glycine [273]. The specific substrate for spinal cord inhibition consists of the synapses located on the terminals of the primary afferent fibers. GABA is the transmitter secreted by these synapses and activates specific receptors, resulting in a decrease in the amount of excitatory transmitter released by impulses from primary afferent fibers, consequently reducing the amplitude of the excitatory postsynaptic potentials.

Benzodiazepines

Benzodiazepines potentiate the inhibitory actions of GABA at pre- and postsynaptic sites in the brain and spinal cord [274]. When presynaptic inhibition is augmented, and it is thought that the release of excitatory transmitters from afferent fibers is reduced, thereby diminishing the stretch and flexor reflexes in patients with bladder spasticity. This is a postulated mechanism of action of the muscle relaxant properties of diazepam at least [275]. Side effects include nonspecific CNS depression, manifested as sedation, lethargy, drowsiness, slowing of thought processes, ataxia, and decreased ability to acquire or store information.

There are few available published papers that provide valuable data on the use of benzodiazepines for the treatment of functional obstruction at the level of the striated sphincter. We have not found the recommended oral dose of diazepam effective in controlling the classic type of DESD secondary to neurological disease. If the cause of incomplete emptying in a neurologically normal patient is obscure and the patient has what appears urodynamically to be inadequate relaxation of the pelvic floor striated musculature (e.g., occult neuropathic bladder, the Hinman syndrome), a trial of such an agent may be worthwhile. The rationale for its use is either relaxation of the pelvic floor striated musculature during bladder contraction or that such relaxation removes and inhibitory stimulus to reflex bladder activity. However, improvement under such circumstances may simply be due to the antianxiety effect of the drug or to the intensive explanation, encouragement, and modified biofeedback therapy that usually accompanies such treatment in these patients.

Baclofen

Baclofen depresses excitation of motor neurons in the spinal cord and was originally thought to function as a GABA agonist [275]. However, its electrophysiological and pharmacological profiles differ radically from those of GABA. Because both GABA and baclofen can produce some effects that are insensitive to blockade by classic GABA antagonists, two classes of GABA receptors have been proposed: the $GABA_A$ receptor (the classic receptor) and the $GABA_B$ receptor. Baclofen does not bind strongly or specifically to classic $GABA_A$ receptors but does to the $GABA_B$ receptors in the brain and spinal membranes. Accordingly, the primary sites of action of baclofen are the spinal cord and brain. Its effect in reducing spasticity is caused primarily by normalizing interneuron activity and decreasing motor neuron activity [159].

Drug delivery often frustrates adequate pharmacological treatment, and baclofen is a good example of this. GABA's hydrophilic properties prevent it from crossing the blood–brain barrier in sufficient amounts to make it therapeutically useful. Baclofen was developed as a more lipophilic analog of GABA; however, its passage through the barrier is likewise limited, and it has proved to be a generally insufficient when given orally to treat severe somatic spasticity and micturition disorders secondary to neurogenic dysfunction [276]. Hachen [250] found that a daily oral dose of 75 mg was ineffective in patients with DESD and traumatic paraplegia, whereas a daily intravenous dose of 20 mg was highly effective. Leyson and associates [235] reported that 73% of their patients with voiding dysfunction secondary to acute and chronic SCI had lower striated sphincter responses and decreased PVRs following baclofen treatment, but only with an average daily oral dose of 120 mg. Intrathecal infusion bypasses the blood–brain barrier and cerebrospinal fluid levels 10 times higher than those reached with oral administration are achieved with much lower doses [277]. Direct administration into the subarachnoid space by an implanted infusion pump has shown promising results, not only for skeletal spasticity but also for DESD and DO. Nanninga and colleagues [278] reported on such administration to seven patients with intractable bladder spasticity: all patients experienced a general decrease in spasticity and the amount of striated sphincter activity during bladder contraction. The action of baclofen on DO is not unexpected, given its spinal cord mechanism of action, and this inhibition of bladder contractility when the drug is administered intrathecally may, in fact, prove to be its most important benefit.

Potential side effects of baclofen include drowsiness, insomnia, rash, pruritus, dizziness, and weakness. Sudden withdrawal has been shown to provoke hallucinations, anxiety, and tachycardia; hallucinations due to reductions in dosage during treatment have also been reported [214]. Development of tolerance to intrathecal baclofen with a consequent requirement for increasing doses may prove to be a problem with long-term chronic usage. Further studies on the long-term efficacy of intrathecal baclofen specifically on the LUT in patients with neurogenic bladder are anticipated.

Dantrolene

Dantrolene exerts its effect by direct peripheral action on skeletal muscle [279]. It is thought to inhibit the excitation-induced release of calcium ions from the sarcoplasmic reticulum of striated muscle fibers, thereby inhibiting excitation-contraction coupling and diminishing the mechanical force of contraction. The drug improves voiding function in some patients with classic DESD and was initially reported to be very successful in doing so [280]. In adults, the recommended starting dose is 25 mg daily, gradually increasing by increment of 25 mg every 4–7 days to a maximum oral dose of 400 mg given in four divided doses. Hackler and colleagues [281] reported an improvement in voiding function in approximately half of their patients treated with dantrolene but found that such improvement required oral doses of 600 mg daily. Although no inhibitory effect on bladder smooth muscle seems to occur [282], the generalized weakness that dantrolene can induced is often sufficiently significant to compromise its therapeutic effects.

Potential side effects other than severe muscle weakness include euphoria, dizziness, diarrhea, and hepatotoxicity. Fatal hepatitis has been reported in 0.1%–0.2% of patients treated with the drug for 60 days or longer and symptomatic hepatitis may occur in 0.5% of patients treated for more than 60 days; chemical abnormalities of liver function are noted in up to 1%. The risk of hepatic injury is twofold greater in women [107].

BTX

BTX, a potent inhibitor of ACh release at the neuromuscular junction, has been injected directly into the striated sphincter to cause relaxation in the treatment of DESD [283]. This application has led to the use of BTX in treating neurogenic and nonneurogenic causes of urethral sphincter hypertonicity that may lead to retention. Injections of 100 units of BTX-A weekly for 3 weeks can achieve duration of effect averaging 6–9 months. Fowler and colleagues [194] used BTX injection in six women with difficulty of voiding or urinary retention secondary to abnormal myotonus-like EMG activity in the striated urethral sphincter. Although voiding did not improve in any patient (attributed to the type of repetitive discharge activity present), three patients developed transient SUI, indicating that the sphincter muscle had, indeed, been weakened. Phelan and colleagues [284] performed a prospective study to assess the efficacy of injecting 80–100 units of BTX-A into the external sphincter of 13 women and 8 men with voiding dysfunction due to various causes, including DESD, pelvic floor spasticity, and bladder hypocontractility. All patients except one were able to void spontaneously, and all but two were able to discontinue catheterization. Similarly, Kuo injected 50 or 100 units of BTX-A into the urethra of 103 patients (55 women) with chronic urinary retention or severe difficulty urinating [202]. The reasons for the LUT voiding dysfunction were quite heterogeneous: DESD, dysfunctional voiding, nonrelaxing urethral sphincter, cauda equina lesion, peripheral neuropathy, and idiopathic detrusor underactivity. Subjectively, 39% had "excellent" results and 46% had "significant" improvement. There was a significant decrease in maximum voiding pressure, MUCP and PVR. In a small, double-blind RCT, the efficacy of BTX-A was compared with lidocaine [285]. This study was performed in 13 patients with DESD secondary to SCI. The injections were performed transperineally. BTX-A was superior to lidocaine, resulting in decreased PVR and MUP. Those treated with BTX-A also had an increase in patient satisfaction. Side effects of BTX were listed in pp. 429–431.

Clonidine

Clonidine is the prototypical α_2-adrenergic receptor agonist. It is considered to be a centrally acting agent with a variety of associated systemic effects including antihypertensive, antinociceptive, and antispasmodic effects. Potential effects on relaxation of the external urethral sphincter (EUS) have been reported previously [257]. Herman and Wainberg [286] administered oral clonidine (400 mcg) in three divided doses over a 16 hour period under monitored inpatient conditions to five patients with SCI with neurogenic DO and quantified effects on the EUS via needle electrodes. They found that clonidine had a profound suppressive effect on volume-induced EMG activity in the EUS in four of five patients. The one patient in whom there were only minimal effects on the EUS had received an intrathecal dose of morphine 2 days before, which the authors feel may have confounded the effects of clonidine in this patient. The authors speculate that the somewhat selective effect of clonidine on the EUS is attributable to postsynaptic suppression of excitatory spinal interneurons (unmasked by the spinal lesion) via the α_2-agonist activity of clonidine. Adverse effects included significant reductions in blood pressure and sedative effects. Further clinical studies on the effects of clonidine on the LUT and striated sphincter (as well as its clinical utility) may be limited owing to its significant effects on blood pressure.

CIRCUMVENTING THE PROBLEM

Antidiuretic Hormone-Like Agents

Endogenous production of antidiuretic hormone (ADH) serves two purposes: stimulation of water reabsorption in the renal medulla and contraction of vascular smooth muscle. A genetic or acquired defect in ADH synthesis or secretion results in central diabetes insipidus, while a defect in the ADH receptor results in nephrogenic diabetes insipidus. A relative lack in ADH is believed to be important in polyuria, specifically nocturnal polyuria [287].

Desmopressin

The synthetic ADH analog, desmopressin (DDAVP), has been used for the symptomatic relief of refractory nocturnal enuresis in children and adults [288]. More recently, it has been explored for the treatment of OAB and incontinence. The drug can be administered by oral, parenteral, or intranasal spray and effectively suppresses urine production for 7–10 hours.

Several small controlled studies on patients with multiple sclerosis and nocturia have consistently reported efficacy of DDAVP at the risk of asymptomatic or minimally symptomatic hyponatremia [289]. Further studies in nonneurological patients have confirmed the efficacy and determined effective dose regimens for the treatment of nocturia [290]. In a phase IIb study on the use of oral DDAVP in the treatment of OAB symptoms, a decrease in frequency and urgency episodes was observed. Patients also reported an improvement in HRQL with only mild side effects including headache. No hyponatremia was reported [291]. Further studies on DDAVP for the treatment of OAB and incontinence are needed.

Given the safety concerns over hyponatremia, it is recommended that the drug not be given in patients older than 79 years of age or to those with 24 hour urine volumes >28 mL/kg. It is also recommended that serum sodium levels be checked at baseline and at 3 and 7 days after starting treatment or changing dose [292]. General precautions including limiting fluid intake from 1 hour before the dose until 8 hours after, periodic blood pressure measurements, and weight measurements to monitor for fluid overload should be instituted. The original intranasal spray has been withdrawn from the market in several countries due to side effects and unpredictable absorption. Side effects include headache, hyponatremia, water intoxication, and rhinitis. DDAVP is contraindicated in patients with baseline hyponatremia and moderate to severe renal impairment [293].

Loop Diuretics

Bumetanide

A similar circumventive approach is to give a rapidly acting loop diuretic 4–6 hours before bedtime. This, of course assumes that the nocturia is not due to obstructive uropathy. A double-blind, crossover RCT of this approach using bumetanide 1 mg was performed in a group of 14 general practice patients [294]. Nocturia episodes per week averaged 17.5; with placebo, this decreased to 12 and with drug to 8. Bumetanide was preferred to placebo by 11 of 14 patients. Side effects include hyperuricemia, hypochloremia, hypokalemia, hyponatremia, hyperglycemia, and serum creatinine elevation [295].

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47 Peripheral Neuromodulation

John Heesakkers and Jetske van Breda

INTRODUCTION

Neuromodulation of the lower urinary tract is extensively applied in patients with overactive bladder (OAB) complaints. The best known and best documented technique is sacral nerve stimulation. Posterior or percutaneous tibial nerve stimulation (PTNS) is the second most extensively documented way of nerve stimulation. The exploration of the best technique of electrical stimulation of the lower urinary, including sex organs, is guided by three principles:

1. Stimulation should be done via the least invasive way. For this reason transcutaneous stimulation with surface electrodes or stimulation probes would suit best.
2. Stimulation should be in an area that is acceptable and not embarrassing for patients.
   This makes sacral dermatomes or legs appropriate areas for stimulation.
3. Stimulation should be practical to apply.
   Continuous stimulation is therefore less ideal and discontinuous stimulation is easier than continuous stimulation

METHODS OF PERIPHERAL NEUROMODULATION

The nerves that innervate the lower urinary tract originate from the lumbar, sacral, and coccygeal segmental nerves from L2 to S4 (Figure 47.1). Afferent and efferent fibers from these segmental sacral roots merge in the periphery outside the spinal cord. After merging, the nerve fibers continue as combined nerves that have lost their segmental innervation pattern. The sciatic nerve is composed of fibers from L4 to S3. The posterior tibial nerve is a part of the sciatic nerve. Peripheral neuromodulation of the lower urinary tract has been attempted via stimulation of those nerves that are related or involved in pelvic organ innervation. These are the pudendal nerve (PN), the dorsal genital nerve (DGN), and the posterior tibial nerve. Peripheral neuromodulation can also be done via the overlying skin or by stimulating the dermatomes that are innervated by the same nerve as the ones that innervate the lower urinary tract.

This chapter describes the clinical practice and developments of the peripheral neuromodulation systems, in particular PTNS, PN stimulation, and DGN stimulation.

PTNS

History

It is an ancient Chinese custom to perform acupuncture of the lower leg. With this technique, developed in China over 5000 years ago, the "energetic harmony" of the urogenital tract might be restored by way of stimulation of specific points. Wilhelmus ten Rhyne (1647–1700) was a Dutch physician who was employed by the Dutch East India Company in 1673 where he encountered eastern traditional medicine. In 1683 he published a book entitled *Dissertatio de Arthritide: Mantissa Schematica: De Acupunctura: Et Orationes Tres* [1]. He wrote about the art of needling for treating diseases including those of the lower urinary tract. He called this technique "acupunctura," and it was the first Western detailed study on that matter.

One of the most commonly used acupuncture points used for gynecological, fertility, digestive, urinary, sexual, and emotional disorders is the *SanYinJiao point*, or spleen 6. It can be translated as "three yin intersection" because it is the meeting point of the three yin channels of the leg: spleen, liver, and kidney. SanYinJiao, SP-6 or spleen 6 is located on the medial side of the lower leg, about 6–8 cm cephalad to the prominence of the medial malleolus. It lies close to the medial crest of the tibia. The location of the SP-6 acupuncture point and the organs affected by this kind of acupuncture have remarkable similarities with PTNS. When electrical current is applied to the acupuncture needle, the technique is called electrical acupuncture. Especially when electroacupuncture is performed with similar stimulation parameters (2–15 Hz, 10–20 mA), it is likely that nerve stimulation is responsible for the clinical effect. Similar effects as with tibial nerve stimulation therefore might be expected on the pelvic organs perhaps as well as on the spleen and on the liver.

The fundamental feature of neuromodulation as compared to acupuncture is that nerves are stimulated and not energy pathways or other routes that do not have any anatomical substrate. Nerve stimulation ideally has an efferent motor effect and an afferent sensory effect. Stimulation of posterior tibial nerve results in great toe flexion or fanning of the toes. The sensory effect is a radiation tickling sensation of the foot sole. McGuire was the first to explore tibial nerve stimulation in 1983 [2]. He performed transcutaneous PTNS in 15 patients with detrusor overactivity (DO) because of a neurological disease.

Inspired by this previous work by McGuire, Marshall Stoller started research on PTNS as neuromodulative treatment in lower urinary tract dysfunction. After initial testing in pig-tailed monkeys, PTNS was later investigated in humans with promising results [3]. This new initiative was the start of the worldwide development and exploration of PTNS.

Historic Overview

5000 BC	Acupuncture of the lower leg in China.
1683 AD	Wilhelmus ten Rhyne writes *Dissertatio de Arthritide: Mantissa Schematica: De Acupunctura: Et Orationes Tres*.
1983	McGuire performs transcutaneous PTNS.
1987	PTNS by Stoller.
1999	Clinical introduction of PTNS.
2006	First publication on tibial nerve implant by van der Pal.
2009	First randomized controlled trial by Peters.

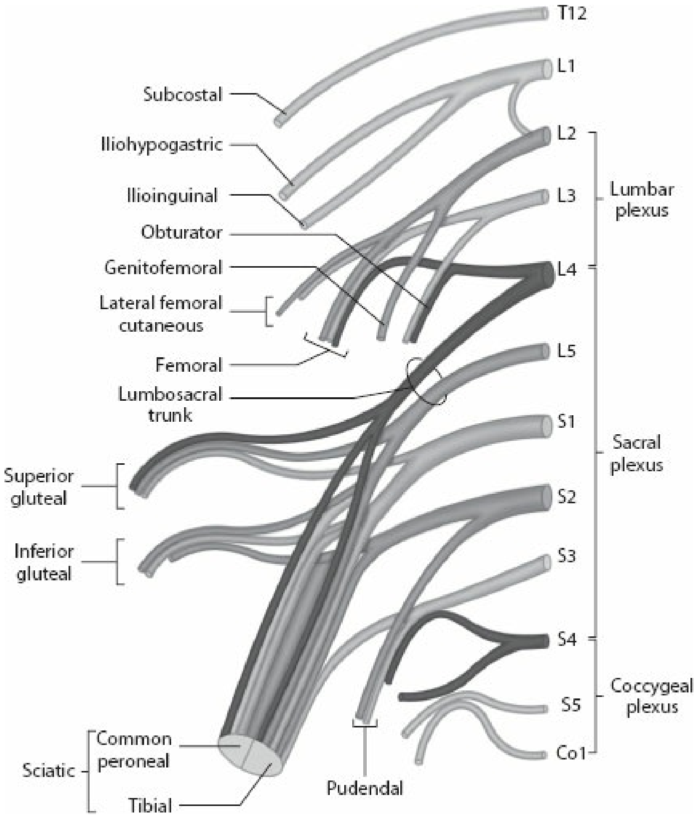

Figure 47.1 Organization of the lower lumbar, sacral, and coccygeal nerve plexus, the merger of the various roots and the most important nerves that branch from the merged nerve plexus. The tibial nerve has its offspring in the sacral roots of mainly S2 and S3.

Technique

PTNS is performed in patients placed in the supine position with the medial malleolus pointing upward. A 34-gauge stainless steel needle is inserted approximately 3–4 cm, about three fingerbreadths cephalad to the medial malleolus, between the posterior margin of the tibia and soleus muscle. The insertion depth is about 2 cm. A stick-on electrode is placed on the same leg near the arch of the foot. The needle and electrode are connected to a low voltage (9 V) stimulator (Urgent PC®, Uroplasty, Inc., Minnetonka, MN) with an adjustable pulse intensity of 0–10 mA, a fixed pulse width of 200 microseconds and a frequency of 20 Hz (Figure 47.2). During the initial test stimulation the amplitude is slowly increased until the large toe starts, to curl or toes start to fan. If the large toe does not curl or pain occurs near the insertion site, the stimulation device is switched off and the stimulation again is switched on for the final proper stimulation phase. If the large toe curls or toes start to fan, stimulation is applied at an intensity well tolerated by the patient. If necessary, the amplitude can be increased during the session. In general, patients undergo 12 outpatient treatment sessions, each lasting 30 minutes 1–3 times per week. If a good response occurs, the patient is offered chronic treatment [4].

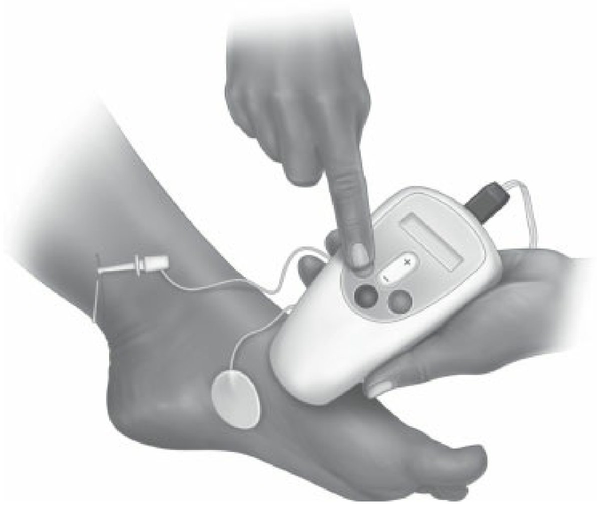

Figure 47.2 Technique of posterior or percutaneous tibial nerve stimulation. (From Heesakkers JPFA, Vierhout ME, *Het urine-incontinentie formularium 2E*, BSvL, Ak Houten, the Netherlands, 2012. With permission.)

Working Mechanism

At the moment, the exact working mechanism of neuromodulation, including PTNS, is still not completely understood. However, it is postulated that symptoms of OAB including incontinence may represent an alteration of the pelvic neuromuscular environment via changes in the inhibitory and excitatory signals of the voiding reflex. It is thought that electrical stimulation of the sacral nerve roots modulates the afferent neural reflex pathways between the spinal cord or pons and pelvic organs. As the ascending sensory pathway inputs and guarding reflex pathway are modulated, storage may be facilitated.

Blok et al. looked at the effects of acute and chronic sacral neurostimulation on PET images of the brain [5]. In the acute phase, brain areas are involved that have to do with sensorimotor learning. These are the areas located in the right postcentral gyrus, the left parietal cortex, the medial prefrontal cortex, and the right insula. Furthermore, there was activation in the ventromedial orbitofrontal cortex and decreased activation in the left medial cerebellum.

However, chronic sacral neurostimulation decreased activity in the cerebellum, midbrain, and adjacent midline thalamus and limbic cortical areas, previously implicated in the control of micturition and urinary storage. They postulated that neuromodulation modulates predominantly areas involved in sensorimotor learning, which might become less active during the course of chronic SN.

In an analogy to sacral neuromodulation, central effects have been studied in PTNS. Finazzi Agro et al. studied the effect of PTNS and sham stimulation on short-latency somatosensory evoked potentials

(SL-SEPs) and long-latency somatosensory evoked potentials (LL-SEPs) [6]. Somatosensory evoked potentials (SEPs) reflect information processing in the brain after stimulation of peripheral somatosensory system. In particular, LL-SEPs seem to provide information on the function of somatosensory associative cortical structures. LL-SEP changes imply that durable stimulation (1 day after treatment) changes in SEP occur. They showed that the amplitude of LL-SEP changes of P80 and P100 waves in the active PTNS group was significantly higher as compared to the placebo group.

The recorded P80 and P100 amplitude increase might reflect long-term modifications in synaptic efficiency through the somatosensory pathway induced by repetitive peripheral nerve stimulation. Long-term potentiation (LTP) and depression (LTD) of excitatory synaptic transmission can contribute to experience-dependent modifications of brain function, including learning and memory. Thus, a plastic reorganization of cortical network triggered by peripheral neuromodulation can be hypothesized as a mechanism of action of PTNS. They concluded that PTNS effects are mediated by suprasacral centers of stimulus elaboration involving cortical associative areas. This is in line with the theories about the working mechanism of sacral nerve stimulation. Such a mechanism of action may, in part, explain the clinical effects of this therapy, which seem to be sustained for an extended period of time (weeks to months) following the conclusion of stimulation.

If one considers applying PTNS for improvement of clinical conditions one has to accept that

- It is possible to positively influence the innervation system of the lower urinary tract by stimulation of the tibial nerve at the ankle
- There is no direct sensation in the bladder area nor motor action of muscles in or adjacent to the pelvic floor during tibial nerve stimulation
- Discontinuous stimulation during a limited period of time once to thrice a week is sufficient to have a beneficial affect

Clinical Results

Since the introduction of PTNS in 1999, several studies have been performed evaluating its effectiveness especially in patients with OAB dry and OAB wet and nonobstructive urinary retention.

Almost all studies on OAB used micturition diaries and general and/or disease-specific quality of life questionnaires to measure the effects of PTNS [7,8]. Subjective success was found in 59%–64% of patients. Objective success, defined most of the time as more than 50% decrease in incontinence episodes and/or micturition frequency, was found in 47%–56% of patients [8,9].

Urodynamic studies especially measured by cystometry may provide more objective data on the efficacy of PTNS. When acute PTNS is performed as soon as DO is observed during cystometry, the suppressive effects in neurological patients are contradictory [10,11].

In these studies, frequency/volume chart data and quality of life scores improved significantly. However, of the participants with pre- and post-treatment urodynamic data, only a few showed complete abolishment of DO [12]. Nevertheless, increments in cystometric bladder capacity and in volume at occurrence of DO were significant. Subjects without DO at baseline appeared 1.7 times more prone to respond to PTNS. The more the bladder overactivity was pronounced, the less these patients were found to respond to PTNS.

Once a positive treatment outcome has been obtained with PTNS, a maintenance program is needed to avoid recurrence of symptoms. One study evaluated the necessity of maintenance therapy by means of a 6-week pause of therapy in successfully treated PTNS patients, leading to over 50% worsening of the main symptoms in almost all patients. Restarting PTNS afterward improved complaints to the level present before the break in treatment [13].

One of the most important studies on PTNS was performed by Peters et al. [14]. The so-called Study of Urgent PC versus Sham Effectiveness in Treatment of Overactive Bladder Symptoms (SUmiT) was a multicenter, double-blind, randomized, controlled trial comparing the efficacy of PTNS to sham through 12 weeks of therapy. The breakthrough was that a validated sham arm was developed and used as a comparator. This was the first time that the net effect apart from the placebo effect could be measured. In two groups of 110 patients, the improvement in global response assessment (GRA), voiding diary parameters, and OAB and quality of life questionnaires were evaluated. The GRA is a self-reported 7-point scale that tells whether an individual perceives a change due to the treatment. Individuals who noted a moderate or marked improvement were regarded as successfully treated patients. Voiding diary parameters after 12 weeks of therapy showed PTNS subjects had statistically significant improvements in frequency, nighttime voids, voids with moderate to severe urgency, and urinary urge incontinence episodes compared to sham. The GRA in the PTNS subjects showed that 55% reported moderately or markedly improved responses as compared to 21% in the sham group.

Another sham-controlled study was performed by Finazzi et al. with similar results [15].

PTNS implies that patients will have to have repeat treatments. The tapering studies show that once every 2 or 3 weeks is sufficient in those patients that benefit from PTNS. Another major question is what the long-term success of PTNS is. Peters et al. followed 50 participants from the SUmiT trial who met the primary effectiveness endpoint after 12-weekly PTNS [16]. These patients were prescribed a fixed-schedule 14-week tapering protocol followed by a personal treatment plan aimed at sustaining OAB symptom improvement. Of this group, 29 patients completed the 36-month protocol and received a median of 1.1 treatments per month. At 3 years 77% maintained moderate or marked improvement in OAB symptoms. Compared to baseline, median voids per day decreased from 12.0 to 8.7, and urge incontinence episodes per day decreased from 3.3 to 0.3. All quality of life parameters remained markedly improved from baseline through 3 years. Minor side effects were described. They were related to needle insertion and consisted of bruising (0.9%), discomfort (1.8%), and bleeding (2.7%).

- PTNS improves OAB symptoms based on voiding diary parameters in 47%–56%.
- Subjective improvement is obtained in about 60% of patients.
- PTNS increases cystometric capacity and delays the onset of, but does not abolish, DO.
- Maintenance therapy is necessary to sustain the effect of therapy.
- PTNS improved bladder symptoms measured with GRA in 55% as compared to 21% in a sham treated group.
- After 3 years, 77% of responding patients to initial therapy experienced moderate to marked improvement on OAB symptoms.

PROGNOSTIC FACTORS FOR PTNS

Little data are available about prognostic factors for success or failure of PTNS. Studies on urodynamic changes by PTNS suggest that in the setting of OAB, without DO, patients are more prone to a successful treatment outcome [12]. Clinical parameters for predicting sacral nerve stimulation (SNS) outcome were also tested in 132 patients treated with PTNS, but showed no significance [17]. Also, a history of sexual and/or physical abuse did not alter PTNS treatment outcome. However, a low total score at baseline in the SF-36 general quality of life questionnaire proved to be predictive for not obtaining objective nor subjective success. Patients with a low SF-36 mental component summary were especially prone to fail. These patients also scored worse on disease-specific quality of life questionnaires, although they had no difference in disease severity compared to patients with good mental health.

- Subjects with mental/cognitive problems don’t seem to be ideal candidates for PTNS

URGENT-SQ: THE PTNS IMPLANT

Rather quickly after the modern clinical development of PTNS, it was recognized that the repeated return to the clinic, once weekly or once bi- or triweekly, would finally lead to a logistic problem with patients returning to the clinic approximately 1–2 times per month. If all successfully treated patients would return every week, this would lead to a jammed outpatient clinic. More importantly, the travel burden for patients would be high and PTNS treatment on demand would not be possible. Therefore, an implant was developed that was placed at the tibial nerve at the ankle and that could be operated via radiofrequency activation with an external stimulator: the Urgent-SQ (Figures 47.3 and 47.4).

The pioneering work was done by van der Pal et al. [18]. They looked at eight patients with refractory OAB who were treated with the Urgent-SQ. After implanting the device, the patients could operate the implant by means of an external stimulator. Patients were evaluated at 3, 6, and 12 months of follow-up. The primary objective was ≥50% reduction in the number of incontinence episodes and/or voids on bladder diary. At 3, 6, and 12 months, respectively, 5, 6, and 4 patients met the primary objective. At 3- and 6-month follow-up, voiding and quality of life parameters had significantly improved. Urinary tract infection, temporary walking difficulties, and spontaneous radiating sensations were reported as adverse events, and there was no local infection, erosion, or dislocation.

Janssen et al. reported about the long-term efficacy and safety of these patients in an open-label study [19]. The seven patients who still had the implant were contacted after nine years and evaluated with an interview, physical examination, ankle x-ray, voiding diaries, and completed questionnaires about adverse events, performance, efficacy, safety, and quality of life with the validated I-QoL. Results showed that six of the seven patients still had sensory and locomotor responses on stimulation at 9-year follow-up. Four patients who had a successful treatment response at one year still used the device. The implants were intact with no migration and/or displacement. Two patients experienced minor discomfort. The conclusion was that after 9 years, the Urgent-SQ implant was a safe therapy for OAB.

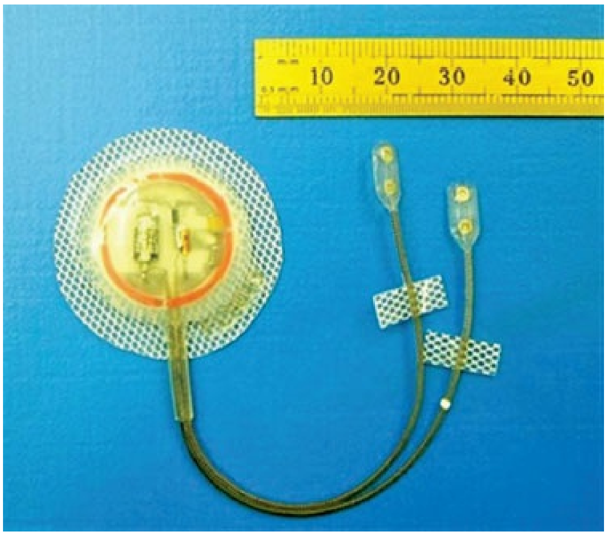

Figure 47.3 The Urgent-SQ implant consisting of an internal electromagnetic pulse receiver; the body, with two leads; and monopolar platinum electrodes.

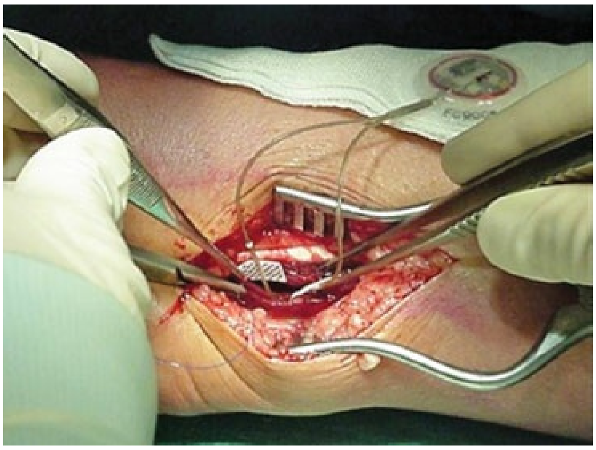

Figure 47.4 Site of implantation during surgery. The two electrodes are placed on opposite sides of the tibial nerve just proximal to the medial malleolus.

- A pilot study reveals that the Urgent-SQ implant appears to be a safe and effective treatment for OAB.

COSTS

Several manuscripts have been published about the cost-effectiveness of the various treatments for OAB, in particular for PTNS and SNS. Various articles show different costs since the medical care systems differ between countries. Leong published that the cost of SNS as a treatment for OAB syndrome in the Netherlands is $15.743 over a 2-year time period [20]. D'Ausilio calculated the 10-year cost for SNS in Italy at €33.897, whereas Staskin compared the costs of PTNS to SNS for OAB syndrome in the United States [21,22]. PTNS was the least costly ($7.565 for a 3-year treatment) compared to SNS ($24.681 for the same treatment period). Chen et al. calculated that 1 year of treatment with PTNS costs $4.375 per patient [23]. Martinson also concluded that PTNS had substantially lower costs compared to SNS in the United States [24]. Although there is variation between countries, it appears that PTNS is less costly as compared to SNS.

FUTURE PERSPECTIVES OF PTNS

PTNS is a minimally invasive, easily accessible neuromodulation technique and has proven its benefit in OAB and nonobstructive urinary retention. Regretfully, in chronic pelvic pain the effects seem to be only modest. At this moment, there is “circumstantial” evidence existing for its efficacy, based on animal studies, and clinical studies including urodynamic parameters. In case PTNS becomes a more established treatment modality, no doubt other indications will be explored. Subjects for further investigation of areas that already have some clinical efficacy data are children, neurological patients, and patients with fecal incontinence.

Almost all research done on PTNS used the same stimulation protocol: PTNS was performed in 10–12 weekly sessions, each lasting for 30 minutes. Stimulation parameters were preset and rather fixed and every time only one needle was inserted. It may well be anticipated that changes in treatment scheme and/or stimulation parameters could lead to a different, possibly even better outcome. The same goes for bilateral instead of unilateral therapy. It is evident that an accelerated stimulation scheme has the advantage of achieving clinical results faster [25]. Regarding stimulation parameters, it is rather widely agreed that pulse intensity in neuromodulation should be set at a well-tolerated level. As it is suggested that frequency is optimal at more unpleasantly low levels (5–6 Hz), studies on PTNS with pulse frequencies below 20 Hz may produce better results [26]. The same goes for changes in pulse duration. Currently, in PTNS, the standard setting is 0.2 milliseconds.

The recent revitalization of the Urgent-SQ creates other possibilities. Efforts should be undertaken to refine the preimplant testing phase in order to decrease the amount of unnecessarily treated patients. Hopefully, this will eventually lead to the ideal implant: an effective and safe, easily controllable device that is operated by patients themselves in flexible, individualized treatment schemes.

Apart from the clinically available and accepted PTNS and SNS treatments, two promising peripheral neuromodulation possibilities nowadays are used in experimental settings: PN stimulation and DGN stimulation.

PUDENDAL NERVE STIMULATION

The PN originates from the S2, S3, and S4 sacral nerve roots. It is a somatic nerve and innervates the external genitalia as well as both the external urethral sphincter and the external anal sphincter. The main trunk passes over the ischial spine and enters Alcock’s canal. Selection of the PN, as a site of stimulation, potentially provides afferent stimulation of S2, S3, and S4. The PN has three major branches, the inferior rectal nerve, the DGN, and the perineal nerve, with a high variation in branching patterns. Afferent PN stimulation has been demonstrated to inhibit the micturition reflex, to abolish uninhibited detrusor contractions, and to increase bladder capacity in animals and humans [26,27]. The potential advantage of PN stimulation compared to SNS is that PN stimulation recruits more afferent fibers. Since the presumed main working mechanism of all types of neuromodulation is in an afferent direction, the recruitment of as many afferent fibers as possible is optimal. Different approaches for electrical stimulation of the PN were described by Martens as is depicted in Figure 47.5 [28].

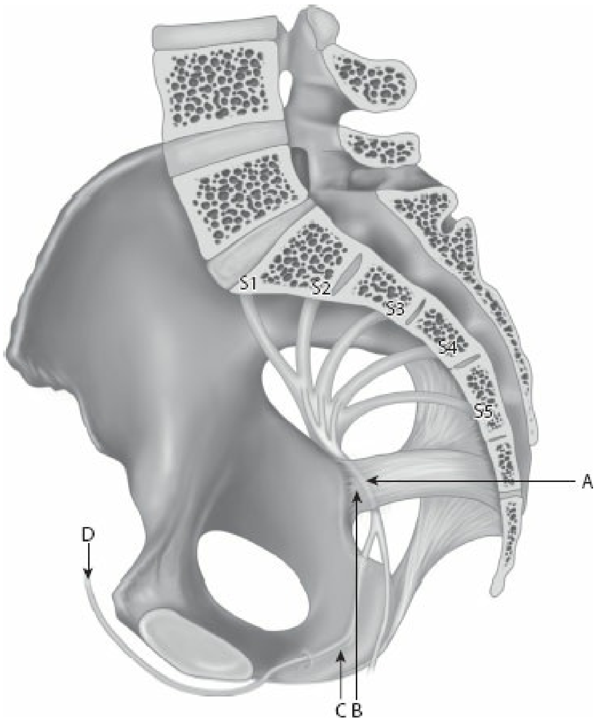

Figure 47.5 Approaches for electrical stimulation of the pudendal nerve (PN) and dorsal nerve of the penis or clitoris. The PN originates primarily from the second, third, and fourth sacral nerve roots (S2, S3, S4), and it sometimes gains contributions from the adjacent roots of S1 and S5. The PN can be accessed for stimulation at the ischial spine by a posterior (A) or perineum approach (B) for insertion of an electrode. With a perineum approach, the PN can also be reached at Alcock's canal (C). The dorsal genital nerve can be stimulated using surface electrodes or percutaneously implanted electrodes (D). (By courtesy of Frank Martens.)

The posterior approach using the ischial spine as a landmark can be accessed by inserting a wire electrode perpendicular at the intersection of a horizontal line from the greater trochanter with a vertical line from the ischial tuberosity tip. When one wants to approach the PN from the perineum, the electrode is inserted perpendicularly to the perineum between the ischial tuberosity and anus.

The use of chronic PN stimulation in refractory neurogenic urgency incontinence with a minimal invasive procedure was first reported by Spinelli in 2005 [29]. Fifteen patients underwent chronic PN stimulation, six with a perineal approach and nine with a posterior approach. Eight patients became continent, two improved by more than 88% and two reduced the number of incontinence episodes by 50%. In 12 patients with a response of >50% improvement in urge incontinence episodes, an implantable pulse generator (IPG) was implanted. At an average follow-up of 6 months, these patients with the implanted IPG perceived the same clinical efficacy as achieved during the screening phase. In the same year, a prospective randomized single-blind, cross-over trial of SNS versus PN stimulation was reported by Peters, including patients with urgency–frequency, urgency incontinence, and nonobstructive urinary retention [30]. Thirty subjects were implanted with a tined lead at S3 and a second electrode was implanted at the PN by the perineum approach. In a blinded, randomized fashion, each lead was tested for 7 days. An overall 50% improvement was considered as a positive response. Twenty-four patients responded to nerve stimulation. Of these, PN stimulation gave overall improvement in symptoms of 63%, whereas those with SNS reported an overall improvement of 46%. Of patients whose symptoms improved more than 50%, 79% desired to have PN stimulation compared to 21% for SNS. On the GRA scale, PN stimulation was superior to SNS for pelvic pain, urgency, frequency, and bowel function. No difference in voiding diary parameters was observed.

Continuous or conditional stimulation can be applied. Continuous stimulation produces stimuli constantly. With conditional stimulation, stimulation takes place when a certain condition such as an involuntary detrusor contraction (IDC) occurs. Conditional stimulation is considered as effective as continuous stimulation to increase bladder capacity, but it reduces stimulation time. This can lengthen the life span of an implanted battery and might prevent habituation to stimulation. Unfortunately, there is not yet a reliable autonomous warning signal for IDC that can be used as a trigger for the stimulation action. So far, only patient-controlled stimulation can be applied. The clinical benefit of patient-controlled stimulation has to be studied in future chronic clinical studies [28].

The literature on PN stimulation for OAB is encouraging but limited and indicates that PNS might be a reasonable option for OAB in the future when more successful long-term clinical results become available.

- PN stimulation still is experimental but has conceptual advantages over other types of neuromodulation.
- Few clinical studies exist that show at least a comparable clinical result as compared to sacral nerve stimulation.
- Broad clinical application and long-term data are awaited for PNS.

DORSAL GENITAL NERVE STIMULATION

The DGN, being either the dorsal penile nerve or the dorsal clitoral nerve, is a branch of the PN. After exiting the Alcock's canal anteriorly, the DGN continues cranially where it contacts the inferior ramus of the pubis and subsequently courses to the inferior border and anterior surface of the body of the pubis. In the male, the nerve courses proximal to the insertion of the cavernous body and continues between the cavernous body and the anterior surface of the pubis to the dorsum of the penis. The nerve divides and runs bilaterally on the dorsal side to the penis between the tunica albuginea and Buck's fascia to terminate in the penile gland. In the female, the nerve travels from the anterior surface of the body of the pubis then pierces the perineal membrane lateral to the external urethral meatus. It traverses along the bulbospongiosus muscle before traversing posteriorly to the crura. The nerve hooks over the crura to lie on the anterolateral surface of the body of the clitoris, before dividing into two cords and terminating short of the tip of the clitoral gland [28,31]. The DGN is running more superficial and therefore perhaps more suited for less invasive stimulation techniques. The mechanism of action of DGNS is thought to be by afferent stimulation of the PN. DGN stimulation is not yet used in daily clinical practice. All publications so far are about experiments in research settings.

Goldman performed DGN stimulation in 21 patients with nonneurogenic OAB using a percutaneously placed electrode [32]. Improvement was defined as a >50% reduction in each of the measured incontinence parameters: 24 hour pad test weight, incontinence episodes per day, pads per day, and the amount of severe urgency episodes. Of the 21 subjects, 19 completed the week of stimulation. In two subjects, the electrode failed, one broke and one dislodged. Of the 19 who completed the home stimulation week, 15 (79%) subjects reported a reduction in incontinence episodes and 9 (47%) experienced a >50% reduction in the number of incontinence episodes. Of those 9, the mean reduction of incontinence episodes a day was 89%. Of the 17 (47%), 8 used less than 50% of their pads per day as compared to pretreatment, whereas 13 (76%) of the 17 subjects who performed a 24 hour pad test had a >50% reduction in pad weight. Eight subjects (47%) were complete dry. With an average reduction of 82%, 13 (68%) had >50% reduction in severe urgency episodes. With regard to side effects, seven patients experienced side effects, ranging from skin irritation to pain and bruising around the electrode exit site. All were mild and recovered spontaneously within 11 days of the implant procedure. This study was the first to demonstrate the feasibility of DGN stimulation via a percutaneous electrode for treatment of urge incontinence in the nonneurogenic population. The results for DGN stimulation in this study are encouraging and seem to be comparable to results of other methods of neuromodulation.

Most of the publications about DGN stimulation were performed in patients with neurogenic detrusor overactivity (NDO). In those studies, good results concerning bladder capacity and suppression of IDC are reported. Martens et al. performed DGNS with a needle electrode in eight spinal cord injury (SCI) patients with DO and reported a success rate of 100% in suppression of one or more IDC with conditional stimulation in neurogenic patients [33]. Opisso compared patient-controlled versus automatic stimulation with surface electrodes in 17 patients with NDO and reported that patient-controlled DGN stimulation is as effective as automatically controlled stimulation to treat NDO [34].

The aforementioned studies for DGN stimulation in neurogenic patients are studies with short-term DGN stimulation in a clinical setting. Recently, Opisso reported a study with subject-controlled DGN stimulation in 11 patients with NDO and urge incontinence at home during 3 days [35]. DGN stimulation was provided with surface electrodes placed either on the dorsal of the penis in males and on or close to the clitoris in females. Eight subjects completed the protocol. Higher bladder volumes with stimulation were seen. None of the subjects reported incontinence episodes on days 4 and 5. This study demonstrated that DGN stimulation in patients with intact bladder sensation is feasible and also suggested a carryover effect.

- DGN stimulation conceptually is an ideal way of neuromodulation since it stimulates afferent nerve fibers.
- All studies to date have been done in a research setting in mostly neurogenic patients.
- Only short time data exist with promising clinical results.

CONCLUSIONS

Peripheral neuromodulation is a proven and accepted treatment for OAB symptoms. PTNS is minimally invasive and not very expensive but it is time-consuming. Therefore, new techniques with implants are being explored. Experimental treatments like PN stimulation and DGN stimulation are promising, but they are still in an experimental phase and the clinical applicability still is limited.

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Sacral Neuromodulation in the Treatment of Female Overactive Bladder Syndrome and Nonobstructive Urinary Retention

J.L.H. Ruud Bosch

Female voiding dysfunctions such as those related to overactive bladder (OAB) syndrome and nonobstructive urinary retention often are refractory to conservative management including drug therapy, behavioral therapy, pelvic floor muscle exercises, biofeedback, noninvasive or minimally invasive neuromodulation, and intermittent self-catheterization. Sacral nerve neuromodulation has proved to be valuable in these situations [1]. In 1997, the Food and Drug Administration (FDA) approved sacral neuromodulation for treatment of refractory urge urinary incontinence in the United States. Subsequently, approval was also granted for the treatment of urgency–frequency syndrome and for nonobstructive urinary retention. The labeling was later changed to include "overactive bladder" as an appropriate diagnostic category [2]. In spite of the fact that its mechanism of action is far from understood [3–6], the list of urological applications now includes refractory urgency incontinence, the urgency–frequency syndrome, nonobstructive urinary retention, interstitial cystitis, and chronic pelvic pain/painful bladder syndrome. The latter two are not FDA-approved indications, but the inclusion of interstitial cystitis is justified by the features of urinary frequency and urgency (with pelvic pain) [2]. The value of sacral neuromodulation (SNM) has now generally been recognized [7], and the therapy has been incorporated in guidelines and treatment algorithms such as those of the International Consultation on Incontinence [8].

MODE OF ACTION OF NEUROMODULATION

The precise mode of action of neuromodulation is unknown. Theoretically, its effects can be explained by modulation of reflex pathways at the spinal cord level [4,9]. However, supraspinal pathways seem to be involved as well [10]. Experimental work in animals, human volunteers, and patients has revealed that at least two mechanisms are important: activation of efferent nerve fibers to the striated urethral sphincter reflexively causing detrusor relaxation [11–13] and activation of afferent nerve fibers causing inhibition of the voiding reflex at a spinal and/or supraspinal level; pudendal nerve afferents seem to be particularly important for the inhibitory effect on the voiding reflex [14–16]. Pudendal afferent activity mapping during neurosurgical procedures of the sacral nerve roots has shown that the S1, S2, and S3 roots contribute 4%, 60.5%, and 35.5%, respectively, of the overall pudendal afferent activity, and it has also been shown that pudendal afferent distribution is confined to a single level (i.e., S2) in 18% of the subjects [17]. A lack of effect of S3 stimulation can therefore be expected in some subjects.

Detailed assessment of the sensory and motor response during lead placement seems to be important for long-term success [18]. This is possible with a two-stage procedure [19] using percutaneous tined lead placement under local anesthesia [20].

Paradoxically, neuromodulation also works in patients with urinary retention in the absence of anatomical obstruction. It has been postulated that neuromodulation interferes with the increased afferent activity arising from the urethral sphincter, restoring the sensation of bladder fullness and reducing the inhibition of the detrusor muscle contraction [21].

SELECTION OF CANDIDATES FOR PERMANENT SACRAL NERVE NEUROMODULATION

Sacral nerve neuromodulation (InterStim^{TM} therapy) differs from other types of neuromodulation by its continuous stimulation and close nerve contact. Its characteristic feature is the implantation of a pulse generator and an electrode lead stimulating one of the sacral nerves, mostly S3. Patients only receive a permanent implant if the preceding percutaneous nerve evaluation (PNE) test is successful or if the effects of the first stage of a two-stage implantation are favorable. In the first stage lead implantation (FS2S), only the definitive electrode is implanted but not the implantable pulse generator (IPG). A test stimulation, currently most often in terms of FS2S, still is the only way by which candidates for a permanent implant can be identified.

Test *Stimulation*

Early attempts to identify factors predicting the success of SNM have largely failed [22]. Later, Scheepens et al., in a multivariate logistic regression model, found that failure to respond to the test stimulation was associated with no previous surgery for intervertebral disk prolapse, longer duration of symptoms before IPG implant (longer than 7 months), neurogenic bladder (vs. no neuropathy), and nonobstructive urinary retention (vs. urinary incontinence), but not to patient age [23]. However, the odds ratios in this study were too low to justify the exclusion from testing of some patient categories. South et al. found a significantly lower percentage of responders to PNE in those older than 65 years. They also found that four or fewer incontinence episodes per day were significantly associated with PNE failure and that urodynamically proven detrusor overactivity in patients with refractory urgency incontinence does not predict the outcome of PNE [24]. Foster et al. suggested that patients with a greater decrease in 24 hour pad weight at initial test stimulation are more satisfied after the implant [25]. Psychiatric disorders also seem to be a predictor of failure [26]. Experienced implanters know that psychological factors constitute an important determinant of their personal bias in the assessment of the result of the test stimulation.

A true-negative test stimulation response of about 20% can be expected based on the neuroanatomical fact that pudendal afferents are confined to the S2 level only in 18% of all subjects [17].

The percentage of patients with urgency incontinence responding to traditional PNE was in the order of 61%–76% in reports of early adopters of this technique [27]. Later reports of traditional PNE quote lower success rates of about 50% [28]. This discrepancy may be related more to patient selection than to the technique of PNE itself. Recent experience with the two-stage implant using a tined lead has resulted in implantation rates of 77%–90% in patients with various indications [18,29,30]. Based on their experience with PNE testing or two-stage testing before tined lead implantation, van Voskuilen et al. [31] concluded that there is an approximately 20% false-negative rate of PNE testing only; however, in this report, the authors had a much lower PNE response rate (20%) than the 54% in a previous report from that institution [32]. One explanation for this difference might be the fact that, previously, 25% of the PNE responders actually underwent more than one PNE session.

Only a well-designed randomized controlled study between PNE and FS2S can confirm whether this is truly due to a better performance of the test.

Interestingly, a report on the results of sacral neuromodulation from a Swiss registry showed that only 74% of patients who tested successfully with traditional PNE went on to a permanent implant without further evaluation, as compared to 97% of patients, who tested successfully with the definitive lead (FS2S) [33]. This suggests that for some reason, either the patient or the investigator was not convinced by the positive PNE result. Of the 21 successful PNE patients who did not immediately proceed to permanent implant, 11 were additionally tested with the definitive lead before implantation was finally performed, but 10 others refused an implant for “personal reasons.” Again, one wonders whether bias toward the testing methods has been at play in this study.

It is clear that it remains difficult to eliminate investigator bias in the interpretation of test stimulation results, even in a randomized study design. And, maybe, this kind of personal view and interaction with the patient is necessary to filter out those individuals who are unsuitable for this type of treatment (like patients with a psychiatric problem) before a point from which return is difficult has been reached. Weil et al. have previously shown that a poor result after permanent implantation is found in 82% of patients with a history of psychological/psychiatric problems as opposed to 28% of patients without this kind of history [26]. In summary, although there seems to be widespread expert opinion that FS2S is better than PNE, there is no solid evidence for this. FS2S is probably considered superior because it results in a higher implantation rate. However, a higher implantation rate after testing is only acceptable if the “additional” patients that are identified with FS2S over PNE, i.e., the presumed false-negatives of PNE, have at least the same long-term outcome as the presumed true-positives of PNE. Unfortunately, there are as yet no conclusive studies that have addressed this issue.

In a mixed group of patients including nonobstructive retention and urge incontinence, Everaert et al. conducted a randomized trial comparing the one-stage and two-stage implant with the original nontined lead [34]. After 24 months of follow-up, they found a false-positive rate of 33% and 14% for the one-stage and the two-stage procedure, respectively. In this study, patients were randomized into one of the two groups only after a successful traditional PNE. Strikingly, all patients randomized to the two-stage implant subsequently passed the FS2S, showing that FS2S testing did not exclude any patients (i.e., presumed false-positives of traditional PNE) from a permanent implant. On the other hand, the difference in failures between the groups was almost entirely due to a difference in early failures (i.e., <3 months after the implant), i.e., 23.8% and 9.5%, respectively, for the one- and the two-stage implant. These conflicting results seem to imply that the sample size of the study was too small to draw solid conclusions. Obviously, a higher implantation rate is also associated with increased costs.

CRITICAL APPRAISAL OF THE RESULTS OF SACRAL NEUROMODULATION BY PERMANENT IMPLANTATION

Multiple case series and several randomized controlled studies of sacral neuromodulation have been reported. However, a completely satisfactory picture cannot yet be drawn in spite of more than 15 years of follow-up in some series. There are several problems with the interpretation of follow-up data of sacral neuromodulation. First, if complete follow-up of all implanted patients is available, the follow-up duration usually is short, and if the follow-up is longer, the percentage of patients that is accounted for is usually low. If those who are lost to follow-up are not in some way included in the final analysis, the reported success rates will be over optimistic and the estimated complication or revision rates will be too low. Second, the variable interpretation of the “>50% improvement over baseline in at least one of outcome measures equals success” criterion makes the comparison of various series difficult. For example, in urgency incontinence, some investigators would call a result successful, only if a >50% decrease in pad use *and* leaking episodes per day is achieved, while others would be satisfied if there is a >50% decrease in pad use *or* leaking episodes per day. Third, some implanters have challenged the “>50%” success criterion and have stated that >80% improvement is more relevant to the patient [35]. It is clear that many implanters have only proceeded with a permanent implant if at least a 75%–80% improvement was noted during test stimulation. This introduces a fourth problem with the evaluation of the clinical results of SNM: if a patient would have proceeded to implant on the basis of an improvement at test stimulation of 75% in one of the outcome measures and if the same patient would subsequently experience an only 55% improvement after 1 year of follow-up, she would still be considered a success in case the “>50%” success criterion is used. So, a report of success using categorical criteria with wide ranges can result in a gross overestimation of the benefits of the treatment. Unfortunately, only a minority of papers report the percentage of patients with urgency incontinence who become and remain dry or the percentage of patients with nonobstructive retention who do not need to self-catheterize at all after the implant. In patients with the urgency–frequency syndrome, it is even more difficult to define what constitutes “cure”: is it those who achieve a normal voiding frequency? But then, what is “normal,” eight or fewer voids?

REFRACTORY URGENCY URINARY INCONTINENCE (UUI)

The results of several case series with a total of 115 patients with urgency incontinence who were treated early in the experience with sacral neuromodulation have been summarized: after a follow-up duration of about 1–3 years, approximately 50% of patients with urgency incontinence without neurogenic causes demonstrate a more than 90% improvement in their incontinence after the permanent implant; 25% demonstrate a 50%–90% improvement and another 25% demonstrate a <50% improvement [27].

In a pivotal multicenter randomized study involving patients with refractory urgency incontinence, half of the patients in whom the PNE test was successful were implanted. Implantation was delayed for 6 months in the remaining patients, who received standard medical treatment and comprised the control group. The stimulation group demonstrated significantly better symptomatic results than the control group at 6 months follow-up [36]. There is a recent interesting report of a prospective randomized, multicenter study, evaluating sacral neuromodulation compared to standard medical treatment in subjects with mild symptoms of OAB. In this study, minimally invasive techniques, including the tined lead, were utilized in a contemporary population. Success was defined as a ≥50% improvement from baseline in average leaks/day. At 6 months, those with urgency urinary incontinence demonstrated a

71% success rate as compared to 47% success in those receiving standard medical treatment (p = 0.03) [37].

Detailed information on the durability of the effectiveness of SNM is relevant, especially in the light of the development of alternative options and the high costs of the treatment. Also, the determination of predictors of success remains important. Subgroups of refractory patients with urgency incontinence such as those following urogynecological surgery or urethrolysis seem to respond well to the treatment after short follow-ups [38,39].

Literature on the long-term results of SNM is relatively scarce. In a prospective Italian national register, 37 patients received an implant for urgency incontinence, and 17 had a minimal follow-up of 12 months. Out of 17 patients (59%), 10 were dry [40]. Three-year results have been reported by Siegel et al: a more than 50% reduction in leaking episodes per day was found in 52.8% of the implanted patients. Furthermore, 46% were considered dry after 3 years [41]. An analysis of a nationwide Swiss registry revealed that 27 of 71 implanted patients with urgency urinary incontinence failed (38%) after a median follow-up of 24 months [33].

There are five publications with a mean or median follow-up of at least 5 years [42–46]. Van Voskuilen et al. described the subjective long-term results in a mixed group of 149 patients (mainly women) [42]. The mean follow-up in the OAB group was 69.8 ± 41.6 months, but it was unclear how many patients had idiopathic urgency incontinence. The authors concluded that SNM gave a prolonged subjective benefit. Voiding diary parameters were not considered. The subject of the study by Scheepens et al. was the efficacy and safety of the two-stage implant technique in a group of 15 patients (also mainly women) with a median follow-up of 5.2 years [43]. Only seven patients had UUI. The number of leaks per day and the number of pads used per day decreased from 9.0 ± 4.3 and 5.0 ± 2.4 to 3.2 ± 3.4 and 1.0 ± 1.3, respectively. Elhilali et al. reported on 52 patients with mixed pathology, after a mean follow-up of 6.5 years. Only six patients had urgency incontinence and only one showed persistent improvement [44]. Van Kerrebroeck et al. reported the 5-year results of a postapproval study, which included patients from the original randomized controlled MDT-103 study, were reported [45]. Of the 96 patients with urgency incontinence, 65 completed the 5-year follow-up, and diaries were available from 54 patients (8 patients had been explanted); of these, 58% and 61% still had successful outcomes concerning the number of leaks per day and the number of pads used per day, respectively. In this evaluation, success was defined as >50% improvement of selected voiding diary parameters as compared to baseline. The percentage of patients who were dry is not reported.

Recently, the results of a prospective longitudinal single-center study with 60 women with idiopathic UUI refractory to conservative therapy who all passed the 5-year follow-up mark were reported by Groen et al. [46]. Five-year success rates of 50% and 53% for the number of leaks per day and the number of pads used per day, respectively, were found. However, only 9 (15%) of the 60 patients were fully continent after 5 years.

The studies with a long-term follow-up deal with patients who were implanted with the original nontined lead. Six-month follow-up in an early study of the tined lead showed results that seemed comparable to the experience with the original lead [47]. The medium-term outcome in patients implanted with the tined lead was reported in patients with refractory urgency incontinence by van Voskuilen et al. [31]. Treatment failure or lost to follow-up was seen in 29.6% after an average of 15.5 months. Sutherland et al. reported on their 11-year experience. The 104 patients in the analysis represent only 44% of the implanted patients between 1993 and 2004. The reasons for not consenting are unknown for what seems to be an exceptionally high percentage of patients not consenting (56%) to a retrospective chart analysis. With a mean follow-up of 22 (range 3–162) months, sustained subjective improvement was more than 50% in 69% of the urge incontinent patients. Of these leads, 47.1% were tined [6]. A recent report of long-term follow-up in a series of 217 patients included more than 10% of patients who were implanted with the tined lead; after a mean follow-up of 47 months, about 70% of the patients with urgency incontinence were a success (i.e., demonstrated ≥50% improvement in leaks/day). However, only 20% were cured, meaning dry [48].

A cure from refractory urgency incontinence has now been reported in 15–20% of patients after a follow-up of 4–5 years [46,48]. A 100% improvement may seem demandingly high as a criterion of success, but is relevant considering the high costs of the therapy and the availability of newer alternatives such as onabotulinumtoxin-A injections [49]. Watanabe et al. showed that 3-year cumulative cost estimates of sacral neuromodulation were about twice as high as those for intradetrusor injection of onabotulinumtoxin-A [50]. The important issue of the patient perspective has recently been surveyed by Balchandra and Rogerson. In their survey, 74% of the 50 women with a mean age of 62 years chose onabotulinumtoxin-A intradetrusor injections over SNM after detailed counseling on the two treatment options ($p < 0.003$) [51].

In a study of 20 patients who had discontinued onabotulinumtoxin-A intradetrusor injections, 14 were implanted with an Interstim system after >50% improvement was achieved in the test phase. After 1 year of follow-up, the improvement was sustained in 11 subjects (55%), and 5 of these had experienced a >90% decrease in leaking episodes [52]. So, sacral neuromodulation may be an option after onabotulinumtoxin-A intradetrusor injections.

Another issue that should be considered is the natural history of urgency urinary incontinence or OAB-wet: Irwin et al. have shown that of women who were classified as OAB-wet in 1992, 49% were dry in 2003, indicating that with time there is a certain percentage of spontaneous resolution, or at least a fluctuating presence of the condition. Therefore, a certain percentage of the improvements seen with treatment may be due to fluctuating symptoms or spontaneous resolution [53].

URGENCY–FREQUENCY SYNDROME

In a multicenter randomized study involving patients with urgency–frequency syndrome, half of the patients in whom the test stimulation was successful were implanted [54]. Implantation was delayed for 6 months in the remaining patients, who received standard medical treatment and comprised the control group. The stimulation group demonstrated significantly better symptomatic results than the control group at 6 months follow-up.

Surprisingly, only a few reports exist on long-term results of SNM in urgency–frequency syndrome. Siegel et al. [41] reported that 2 years after implantation, 56% of the patients with urgency–frequency syndrome showed a more than 50% reduction in voiding frequency. Elhilali et al. reported persistent improvement in 10 of 22 (45%) patients with urgency–frequency syndrome after an average follow-up of 6.5 years [44].

The 5-year results of a postapproval study, which included patients from the original randomized controlled MDT-103 study, were reported [45]. Success was defined as >50% improvement of selected voiding diary parameters as compared to baseline. Of the 25 patients with urgency–frequency syndrome, 5-year follow-up diaries were available from 11 patients (7 patients had been explanted), and 40% of these still had a successful outcome concerning the number of voids per day. The average number of voids had decreased from 19.3 to 14.8, but it is unclear whether any patient experienced normalization of voiding frequency [45].

The recent report of Peeters et al. showed that after a mean follow-up of 47 months, 68% of patients with urgency–frequency syndrome demonstrated ≥50% improvement. However, only 33% were cured, meaning no urgency and a normal daytime frequency [48].

NONOBSTRUCTIVE URINARY RETENTION

Jonas et al. reported that 68 of 177 nonobstructive retention patients responded to traditional PNE with a greater than 50% improvement. Of the implanted patients, 69% eliminated catheterization at 6 months follow-up, and an additional 14% had a greater than 50% reduction in catheterization volume. At 18 months follow-up, catheterization was completely eliminated in 58% of 24 evaluable patients [55]. Swinn et al. reported a 68% success rate with PNE in 38 women, mostly with Fowler's syndrome [21]. The same group reported their long-term results in 60 implanted women. After a mean follow-up of 48 months, 72% voided spontaneously and 50% did not need to perform self-catheterization [56]. Another group reported their results in 20 implanted women. After a mean follow-up of 41 months, 86% voided spontaneously and 55% did not need to perform self-catheterization [57].

The 5-year results of a postapproval study of the original randomized controlled MDT-103 study were recently reported. Success was defined as >50% decrease in the number of catheterizations per day as compared to baseline. Five-year follow-up diaries were available from 22 of 31 patients with nonobstructive urinary retention (1 patient had been explanted), and 58% of these still had a successful outcome. However, the percentage of patients that did not have to catheterize at all was not reported [45].

Kessler and Fowler reviewed the results of SNM for urinary retention and found that the success rate ranged between 55 and 100% after a follow-up duration of 43 and 15 months, respectively [58]. Recently, Peeters et al. reported on 93 patients with nonobstructive urinary retention: after a mean follow-up of 47 months, 58% of the patients did not need to catheterize anymore [48].

They also found a higher long-term success rate in patients implanted for Fowler's syndrome than in those with idiopathic retention, with 62.5% and 53%, respectively, not needing to self-catheterize.

In summary, a more than 50% reduction in the number of catheterizations is found in 58%–86%. The cure rate, that is, the percentage of patients not needing to catheterize at all, is around 50%–58% after 41–48 months of follow-up.

INTERSTITIAL CYSTITIS

Several authors performed permanent implantations of the InterStim^{TM} device for treatment of interstitial cystitis. Some investigators report good results with up to 75% improvement in symptoms [59–61], including a 20% "cure" rate [60]. However, follow-up in these studies was short (range 5.6–14 months). Berman et al. could not confirm these results [62]. Only 2 of 13 patients (25%) were pleased or delighted with the InterStim device. A randomized crossover trial of sacral versus pudendal nerve stimulation (PNS) (with the InterStim system) for interstitial cystitis indicated that overall symptom reduction with PNS might be somewhat better than with sacral nerve stimulation (59% vs. 44%; $p = 0.05$) [63]. Of those with a permanent implant, 13 of 17 chose the pudendal lead. The 17 patients were followed for 6 months: 3 did not complete follow-up visits, and in the remaining patients, the number of voids decreased by 41% for PNS and 33% for SNS (statistically not different).

Battery longevity in a Medicare population after sacral neuromodulation was reported by Cameron et al., who noted that 11 of 19 batteries implanted for interstitial cystitis were removed and the odds of explantation in interstitial cystitis patients were 10.5 (95% CI: 3.9–28.4) [64].

The limited evidence in interstitial cystitis patients seems to indicate that sacral nerve neuromodulation leads to an initial symptom improvement but is not very successful with longer follow-up.

ADVERSE EVENTS

The necessity to reposition the electrode after migration was reported in about 20% of patients in the early experience with SNM [32,65]. Pain at the site of the pulse generator or the lead or in the leg is the most frequently reported problem. Siegel et al. reported adverse events for 219 InterStim-implanted patients [41]. The majority of events observed were pain at the stimulator site (15.3%), new pain (9%), pain at the lead site (5.4%), suspected lead migration (8.4%), infection (6.1%), transient electric shock (5.5%), and adverse changes in bowel function (3%). Dasgupta et al. also reported a high overall adverse event rate of 51.6% [66].

In a review of randomized trials and case series, Brazzelli et al. noted a 33% surgical revision rate in 855 patients, with pain at the stimulator site being the most common problem, accounting for 25% of the surgeries [67]. Van Voskuilen et al. reported a surgical revision rate of 48.3% (excluding pulse generator replacements) after an average follow-up of 64.2 months [42]. During a 7-year study period, 26 surgical revisions (including 8 explants) had to be performed in 55 women who had been implanted for refractory voiding dysfunction (47.3%) [68].

Sutherland et al. reported on their 11-year experience in 104 patients. In this population, 47.1% of the leads were tined [6]. A 53% adverse event rate was reported. Notably, the adverse event rates associated with tined and nontined leads were 28% and 73%, respectively. However, the follow-up duration was quite different. The average follow-up of the tined lead versus the nontined lead group is approximately 1–1.5 years versus 5–5.5 years. This difference can at least partly explain the difference in adverse event rates. The tined lead is not free from complications and lead migration has been reported in 2.1% [69], but this is less than the 8.4% suspected lead migration rate reported with the original lead [41].

CONCLUDING REMARKS

Neuromodulation can be very beneficial for some patients with an OAB syndrome or nonobstructive urinary retention and should be considered before applying more invasive, nonreversible treatments. However, the durability of the initial success is probably overrated in most reports. The cure rate in patients with refractory urgency incontinence is around 15%–20% at 4–5 years of follow-up [46,48]. In patients with nonobstructive urinary retention, the cure rate at 3.5–4 years is about 50%–58% [48,56,57]. It is difficult to define cure in patients with the urgency–frequency syndrome; a normal daytime voiding frequency seems to be achievable in about a third of the patients [48]. The published reoperation rate approaches 50% after an average follow-up of 5 years [42]. The effect on the quality of life is unclear [7]. Unfortunately, the true cost/benefit ratio of this expensive type of treatment is not known [35].

It is still unclear how best to choose patients for this procedure, since no predictors of success have been identified. Technical advances such as the use of the tined lead, the two-stage implant, the smaller InterStim II pulse generator, buttock placement of the pulse generator, and the less invasive partially percutaneous technique seem to have decreased the necessity for revision [28,70]. However, higher success rates with the definite implant are not to be expected with these technical modifications, provided that the sacral nerve is stimulated adequately when using the older technique.

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49 Injectable Bulking Agents in the Treatment of Female Stress Urinary Incontinence

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INTRODUCTION

A multitude of options exist for the management of female stress urinary incontinence (SUI), such as pelvic floor muscle training (PFMT), urethral suspension procedures, urethral slings, and urethral bulking agents [1–3]. Careful patient education regarding the etiology and natural history of SUI as well as the physiology of urinary storage and voiding is extremely helpful in setting shared goals with the patient regarding all management options. Current guidelines recommend, at a minimum, a focused history and physical exam; an objective demonstration of SUI and urinalysis; and an assessment of postvoid residual, with additional diagnostic testing (urodynamic evaluation, cystoscopy, imaging, etc.) being utilized on a case-by-case basis [1–3].

For bothersome SUI, a shared patient decision on which management strategy to pursue is made after thorough discussion of the many options available and their attendant risks and benefits. Presently, a first-line approach with noninvasive treatment via behavioral management and PFMT may allow some women to avoid surgical intervention, albeit, via postal surveys at 15 years, the effectiveness of this management does not appear sustainable [4].

For many patients choosing bulking agents, a desire for a simple in-office injection technique with immediate, albeit not permanent, result may be paramount. Others, based on realistic goals, choose urethral bulking having undergone one or more prior procedures with less than a satisfactory outcome and are not interested in enjoining more invasive procedures. Some patients may not be candidates for other procedures due to fragility or medical comorbidities. Less commonly, patients may have a poorly coaptable, fixed urethra [5], i.e., a “pipestem” urethra [6], therein reducing the efficacy of procedures dependent upon the augmentation of closure mechanisms by reducing urethral hypermobility with stress events.

INDICATIONS

Bulking agents are used where bothersome urinary incontinence results from poor intrinsic sphincter function, often quantified by the determination of the abdominal leak-point pressure or maximum urethral closure pressure (MUCP) [7]. Notably, there is a lack of high-quality evidence correlating the results of urodynamic studies with treatment outcomes for patients with SUI [8,9]. As such, complex urodynamic-derived criteria are generally not required prior to the use of bulking agents. The determination of the postvoid residual volume, however, is recommended prior to the use and reinjection of bulking agents [9], both diagnostically and to reduce adverse events, as the application of bulking agents in the setting of an elevated postvoid residual may lead to outlet obstruction and overflow incontinence [10].

Bulking agents may be used as primary treatment and, importantly, do not hamper the subsequent use of surgical procedures when and if necessary to complement sphincteric competence [11]. Notably, bulking agents for female SUI have the uncertain honor of having more English-language review articles since 2000 [12–24] than primary RCTs [25,26–31].

In addition to use as a primary treatment, several reports support injection of bulking agents as an effective adjunct for many difficult clinical scenarios, including secondary application following failed surgical procedures [32–34] and following radical pelvic surgery in both men and women [35,36], in patients with spinal cord injuries [37,38], or for continent stomas [39] that lack the desired level of continence due to insufficient closure pressures. As with use in a primary setting, large high-quality studies of bulking agents in the aforementioned challenging situations are lacking. Additionally, effective soft-tissue bulking has been reported in pediatric vesicoureteric reflux [40–43], fecal incontinence [44–49], cosmetic procedures [50,51], and gastroesophageal reflux [52].

MECHANISM OF ACTION

The urinary sphincter is a complex and naturally complementary closure mechanism to the varying pressures placed across the pelvic floor. Coaptation of the urethral lumen allowing for a watertight seal involves the physical properties of the intrinsic softness of the mucosa [5], supportive connective tissue, normal vascularity [53,54], neural integrity, and adequate function of surrounding smooth and striated muscle to provide resistance to these variable intra-abdominal forces. The voluntary sphincters are necessary for active continence; hence, strength training these voluntary muscles with pelvic floor muscle contractions [55,56] allows for heightened closure pressures during momentary and nonsustained increases in abdominal pressure, as occurs with coughing, sneezing, and other Valsalva activities.

Bulking agents work by increasing resistance to intra-abdominal forces via the soft-tissue filler properties of the injectable agent [57]. The capacity to bulk soft tissue is inherently limited. Hence, improvement of continence may be limited if the degree of incontinence is severe. Poor tissue compliance may not accommodate sufficient soft-tissue fill for complete continence. Though only case reports exist, poorly coapting soft tissues due to neural damage, in postprostatectomy incontinence [36,58–61] or stomas, may achieve effective soft-tissue fill with a bulking agent.

Injected autologous cells of skeletal muscle (muscle-derived cells [MDC]) may provide an additional benefit to soft-tissue bulking including a dynamic element of muscular contraction and potentially enhanced resting tone.

HOW HAVE RESULTS BEEN QUANTIFIED?

Several comparative trials have measured the efficacy using the Stamey Urinary Incontinence Scale [62], which is likely associated with a poor discrimination index [63] to detect changes in continence (i.e., integrals are broad, as in 1, leakage with vigorous activity, versus 2, leakage with minimal stress). More recent trials have included more sensitive and appropriate measures of change in continence, including pad tests, validated questionnaires, and patient perception of effectiveness [64].

Most comparative trials are noninferiority trials [65] with their inherent limitations and used Contigen^{TM} (no longer available) as the comparator.

Current literature does not demonstrate any significant difference in efficacy or complications between currently accepted bulking agents [3]. Bulking agents' effectiveness tends to decrease over time. Anticipated efficacy for patients treated with collagen without concomitant prolapse treatment has been reported to decline over time, from 48% at 12–23 months to 32% at 24–47 months [66]. A recent systematic review of response rates at 12 months with experienced surgeons approached 30%–40% dry, with twice that percentage dry/improved. Unfortunately, none of the current bulking agents have proven durable; several of the RCTs are notable in that they were designed to end at 12 months after the last injection.

Using all measures, bulking agents are less effective and less durable than other procedures but remain less invasive with lower complication rates [67].

WHICH BULKING AGENT TO CHOOSE?

Each of the available bulking agents is similar in benefits/risks/burdens [3]. In an unusual trial of multiple agents, a 12-month analysis of over 800 cases of urinary transurethrally applied glutaraldehyde-cross-linked collagen (n = 312), nonanimal stabilized hyaluronic acid/dextranomer (NASHA/Dx) (n = 54), ethylene vinyl alcohol (EVOH) (n = 104), and polyacrylamide hydrogel (n = 44) demonstrated that the objective and subjective measures were similar for each group, with negative pad tests in over 70% of these women [68]. For most agents, the published prospective randomized trials have been industry sponsored and therefore limited to one or two randomized trials. Much of the other referenced literature details durability and adverse events.

However, the technique of bulking agent injection requires a measured degree of expertise. Given that each bulking agent has characteristics specific to its application, most centers choose a bulking agent and become facile with that agent. Impaired durability of the bulking agents is a greater challenge than current safety issues.

Currently, the availability of injectable agents varies considerably around the world from country to country due to differential regulatory environments. As of 2016, commercially available agents include the following:

- *Polydimethylsiloxane macroparticles suspended within a bioexcretable carrier hydrogel of polyvinylpyrrolidone* (Macroplastique^{TM}, Cogentix Medical, Minnetonka, MN).

  Requiring a pressurized injection system, 247 females with intrinsic sphincter deficiency in a multicenter study were randomized 1:1 and treated with Macroplastique versus Contigen® serving as a control. At 12 months, the cure/dry rate was statistically better at 36.9% for those treated with Macroplastique versus 24.8% in the control group [28]. In a rare study following a study group out to 24 months, 33 of 38 of the patients achieving dry/continence at 12 months remained dry at 24 months. An additional 12 of 29 patients, who were judged improved at 12 months, were dry at 24 months [69]. The Macroplastique Implantation Device, a specialized pressured syringe and applicator, allows for outpatient transurethral cystoscopic injection under direct vision. Sterilization of the reusable injector system requires enzymatic cleaning, disinfection, and autoclaving, which may not be available within the outpatient or clinic setting.
- *Calcium hydroxylapatite (CaHA)* (Coaptite^{TM}, Boston Scientific Corp., Natick, MA).

  A multicenter RCT of 296 women, also using the poorly discriminatory Stamey Urinary Incontinence Scale to assess outcomes, found that 63.4% of patients injected with CaHA achieved an improvement of one Stamey score compared with 57% of patients injected with Contigen^{TM} [70]. The material is injected with a disposable 21-gauge needle under cystoscopic guidance and readily adapted to the outpatient or clinic setting.
- *Zirconium-coated Carbon beads* (Durasphere® EXP, Coloplast Corp, Minneapolis, MN).

  In a noninferiority trial with Contigen^{TM} as the comparator, Durasphere® achieved a nonstatistically significant improvement of one or more Stamey grade in 80% of the 61 women treated, compared with 69% of the 68 women treated with Contigen^{TM} [31]. The initial reports utilized a needle system that was cumbersome; the newer formulation ("EXP") and better needle design have facilitated these injections in the outpatient setting.
- *Polyacrylamide hydrogel (PAHG)* (Bulkamid^{TM}, Contura, International A/S, Soeborg, Denmark).

  Periurethral injections of Bulkamid^{TM} appear safe and effective in the short term in two single-arm 12-month studies of 135 and 82 women demonstrating objective improvement on pad tests [71] and in subjective measures (visual analog scales, validated questionnaires) [71,72]. A recent multicenter RCT of Bulkamid^{TM} vs. Contigen^{TM} in a 2:1 randomization demonstrated noninferiority of Bulkamid ^{TM} to Contigen^{TM} with 47.2% and 50% of patients treated with Bulkamid^{TM} versus Contigen^{TM} achieving zero incontinence episodes, respectively, and 77.1% versus 70% of patients treated with Bulkamid^{TM} versus Contigen^{TM}, respectively, cured/improved.
- *Porcine dermal implant* (Permacol^{TM}, Covidien plc, Dublin, Ireland).

  In a 6-month RCT of 50 women, Permacol^{TM} formulated for injection was compared with Macroplastique^{TM} again using the weakly discriminating Stamey Urinary Incontinence Scale coupled with a validated questionnaire. They reported that 64% and 60% of the Permacol-treated patients achieved improvements in these respective outcome measures versus 46% and 42% improving in the Macroplastique^{TM} group [30].

NOT AVAILABLE

- *Glutaraldehyde-cross-linked bovine collagen (Contigen^{TM})* has been the standard against which other agents have been compared; unfortunately, the bovine collagen is no longer available. Furthermore, the product is immunogenic requiring a negative skin testing 30 days prior to bulking agent injection.
- *Autologous fat* should no longer be used due to ineffectiveness against injected saline

demonstrated in a randomized trial [73]. A fatal pulmonary embolism [74] and a fat embolism syndrome [75] argue strongly against its use; of note, the fat embolism syndrome was associated with an injection with 14G needle using a periurethral approach. Of note, autologous fat remains widely used in cosmetic procedures and purportedly retains 60% of its bulk over time. This result has not been translatable to safe or efficacious use in urinary incontinence.

- *NASHA/Dx (Zuidex*^{TM}): With a high rate of pseudoabscess formation precluding its use [27], *Zuidex* has been used with [27] or without [76] the Implacer device, a noncystoscopic transurethral injection device. However, the Deflux^{TM} formulation of NASHA/Dx is effective and safely used in pediatric vesicoureteric reflux.
- *EVOH copolymer (Uryx*^{TM}): Uryx is used much more extensively in vascular and interventional studies in an alternative formulation; it has also been studied as a potentially reversible compound injected into the vas deferens [77] or fallopian tube [78] for sterilization. It was withdrawn from the SUI marketplace due to frequent reports of urethral erosion of the material [79].
- *Polytetrafluoroethylene (Polytef*^{TM}): Polytef was associated with migration in animal studies [80] and is no longer used in routine clinical practice [81].

TECHNIQUES

Bulking agents have been injected periurethrally (peristomal), transurethrally (transluminally), or combined [64], in the midurethra [27] and at the bladder neck [82], both in retrograde [83] and antegrade fashion [84], and with cystoscopic guidance in most [85], but not all [86]. Standardization of techniques has hampered comparison of results.

Achieving higher "maximum squeezing" opening pressure correlates with improved continence after bulking agents. It has therefore been suggested that agents should be injected on the luminal side from the sphincter and at the high-pressure region of the sphincter [57].

A bulking agent theoretically achieves a gradual increase in the central filling of the urethral soft tissue, as may be measured by an improvement in MUCP [57,68]. Increasing volume of the injected bulking agent would subsequently result in decrease in luminal closure pressure if the bulking agent either overbulked the region [47] or conversely extravasated. Notably, success rates have been reported to decrease with an increased number of injection sites, likely due to extravasation [87]. Injection of the material, therefore, should be slow and deliberate in order to maximize fill and reduce disruption of the fragile soft tissue. Sequential injections are preferable to bursting the soft-tissue *envelope* created by the bulking agent. Therefore, it may be useful to think of reaching a "sweet spot" with the volume injected: too little is ineffective at raising the intraluminal closure pressures, and too much will burst the envelope containing the bulking agent.

Transurethral injections directed nearer to the bladder neck may be associated with less urinary retention compared with periurethral injections as is reported in some studies comparing methods. It has been theorized that the greater volume reported in most comparative trials of the periurethral injection may be an associated cause [88]. Others have suggested that a luminally placed bulking agent might allow for higher degrees of soft-tissue creep (i.e., resistance to deformation by stressors) than a periurethral application, thereby implying higher efficacy of a transurethrally placed agent [88]. Others report no statistical difference between the effectiveness of the periurethral versus transurethral approach to injection [88,89].

In the transurethral technique, the bulking agent may be injected at the bladder neck or the midurethra under cystoscopic guidance. There is insufficient comparative data to support bladder neck versus midurethral injection. In the transurethral cystoscopic approach, the urethral mucosa is punctured distal to the chosen injection locale in the urethra. Prior to the puncture, the urethra and bladder are inspected and the scope is then withdrawn to the distal urethra. The middistal portion of the urethra is punctured with the bevel of the needle toward the lumen at a 30°–45° angle. The needle is transluminally advanced into the submucosa, but not to the muscularis. The angle is subsequently dropped parallel to the path of the urethra, and the needle is advanced approximately 1 cm within the submucosal layer with slow deliberate injection of the material aided by visual deformation of the tissues and halting further injection particularly if blanching of the mucosal vessels is observed.

The bulking agent is more effective in a circumferential distribution [90]. Submucosal hydrodissection with lidocaine may be performed prior to injection [91] to reduce discomfort and to prepare the envelope for the agent. Once the injection is completed, the needle is held in position for several seconds prior to withdrawal, in order to allow for equilibration of pressures within the receiving soft-tissue envelope and to reduce extravasation from the needle site [91]. While failure rates have been reported to increase with the number of puncture sites [83], presumably due to the loss of the bulking agents through these punctures, several industry-recommended techniques include three-site injections (e.g., Macroplastique).

Contraindications to the use of a bulking agent in an appropriately selected patient include an active urinary tract infection or known hypersensitivity to the agent or any of its components. Bulking agents have been successfully and safely injected in fully anticoagulated patients, albeit with a theoretical concern for an increased risk of ongoing hematuria or urinary retention in the setting of a periurethral hematoma (personal experience).

COMPLICATIONS

Currently, available bulking agents have an acceptably low rate of acute and chronic complications. The most common adverse event is temporary urinary retention with major adverse events being rare [62,63,84]. Acute urinary retention has been reported in up to 24% of patients in a study of Durasphere and thus deserves mention during patient counseling. Additionally, it should be noted that retention in this setting is transient, for instance, lasting 7 days or less in most series [24,63]. Other adverse events that may be commonly encountered include postoperative dysuria, hematuria, uncomplicated urinary tract infection, and de novo urinary urgency, which typically resolve with conservative management [62,63,92,93]. Aspiration or incision and drainage of the injected agent is associated with 100% return of the patients prior sphincteric incontinence [94].

A few specific long-term complications that are quite rare, typically reported as single cases or small series, merit consideration as well. Urethral prolapse, potentially from disruption of support between the urethral mucosal and muscle wall with urethral bulking, has been reported [95–99]. Periurethral masses, variously described as periurethral pseudocyst [100] or sterile pseudoabscess [48,75,76,100–105], may be large and symptomatic and are associated with outlet obstruction [106] and/or pain [75]. Treatment of these lesions with aspiration [94] is associated with symptomatic pseudoabscess reoccurrence and thereby may require definitive transurethral, transvaginal, or retropubic incision and drainage [76]. These masses, if draining spontaneously into the urethral lumen, might progress to a de novo urethral diverticulum [107,108]. Extremely rare is a single case report of an infectious abscess [104]. As several agents require high-pressure injector systems, particle migration into local and distant lymph nodes may occur [109] and be visibly confirmed if the bulking agent is able to be imaged. Embolization may also occur, though only autologous fat has been reported to result in pulmonary embolism [75] and death [74]. Bulking agents can be inadvertently injected into the periurethral venous plexus.

All bulking agents could be erosive, resulting either from a property of the injected agent [110] or of the surrounding tissue [111,112] and may result in the extremely rare complication of fistula formation. Transvaginal incision and drainage of a pseudoabscess carries this theoretical risk.

Adverse events have also been reported outside of the urologic and gynecological literature, such as in plastic surgery series, but are likewise rare [113,114].

IMAGING

Bulking agents will cause deformation of the normal tissue planes on imaging [115,116]. These may be radiographically opaque (Durapshere™, Coaptite™). Of greater concern is the normally functioning bulking agent occasionally misinterpreted as a complex soft-tissue mass suggestive of malignancy, periurethral abscess, or urethral diverticulum. There are no known reports of mutagenicity or malignancy in association with any of the bulking agents. If a history of a bulking agent injection is unknown, misdiagnosis of a bulking agent as a diverticulum or soft-tissue fluid collection is not uncommon [117].

RESEARCH

The reconstructive and regenerative medicine literature includes multiple reports of other soft-tissue bulking agents. Thus, the nonurological literature may be instructive in the development of other agents for the treatment of SUI [118,119]. As an example, polymethylmethacrylate microspheres in miniswine were found to be safe at necropsy [120]; however, subsequent human studies report complications in soft tissues [121].

The pelvic floor specialist has been told to look for a durable bulking agent. However, this is in contradistinction to much of the cosmetic literature that is searching for temporary soft-tissue fillers, such as poly-l-lactic acid or hyaluronic acid fillers. The cosmetic and plastic surgeons work under the assumption that all such soft-tissue agents will be temporary due to progression of the soft-tissue changes occurring with aging [93]. Although these age-progressive soft-tissue changes have not been quantified in the female continence mechanism, perhaps changes in the host tissue relate to the nondurability of the effect of bulking agents used for incontinence. Evaluation of longitudinal changes in the abdominal leak-point pressure in a cohort population with SUI not electing treatment might alter our expectations for an agent's durability and for planned retreatment.

Autologous cells: Given the relatively poor efficacy and durability with bulking agents as compared to other invasive therapies for SUI, autologous cells represent a promising therapy. Unfortunately, early work in this area was compromised by a lack of research integrity [92]. The rapidly expanding regenerative medicine literature will potentially lead to advances in this field for SUI [122]. Incontinence studies using autologous MDC are early, but promising. Obtained by needle biopsy of the quadriceps femoris muscle and subsequently expanded and injected into the urethral sphincter, MDC injection was safe in 8 women followed for 18 months. A dose–response curve was suggested in 8 of 9 patients in the high-dose group reported zero to one leaks in a 3-day diary compared to 5 out of 15 in the low-dose group [123]. A 2-year follow-up of 16 women injected with autologous upper-arm MDC also reported reasonable safety, but efficacy again suggested a dose–response effect with a modicum of efficacy (questionnaire based). Many of these studies are not designed to determine if the injected muscle cells are viable or functional [124] that leads to the hypothesis that these interventions exert their favorable effects simply by providing passive tissue bulking [125]. Other studies are underway in the United States. (https://clinicaltrials.gov. Search bulking agents, wherein there are nine open trials, accessed July 23, 2014.)

FUTURE RESEARCH

Future areas of research regarding urethral bulking may include the following:

1. Improved reporting
   a. Standardization of patient populations and outcomes such that bulking agents may be accurately compared with each other and with other treatment modalities
   b. Kaplan–Meier curves for bulking agents beyond 12–24 months
2. Large cooperative reports of the use of bulking agents in alternative clinical situations, such as
   a. Sphincteric urinary incontinence due to spinal cord injury or pudendal injury
   b. Postprostatectomy incontinence with either anastomotic regions or resected areas that retain both tissue compliance and expandability
   c. Continent stomas or neobladder anastomotic regions that lack effective seal for achieving dryness
3. High-quality studies on MDC to establish their durability and potentially enhanced continence beyond a pure tissue bulking agent

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50 Use of Botulinum Toxins in the Management of Female Voiding Dysfunction

David Ginsberg and Ellen Goldmark

INTRODUCTION

Botulinum toxin (BoNT) was initially FDA approved for the treatment of strabismus in 1989. Over time, its use has expanded for the treatment of a variety of multiple conditions, including migraine headaches, limb spasticity, cosmetic surgery, muscular dystonia, and lower urinary tract dysfunction [1]. The first urological application for BoNT was reported in 1988 for the treatment of detrusor sphincter dyssynergia (DSD) [2]. In 2000, BoNT serotype A (BoNT-A) was described as being an effective treatment for patients with detrusor hyperreflexia secondary to spinal cord injury (SCI) with urinary incontinence between intermittent catheterization [3]. It was not until over a decade later, in August 2011, that BoNT-A finally received FDA approval for the treatment of urinary incontinence due to neurogenic detrusor overactivity (NDO) in patients who had an inadequate response or were unable to tolerate anticholinergic medications [4,5]. Shortly thereafter, in January 2012, the FDA approved the use of BoNT-A in patients with overactive bladder (OAB) with symptoms of urge urinary incontinence (UUI), urgency, and frequency in adults who have an inadequate response to or are intolerant of an anticholinergic medication [6].

Off label, it is used in women with frequency/urgency and no evidence of DO, interstitial cystitis/painful bladder syndrome (IC/PBS), and DSD. The use of BoNT-A for the treatment of a variety of female urological conditions has provided an alternative to major reconstructive surgery in patients with NDO as well as relief from bothersome OAB symptoms in women who have failed medical therapy.

Biology and Mechanism of Action

Clostridium botulinum is a Gram-positive anaerobic bacterium, whose strains produce seven immunologically distinct neurotoxins (types A–G). It was first isolated by van Ermengem in 1897 [7]. Types A and B have been used to treat medical conditions, with type A being used most often as it is relatively easily obtained and stable. The neurotoxin component is synthesized as a biologically inactive single-chain polypeptide activated by cleavage of the polypeptide chain into a 100-kDa heavy chain and a 50-kDa light chain linked by a disulfide bond [8,9]. There are a variety of type A botulinum toxin products available; these products are not equivalent and the doses are not interchangeable. Table 50.1 summarizes what is currently commercially available in various countries around the world. OnabotulinumtoxinA (Botox, Allergan, Irvine, CA) is the only botulinum toxin product approved for use in the lower urinary tract in the United States.

Under normal circumstances in striated muscle, each muscle fiber is innervated by a single motor neuron at a site near the middle of each muscle fiber. This is termed the motor end plate. Within each nerve terminal are cystoplasmic vesicles containing Ach transmitter molecules. The Ach collects within clusters of these synaptic vesicles and each vesicle aligns with a patch of dense material forming an active zone. At the active zone in response to a propagated neural impulse, vesicles fuse with the plasma membrane resulting in the release of the Ach transmitter molecules into the synaptic cleft. The Ach diffuses across the synaptic cleft, binding to and stimulating the postsynaptic Ach receptors on the muscle cell. This results in a muscle contraction [10]. Three intracellular membrane-associated proteins are required for the binding of Ach-filled vesicles to the presynaptic active zone and exocytosis of Ach into the synaptic cleft: synaptobrevin, synaptosomal-associated protein 25 (SNAP-25), and syntaxin. The three proteins and the synaptic vesicle form the soluble *N*-ethylmaleimide-sensitive factor attachment protein receptor (SNARE) complex [11].

Both the light chain and the heavy chain of the BoNT molecule have specific roles in creating its physiological effect. After injection, BoNT is taken up by nerve cells via the heavy portion of the molecule. Its heavy chain is involved in the binding of the neurotoxin and in the transportation of the neurotoxin into the neuronal cytosol (endocytosis). Once the molecule is intracellular, its light chain is responsible for the cleavage of the intracellular protein SNAP-25 that prevents formation of the SNARE complex and thus prevents binding of the synaptic vesicle to the cell membrane and release of Ach [12–14]. Without the release of Ach into the synaptic cleft, there is no muscle contraction.

BoNT-A Use in Neurogenic Detrusor Overactivity

NDO refers to the urodynamic finding characterized by involuntary detrusor contractions (IDCs) during the filling phase of urination, which may be spontaneous or provoked, due to a relevant neurological condition [15,16]. It is critical that patients with NDO maintain low bladder pressure during storage and voiding to prevent upper tract complications, recurrent urinary tract infection (UTI), bladder stones, and vesicoureteral reflux (VUR). Anticholinergics have traditionally been the mainstay of treatment in patients with NDO; however, these medications may cause and/or exacerbate dry mouth, as well as constipation, already an issue in this patient population [11]. Additionally, many patients continue to experience urinary leakage despite maximum medical therapy. The treatment goal of using BoNT-A in patients with NDO due to SCI is often to cause urinary retention. In such patients, initiation of intermittent catheterization is necessary to effect bladder emptying. The first paper to demonstrate success of onabotulinumtoxinA in patients with NDO was published by Schurch et al. in 2000. Despite maximum medical therapy, 21 patients with SCI and NDO with incontinence were found to have a significant increase in maximum cystometric capacity (MCC) and a mean decrease of maximum detrusor pressure following injection of 300 units of onabotulinumtoxinA. Incontinence was resolved in 17 of 19 patients and the clinical effect was still present at 9 months in the 11 patients who were still being followed [3].

Table 50.1 Different Forms of Botulinum Toxin (Serotype A) in Clinical Use

	OnabotulinumtoxinA	**AbobotulinumtoxinA**	**IncobotulinumtoxinA**
Commercial name	Botox® (Allergan, Irvine, CA)	Dysport® (Ipsen, Paris, France)	Xeomin® (Merz, Frankfurt, Germany)
Units/vial	100	500	100
Available doses	50, 100, 200	300, 500	50, 100

Subsequently, Schurch et al. performed a randomized placebo-controlled study of onabotulinumtoxinA in patients with NDO and urinary incontinence. Patients received either 200 or 300 U of intradetrusor onabotulinumtoxinA or placebo (saline) injections. The two treatment groups had significant posttreatment decreases in incontinence episodes, while the placebo group did not. The study was not powered to demonstrate a difference in efficacy between 200 and 300 U doses, but the similarity between the doses lead to further evaluation for the treatment of NDO with the 200 U dose [17].

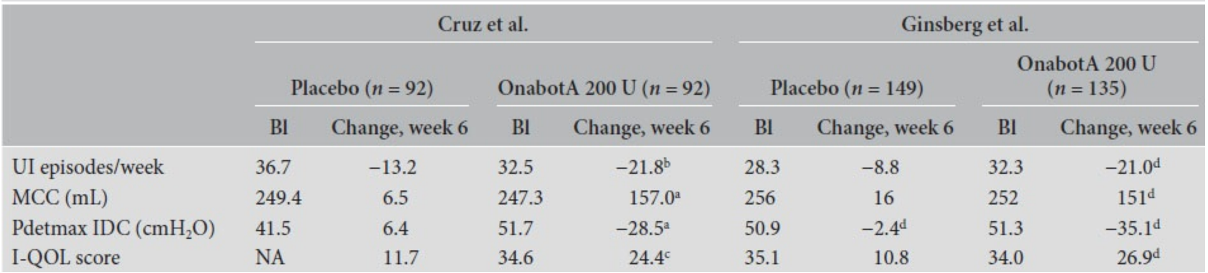
FDA APPROVAL FOR NEUROGENIC DETRUSOR OVERACTIVITY

Two large, multicenter, double-blind, randomized placebo-controlled trials were subsequently performed with the intent of obtaining an FDA indication for NDO. A total of 691 patients with NDO secondary to multiple sclerosis (MS) (n = 381) or SCI (n = 310) were evaluated. The primary endpoint of the studies was a change from baseline in the mean number of urinary incontinence episodes/week at week 6. Adverse events were recorded. Patients who received 200 and 300 U of onabotulinumtoxinA demonstrated significant improvements over placebo, with a decrease of mean urinary incontinence episodes. Median time to patient request for retreatment was 36.5 and 42.1 vs. 13.1 weeks for onabotulinumtoxinA vs. placebo in the two studies. The need for new onset intermittent catheterization (for patients not on IC at baseline) was approximately 25% higher in the treatment groups as compared to placebo [4,5] (see Table 50.2).

Prior to the introduction of BoNT-A for NDO, female patients who failed medical therapy were offered indwelling catheterization, diapers/pads, or major reconstructive surgery with a bladder augmentation or other urinary diversion [18]. The introduction of BoNT-A in this patient population has provided an alternative, less-invasive treatment option for patients with NDO and medication refractory urinary incontinence. It is likely that in years to come, bladder augmentation will be reserved for patients with refractory detrusor overactivity or impaired compliance that have failed treatment with BoNT-A [19].

A particularly difficult subpopulation of women with NDO are those suffering from MS. Studies show that the prevalence of women to men with MS is >2:1 [20]. This population of patients often experience bothersome NDO coupled with incomplete bladder emptying and, depending on their disease, may lack the manual dexterity to perform self-catheterization. The risk of urinary retention is approximately 25% in patients with NDO given 200 U of onabotulinumtoxinA and 5% in patients with OAB given 100 U of onabotulinumtoxinA (and will be discussed later in the manuscript). Based on these data, we routinely treat women with NDO secondary to MS who are not already on clean intermittent catheterization (CIC) and do not have an elevated postvoid residual (PVR) at baseline with the 100 U dose [4,5,21,22]. Although optimal efficacy may be compromised with the lower dose, the avoidance of urinary retention in many of these patients is crucial as the compromise of upper extremity dexterity seen in many individuals with MS makes intermittent catheterization challenging and could potentially render such patients dependent on indwelling catheterization. This is an area that is presently being studied.

Table 50.2 Comparison of Two Multicenter, Double-Blind, Randomized Placebo-Controlled Trials Leading to FDA Approval for Neurogenic Detrusor Overactivity



	Cruz et al.				Ginsberg et al.			
	Placebo ($n = 92$)		OnabotA 200 U ($n = 92$)		Placebo ($n = 149$)		OnabotA 200 U ($n = 135$)	
	Bl	Change, week 6	Bl	Change, week 6	Bl	Change, week 6	Bl	Change, week 6
UI episodes/week	36.7	−13.2	32.5	−21.8[b]	28.3	−8.8	32.3	−21.0[d]
MCC (mL)	249.4	6.5	247.3	157.0[a]	256	16	252	151[d]
Pdetmax IDC (cmH_2O)	41.5	6.4	51.7	−28.5[a]	50.9	−2.4[d]	51.3	−35.1[d]
I-QOL score	NA	11.7	34.6	24.4[c]	35.1	10.8	34.0	26.9[d]

Abbreviation:Bl, baseline.

[a] $p < 0.001$.

[b] $p < 0.01$.

[c] $p < 0.001$ vs. placebo.

[d] $p < 0.05$ vs. Placebo.

BONT-A AND OAB

As noted previously, BoNT-A was approved for the treatment of refractory UUI in January 2012. OAB is defined as a complex of symptoms comprised of urinary urgency with or without urge incontinence, urinary frequency, and nocturia. Urinary urgency is the sudden onset or desire to pass urine, which is difficult to hold. Frequency is the passage of urine, which is greater than the amount considered to be normal, usually more than 8 voids/day. UTI and other GU pathology must be excluded prior to giving a patient a true OAB diagnosis (ICS, 2005) [23]. Treatment options for OAB include behavioral modification, anticholinergic therapy, Beta-3 agonists, sacral nerve stimulation (SNS), BoNT-A, and posterior tibial nerve stimulation (PTNS). Although it is true that significant progress has made in the treatment options for OAB over the past decade, each option has a risk/benefit profile and providers must help patients select the treatment best for them. Some patients are unable to tolerate side effects from anticholinergic medications (dry mouth, constipation), and some do not experience desired treatment effects. Recent FDA approval of the new Beta-3 agonist for OAB does provide an alternative to anticholinergic medical therapy but does not always provide the desired effects. SNS requires a permanent implant placed in the operating room and PTNS, although with few risks, does require 12 consecutive in office treatments, followed by monthly maintenance visits for continued benefit. BoNT-A can be administered in the office with local anesthesia, although it does require a cystoscopy to administer as well as repeat injections to maintain effects chronically.

OAB EPIDEMIOLOGY AND FINANCIAL IMPLICATIONS

OAB prevalence is estimated to impact 12.9% of women, with nearly half (48%) reporting symptoms of incontinence. Additionally, there is a financial burden associated with OAB [24]. Patients with urinary incontinence have been shown to have higher health-care resource utilization and lower health-related quality of life and productivity [25]. Direct costs of OAB relate to its diagnosis and treatment, and indirect costs include lost time from work and impaired work performance, with additional patient-related factors such as depression, sleep disturbance, skin infection, and UTI [26–28]. A review of the literature by Coyne et al. described a cost analysis incorporating OAB with UUI prevalence rates as well as data on the use of each cost component to calculate annual direct costs in patients older than 25 years. From this, the total cost of OAB in the United States in 2007 was estimated at $65.9 billion, of which indirect costs accounted for 22.1% [29]. The projected cost of OAB in the United States is $76.2 billion in 2015 and $82.6 billion in 2020 [30]. One study has shown that lost productivity costs due to OAB are as high as $841 million dollars/year [31]. With the economic and human burden associated with OAB, one can see how the FDA approval of BoNT-A may prove to be valuable over time.

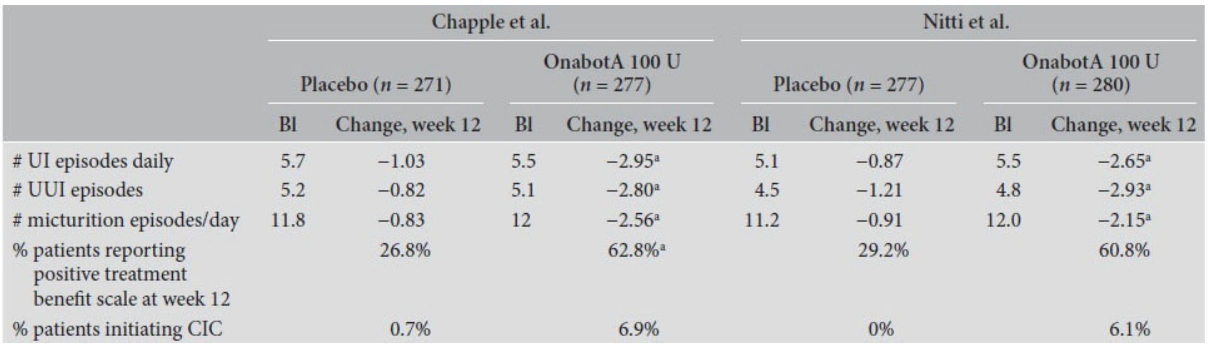
FDA APPROVAL FOR BONT-A FOR IDIOPATHIC DETRUSOR OVERACTIVITY

Though not an FDA regulatory trial, the first clinical study for idiopathic detrusor overactivity (IDO) and BoNT-A was reported in 2001. Radziszewski et al. treated seven patients with IDO with 300 U of abobotulinumtoxinA and demonstrated that all patients achieved continence after 1 month [32]. Since then, multiple large, placebo-controlled studies have been performed to evaluate the efficacy and safety of BoNT-A for UUI.

Two large, phase III, placebo-controlled studies were conducted involving a total of 1105 patients with OAB and UUI refractory to antimuscarinic therapy. Patients were randomized to receive 100 U onabotulinumtoxinA injections vs. placebo. Patients with idiopathic OAB who experienced three or more urgency UI episodes/3-day period and an average of eight or more voids/day were enrolled. Patients had failed prior treatment with anticholinergic medication due to either lack of efficacy or intolerability of side effects. Notably, urodynamics were not performed in these trials. These studies showed that onabotulinumtoxinA improved continence vs. placebo with a statistically significant decrease in the daily frequency of urinary incontinence episodes vs. placebo. A significant improvement was also seen in a variety of other secondary outcomes such as frequency and urgency as well as quality of life (Table 50.3). Temporary urinary retention requiring the initiation of CIC was more common in the treatment arms of both studies and was approximately 6% greater in the treatment arm. While outcomes were not stratified according to gender, it is likely that these results are applicable to most female patients with urgency urinary incontinence secondary to OAB as the majority of patients in the studies (90% and 88%) were women (see Table 50.3) [21,22].

Prior to onabotulinumtoxinA receiving FDA approval for use in urgency incontinence, Brubaker et al. performed a multicenter trial in women with refractory urge incontinence (defined as having failed at least two anticholinergic medications and at least one supervised behavioral therapy), detrusor overactivity incontinence, and >6 episodes of urge incontinence/3 days. Patients were treated with 200 units of onabotulinumtoxinA or placebo (28 BoNT-A arm, 15 placebo). The primary endpoint was improvement in urge incontinence symptoms 2 months after treatment. A total of 60% of patients treated with onabotulinumtoxinA showed improvements in the Patient Global Impression of Improvement, with a median duration of response 373 days compared with 62 days or less in the placebo group. Because interval analysis revealed 43% of patients receiving onabotulinumtoxinA experienced an elevated PVR requiring initiation of CIC (defined as a PVR >200 cc), the study was placed on hold. It is important to note that the patients were injected with 200 U of onabotulinumtoxinA, double the FDA-approved dose for OAB, and that an elevated residual was arbitrarily defined as 200 cc and did not evaluate whether or not these patients were symptomatic. The study concluded that women with IDO experienced a decrease in urge incontinence episodes with 200 U onabotulinumtoxinA, although with increased PVR and UTI [33].

Table 50.3 Comparison of Two Multicenter, Double-Blind, Randomized Placebo-Controlled Trials Leading to FDA Approval for Overactive Bladder and Urge Urinary Incontinence Refractory to Antimuscarinic Therapy



	Chapple et al.				Nitti et al.			
	Placebo ($n = 271$)		OnabotA 100 U ($n = 277$)		Placebo ($n = 277$)		OnabotA 100 U ($n = 280$)	
	Bl	Change, week 12	Bl	Change, week 12	Bl	Change, week 12	Bl	Change, week 12
# UI episodes daily	5.7	−1.03	5.5	−2.95[a]	5.1	−0.87	5.5	−2.65[a]
# UUI episodes	5.2	−0.82	5.1	−2.80[a]	4.5	−1.21	4.8	−2.93[a]
# micturition episodes/day	11.8	−0.83	12	−2.56[a]	11.2	−0.91	12.0	−2.15[a]
% patients reporting positive treatment benefit scale at week 12		26.8%		62.8%[a]		29.2%		60.8%
% patients initiating CIC		0.7%		6.9%		0%		6.1%

Abbreviation:Bl, baseline.

[a] $p < 0.001$.

COMPARISON OF BONT-A TO ANTICHOLINERGIC THERAPY

Comparison of onabotulinumtoxinA with anticholinergic therapy was studied by Visco et al. in a double-blind, placebo-controlled randomized trial in women with idiopathic urge incontinence who had not necessarily failed oral drug therapy [33]. Women with five or more episodes of UUI per 3-day period were randomized to daily oral anticholinergic plus one intradetrusor injection of saline vs. one intradetrusor injection of 100 U onabotulinumtoxinA plus oral daily placebo. The primary outcome was the reduction from baseline in mean episodes of urgency urinary incontinence per day over a 6-month period. The study demonstrated that the women in the onabotulinumtoxinA arm of the study were significantly more likely to report complete resolution of UUI (27% vs. 13%, $p = 0.003$) than those in the anticholinergic group. Both groups had improvement in quality-of-life measurement, without a statistically significant difference between groups. Both oral anticholinergic therapy and onabotulinumtoxinA were associated with similar reductions in the frequency of daily episodes of UUI. The onabotulinumtoxinA group was more likely to have transient urinary retention and UTI, while the antimuscarinic arm reported more dry mouth [34]. While interesting, it is not clear how applicable these data is clinically as onabotulinumtoxinA is presently approved for patients that have failed treatment with anticholinergics, which is not the group studied in this paper.

BONT-A USE IN OAB WITHOUT DO

Although not FDA approved for the indication, BoNT-A may be considered in women with symptoms of urgency/frequency without urodynamic demonstrable DO. BoNT-A use in women with urgency/frequency provides an alternative treatment method for women who have failed medical therapy and desire additional therapy but do not wish to undergo other treatments for refractory OAB including sacral neuromodulation or PTNS. The use of BoNT-A for frequency/urgency without urge incontinence has not been well studied; however, a study by Kanagarajah et al. evaluated 32 patients with OAB with [13] and without [19] incontinence and no evidence of detrusor overactivity on urodynamics. Patients were randomized to receive 100 or 150 U of onabotulinumtoxinA. A statistically significant number of OAB-dry patients had improvement in urinary frequency and OAB-wet patients reported statistically significant improvement in incontinence episodes [35]. According to the AUA/SUFU OAB guidelines, if a patient fails first- and second-line treatments (behavioral therapies and medications), third-line treatments include SNS, PTNS, and BoNT-A injection [36]. It is important to note that of these three treatment options, SNS and PTNS are FDA approved for frequency/urgency (with or without urinary incontinence); onabotulinum toxin is approved for urgency incontinence refractory to antimuscarinics.

BONT-A AND DETRUSOR SPHINCTER DYSSYNERGIA

In addition to its FDA-approved use in patients with NDO, individuals with suprasacral cord lesions, specifically SCI, or MS may suffer from DSD, with the end result of troubling urinary incontinence coupled with incomplete bladder emptying. Although not FDA approved for the indication, several papers describe the off-label use of intraurethral injection of BoNT-A to reduce urethral resistance and improve bladder emptying [37,38]. A prospective study by Schurch et al. evaluated 24 patients with SCI and urodynamically proven DSD, given one of three treatment protocols each receiving at least 25 U of onabotulinumtoxinA using intraurethral or transperineal injections. Ultimately, 50 transurethral and 25 transperineal injections were performed. All but 3 of the 24 patients demonstrated urodynamic improvements after onabotulinumtoxinA injection. Improvements included decreases in maximum urethral pressure during DSD, duration of DSD, and basic urethral sphincter pressure measurement (decreases of 48%, 47%, and 20%, respectively). Of the 24 patients, 9 had a decrease in PVR. The authors noted that this treatment could be considered for patients who are unable to perform CIC or those that do not desire sphincterotomy [39]. Of note, this may be less of an issue with female patients who generally do not have problems with elevated pressures related to DESD and who do not have the options of reflex voiding to a condom catheter. This was demonstrated in the MS population by Lemack et al. who noted that women with MS rarely have issues with upper tract deterioration due to elevated detrusor pressures [40].

BONT-A AND IC/PBS

Although not FDA approved for this indication, the use of BoNT-A in the treatment of IC/PBS has been described. IC/PBS is presently defined as “an unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptoms of more than 6 weeks duration, in the absence of infection or other identifiable causes” [41]. The pathophysiology of IC/PBS is incompletely understood and is a condition very frustrating to patients suffering from the disease as well as practitioners who often feel treatment options are insufficient. Current treatments are usually unsuccessful at completely alleviating bladder pain and increasing functional bladder capacity [42]. Current management of the condition is directed at palliation of symptoms and relief of pain [43]. A theory behind the mechanism of BoNT-A use in this condition is its decrease in adenosine triphosphate release from urothelial cells. In chemically induced cystitis in rats, injection of BoNT-A into the detrusor muscles increased bladder capacity and compliance [37]. In patients with IC/BPS, inhibition of the neuroplasticity of sensory fibers in the suburothelial space by intravesical BoNT-A injections may target pain and sensory urgency [38]. Based on these principles, several studies have shown that BoNT-A injection in the bladder wall can decrease the intensity of pain in patients with IC/PBS refractory to standard treatments [44–46]. Although a recent review by Mangera et al. concluded that there was a lack of high level of evidence for the use of BoNT-A in IC/PBS, the literature does describe its use [47]. According to the AUA guidelines, BoNT-A use for the treatment of IC/PBS is a fifth-line treatment option, to be used once most other therapies fail [48].

Kuo et al. compared the therapeutic results of onabotulinumtoxinA 100 or 200 U plus hydrodistention vs. hydrodistention alone. A total of 44 patients received suburothelial injection with 200 U (n = 15) or 100 U (n = 29) of onabotulinumtoxinA followed by cystoscopic hydrodistention 2 weeks later. The control group (n = 23) received hydrodistention without onabotulinumtoxinA injection. All three groups had a decrease in symptom score, but pain scale reduction, functional bladder capacity, and cystometric bladder capacity increased only in the two onabotulinumtoxinA groups at 3 months. There was no benefit in using a 200 U vs. 100 U dose of onabotulinumtoxinA in the study in terms of pain relief or increased bladder capacity; however, the higher dose did lead to an increased incidence of urinary retention and difficulty voiding [1,45].

Pinto et al. performed a prospective study to evaluate for the efficacy and safety of repeated intratrigonal injection of onabotulinumtoxinA in patients with IC/PBS by looking at 16 women with symptoms refractory to standard therapy, who received four consecutive injections of 100 U onabotulinumtoxinA 4 months apart. The outcome measures were pain visual analog scale, O’Leary-Sant score, 3-day voiding diary, and quality-of-life questionnaire. The mean decrease in pain score, O’Leary-Sant Score, and urinary frequency and mean increase in voided volume and quality of life were similar after each treatment. Individual symptom relief lasted 6–12 months with average duration of 9.9 ± 2.4 months. Although the study included only a small number of patients, this suggests that there may be some efficacy of onabotulinumtoxinA with repeat injections used for IC/PBS [46].

A literature review by Tirumuru et al. looked at a total of 10 (three randomized controlled trials and seven prospective cohort studies) studies that evaluated a total of 260 patients with IC/BPS treated with onabotulinumtoxinA. Eight of the studies reported improvement in symptoms. Of the 260 patients, 19 required intermittent catheterization at some point after injection. The authors concluded additional studies are needed to clearly determine the benefit for onabotulinumtoxinA use in patients with IC/PBS

[1,49]. In addition, the potential need for regular intermittent catheterization due to temporary incomplete bladder emptying/retention cannot be minimized in this very difficult to treat patient population who often find catheter placement to be very uncomfortable.

Lee et al. evaluated the use of onabotulinumtoxinA in 40 patients, who had failed conventional treatments for ulcer-type (*n* = 10) and nonulcer-type (*n* = 30) IC/BPS. Patients received four sets of 100 U intravesical onabotulinumtoxinA injections every 6 months. After 6 months, 15 patients with nonulcer IC/BPS demonstrated GRA scores ≥2 (previously defined as successful treatment outcome) with the remaining 15 patients with scores <2. All patients in the ulcer group had GRA scores <2, consistent with treatment failure. After injections, all 30 patients with nonulcer-type IC/BPS demonstrated decreased pain scores, frequency episodes, and increased functional bladder capacity, while none of the patients with ulcer-type IC demonstrated any clinical or urodynamic variable improvement. At the conclusion of the study, all 10 patients with ulcer-type IC underwent transurethral cauterization of the ulcers with resultant pain relief. The conclusion of the study was that onabotulinumtoxinA injections might help with pain relief in some patients with nonulcer-type IC, but not in patients with ulcer-type IC [50].

TECHNIQUE OF INJECTION

Different injection techniques have been utilized in the literature, with authors advocating a spectrum of techniques including variables such as depth of injection, volume of diluent, and location template for injection [51,52]. The standard template for most studies including those that led to FDA approval includes a submucosal injection involving the majority of the posterior and lateral walls of the bladder without injection of the trigone (see Figure 50.1).

In most studies, injection of the trigone has been avoided due to the theoretical concern of new onset VUR [11]. A recent randomized controlled trial evaluated the location of injection using abobotulinumtoxinA at 500 U with patients receiving either 20 × 1 mL injections throughout the bladder sparing the trigone or 5 × 1 mL injections in the trigone and 15 × 1 mL injections throughout the bladder. The OAB symptom score was improved up to 26 weeks postprocedure with significant improvements in favor of the group that received injections in the trigone, with neither group developing VUR [51,53].

Another variation in technique of administration is suburothelial vs. intradetrusor injection. A small study evaluated 32 patients with SCI and NDO with all patients receiving 300 U of onabotulinumtoxinA. One group received injections at 2–4 mm depth visualized by ultrasound without suburothelial blebs or bulking seen with injection, while the other group received suburothelial injections, which demonstrated bulking of the urothelium with injection. No significant difference in bladder diary and urodynamic parameters was seen; however, improvement in bladder compliance seemed better in the intradetrusor group [53].

ADVERSE EVENTS

The most commonly seen adverse events associated with BoNT-A injection are incomplete bladder emptying and UTIs. UTI is reported at a rate of between 2%–32% and is usually associated with an elevated PVR [1,54]. Systemic side effects such as generalized weakness have been reported after bladder injection, although this is rare and appears to be related to the dose of the toxin or the formulation used [1,17,55]. A black box warning mandated by the FDA cautions that the effects of the botulinum toxin may spread from the area of injection to other areas of the body, causing symptoms similar to those of botulism. These symptoms include potentially life-threatening swallowing and breathing difficulties and even death. The symptoms that prompted the warning had mostly been reported in children with cerebral palsy being treated with the high doses of the drug for muscle spasticity; however, reports of muscle weakness postinjection for neurogenic bladder has been reported, although with doses higher than the FDA-approved dose of 200 U [55].

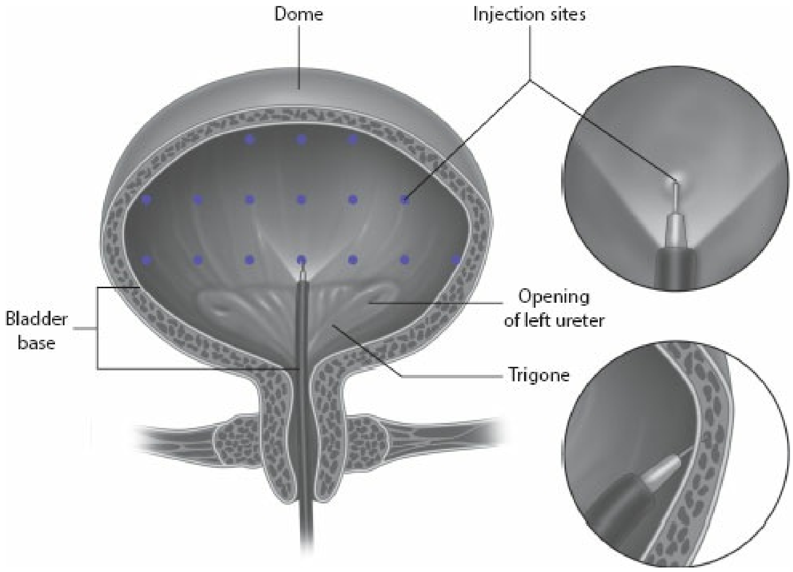


Figure 50.1 OnabotulinumtoxinA injections were administered cystoscopically in detrusor, sparing trigone. (From Ginsberg D et al., *J Urol*, 187(6), 2131, 2012. With permission.)

DOSING

According to the Botox® prescribing information, an individual is not to exceed 360 U of Botox in a 3-month interval for all indications combined. The maximum dose of administration for FDA-approved urological uses is 200 U; however, many patients may be receiving BoNT-A injections for alternative uses (spasticity, cosmetics, etc.). The highest dose studied by the manufacturer in clinical trials is 360 units; thus, that is the highest dose that has been safely studied. Maximum doses are based on the dose at which efficacy plateaus or the dose at which significant adverse events become too frequent [56]. A recent abstract reviewed 13 patients that underwent injection of greater than 360 units for a variety of indications over a 3-month time period and there were no life-threatening adverse events noted [57].

Since BoNT-A is derived from foreign (nonself) proteins, there is a theoretical risk of the development of antibodies from the recipient due to an induced immunological response. The concern with antibody development with BoNT-A is a reduction of therapeutic benefit to the patient. The incidence of neutralizing antibody production (induced antibodies that block the action of BoNT-A) is very uncommon, with rates reported around 4.7% in the original clinical trials predating its use in the urinary tract, which importantly was a BoNT-A formulation known to be significantly more immunogenic than the current clinical formulation. The rates of neutralizing antibody production are now thought to be approximately 1% across various indications [56].

The 12-week interval injection period was based on clinical trial protocols, keeping in mind the avoidance of the potential additive drug effect with minimization of the theoretical potential for antibody generation.

Finally, there is no evidence to support the notion that there is decreased efficacy of BoNT-A with repeated injections. Prior literature has shown continued efficacy with repeat injection of BoNT-A for both NDO and OAB/urgency incontinence [58,59]. In addition, the formulation of anti-Botox antibodies was not identified in any of the phase III trials for NDO or urge incontinence.

CONCLUSION

Since its FDA approval in 2011, BoNT-A has demonstrated therapeutic benefit for patients with NDO and UUI secondary to OAB refractory to alternative treatments. Although not FDA approved for IC/PBS, DSD, or frequency/urgency, certain studies do demonstrate benefit in selected patients. Patients should be counseled regarding the risk of UTI and urinary retention, with volitional voiders receiving treatment aware of the potential need to perform CIC for an elevated PVR. Although some questions remain regarding the optimal injection technique and optimal dose, with time more information likely will become available.

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Section VI

Associated Disorders

51 The Overactive Bladder

Marcus J. Drake

INTRODUCTION

Overactive bladder (OAB) syndrome is defined as urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence (UUI), in the absence of urinary tract infection (UTI) or other obvious pathologies [1]. Thus, OAB is a clinical diagnosis derived from a symptom complex centered on urinary urgency and does not require confirmatory urodynamic evaluation. Strictly speaking, "frequency" is simply the number of times someone passes urine in a defined time period; the relevant OAB symptom of passing urine too often by day is "increased daytime frequency (IDF)," and this would been more appropriate phrasing in the definition [2]. An alternative name for OAB is urgency syndrome [1].

The personal and socioeconomic burden of OAB is considerable. OAB is highly prevalent and, while not life threatening, it is associated with a significant adverse effect on quality of life (QoL), sleep quality, and emotional well-being [3,4]. OAB has been proposed to have a greater negative effect on health-related QoL than some other chronic conditions, such as diabetes mellitus, hypertension, asthma, or depression [5,6]. The estimated economic cost attributable to OAB in the United States was estimated at $12 billion per annum in 2003 [7], and this is likely to rise with aging population demographics. The real cost also needs to consider indirect or intangible costs (e.g., loss of earnings, self-purchase of containment products, and reduced productivity). Higher OAB symptom severity is associated with a greater risk of falls [8], especially in the elderly, and this may mean collateral effects, such as fractures, have to be considered in the overall population health burden of OAB. Growing awareness of the scale and impact of OAB has driven recent advances in our understanding of the assessment, pathophysiology, and management of this common and challenging condition.

TERMINOLOGY

Standardized terms to describe OAB and its constituent symptoms were reviewed by the International Urogynecology Association and the International Continence Society (ICS) in 2010 [1]. OAB signifies the presence of lower urinary tract symptoms (LUTS) during the storage phase of the micturition cycle. The constituent symptoms comprise the following:

- *Increased daytime urinary frequency*: Complaint that micturition occurs more frequently during waking hours than previously deemed normal by the woman.
- *Nocturia*: Complaint of interruption of sleep one or more times because of the need to micturate. Each void is preceded and followed by sleep.
- *Urgency*: Complaint of a sudden, compelling desire to pass urine, which is difficult to defer.
- OAB itself remains a symptom complex, and the underlying diagnosis may be related to a number of other conditions, with an overlap with voiding dysfunction in particular.

Detrusor overactivity (DO) is a urodynamic diagnosis [1], indicating the occurrence of involuntary detrusor contractions during filling cystometry. These contractions, which may be spontaneous or provoked, produce a wave form on the cystometrogram, of variable duration and amplitude. The contractions may be phasic or terminal. Symptoms, for example, urgency and/or urgency incontinence, may or may not occur. Neurogenic DO is the term used to describe DO in the presence of a relevant neurological condition. Sometimes, DO and DO incontinence can be triggered by a physical stress such as a cough [9] ("stress-provoked DO"); this should be classified as DO, not misinterpreted as representing stress urinary incontinence (SUI).

Urinary incontinence (the symptom) is the complaint of involuntary loss of urine [1]. It is classified according to the situation(s) reported to cause the urine loss. For OAB, UUI is the complaint of involuntary loss of urine associated with urgency. Mixed urinary incontinence (MUI) is the complaint of involuntary loss of urine associated with urgency and also with effort or physical exertion or on sneezing or coughing. In other words, MUI means the coexistence of UUI and SUI in the same person. A person with OAB not causing incontinence ("OAB dry") who has SUI should not be categorized as having MUI. The relationship between the OAB constituent symptoms and the three types of incontinence mentioned earlier is illustrated in Figure 51.1.

The standardized terms helped to gain coherence in a field that had previously been notable for varied and sometimes conflicting terminology. The term "unstable bladder" was previously generally used to describe both patients with involuntary detrusor contractions during bladder filling on cystometry and also patients presenting with urgency and storage LUTS, who were often treated without urodynamic evaluation. In addition, there were potential misconceptions and negative connotations for patients with the word "unstable." Thus, "overactivity" is the current preferred descriptor.

EPIDEMIOLOGY

In population-based studies, storage urinary symptoms have been reported in 17.4% of women in Europe over the age of 40 [6] and 16.9% women in the United States over the age of 18 [4]. This equates to around 49 million people in Europe and 33 million people in the United States with OAB. Prevalence rises with age, increasing to 31% of women over the age of 75 [6]. Since ongoing expansion of the aged population is foreseeable, OAB will increasingly present a major health-care challenge.

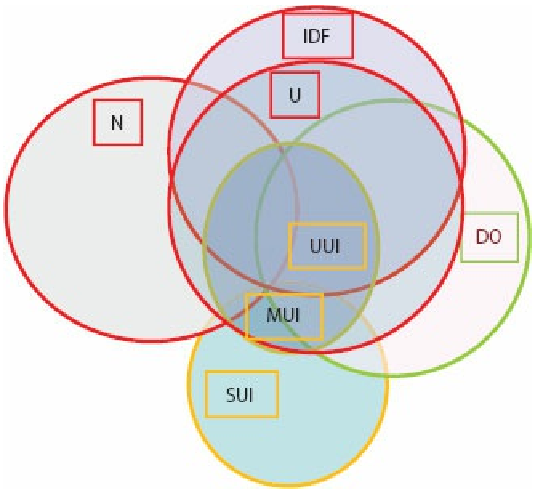

Figure 51.1 The relationship between overactive bladder and incontinence. The symptoms of OAB (outlined in red) are urgency (U), IDF, and nocturia (N). Quite a lot of nocturia is due to nocturnal polyuria unrelated to OAB, so the nocturia ring is shown having a substantial area that does not overlap with the urgency ring. Likewise, the IDF ring does not fully overlap with urgency. There are three major categories of incontinence outlined in orange. UUI is fully within the urgency ring. SUI can occur as an isolated symptom or can be associated with urgency; however, only if SUI occurs with UUI should it be termed MUI. DO (in green) is a urodynamic observation; it usually occurs with urgency, but it can be asymptomatic, and it may be observed in association with SUI.

The EPIC study [10] was a large population-based study quantifying lower urinary tract symptoms according to the current terminology. In 58,139 adults aged 18 or over in Canada, Germany, Italy, Sweden, and the United Kingdom, OAB was reported by 11.8% of the population (12.8% of women and 10.8% of men). Under the age of 60, OAB was more common in women, and over the age of 60, it was more common in men. Of women with OAB, 49.2% were incontinent (OAB wet), compared to 28.7% of men.

Overall, the greatest burden at population level results from urgency, while UUI is the more bothersome for individuals [11]. In a recent systematic review, prevalence ranges of UUI were found to be 1.8%–30.5% for European populations, 1.7%–36.4% for U.S. populations, and 1.5%–15.2% for Asian populations [12]. UUI is associated with depression, UTIs, increased body mass index, and diabetes; furthermore, there is an increased risk of falls in elderly individuals and even deaths [13].

Although OAB symptoms are common, affected people may be reluctant to discuss them. It is estimated that 60% of individuals with storage LUTS seek healthcare, while only 27% receive treatment [6]. Reasons for delay in seeking advice include acceptance of symptoms as being a normal part of aging, particularly in older patients, and the prospect of surgical treatment. Embarrassment and reluctance to discuss the problem with the general practitioner are very common and may be more so in women if the general practitioner is male. One-fifth of women consult a doctor within a year of symptoms becoming troublesome, a third delay for up to 5 years, and a quarter wait for more than 5 years [14]. Consequently, there may be a substantial population of patients with untreated OAB.

PHYSIOLOGY AND PATHOPHYSIOLOGY

The scientific focus in explaining the basis of urgency incontinence symptoms has previously been on DO, which can be evaluated urodynamically and provides an objective and demonstrable abnormality, relevant in both the clinical setting and in animal models. Two main hypotheses have for some time underpinned the understanding of the motor aspects of DO. The first arise from the long-standing recognition of the crucial role of the pontine micturition center (PMC) and the periaqueductal gray (PAG) in controlling the storage function of the bladder and the switching of the lower urinary tract from storage to voiding. The overarching regulatory control intuitively leads one to assume that lower urinary tract problems may derive from alterations in the neural regulatory circuits—the "neurogenic hypothesis" [15]. This neurogenic dysfunction could derive from alterations in the balance of excitation and inhibition or from reorganization of reflexes. Certainly, such changes do appear to be critical in urinary incontinence in many clinical situations. However, it is clear that detrusor muscle itself shows significant changes in its properties in DO—the "myogenic hypothesis" [16]. Receptors on the surface of the smooth muscle are altered in response to various physiological challenges, for example, partial denervation. As a consequence, the muscle can become abnormally excitable, a feature that has been established in animal models of bladder outlet obstruction–induced DO. In addition, the abnormal excitation can spread over an excessive distance, so a substantial proportion of the bladder wall can contract simultaneously, hence giving rise to DO. The increased excitability and abnormal propagation of excitation, perhaps as a consequence of partial denervation, underpins the myogenic hypothesis of DO [16].

In contrast to DO, the emphasis in OAB syndrome is shifted away from the motor side toward the sensations, which patients find most bothersome. Changes in the afferent nerves could in theory give rise to excessive sensory information coming from the lower urinary tract [17]. The afferent nerves within the bladder wall are surprisingly complex and can express a range of transmitters and receptors. Furthermore, nearby cell types could contribute to the generation of sensory information; the urothelium itself and nearby interstitial cells both represent interesting possibilities for modulating the sensitivity of sensory nerve function [18]. Finally, other chemical mediators released within the vicinity of the afferent nerves could alter transmission of sensory activity. Alteration in sensory nerve sensitivity, such that a greater degree of sensory information is transmitted from the bladder than would be expected for a given bladder volume, underpins the "afferent hypothesis" of OAB [17].

The motor and afferent arms converge in the integrative peripheral autonomy hypothesis [19], which focuses on interactions between different cell types in the bladder wall. It describes the presence of localized contractions in the normal bladder and exaggerated localized activity in models of OAB [20] and in humans [21], asserting that such change is a result of increased excitability not only in the muscle but also in the other relevant cell types (interstitial cells and ganglia). Furthermore, excitation can propagate through various cellular channels, including muscle-to-muscle communication (as in the myogenic hypothesis), interstitial cell networks, intramural nerve trunks, or waves of excitation through the urothelium. Widespread propagation of abnormal excitation will give rise to DO, while increased localized distortion will stimulate the sensory nerves and underpin urgency. The relative balance of localized excitability and wider propagation may explain why some people report significant urgency but are not found to have DO on urodynamic testing, while other people have significant urodynamic DO but relatively little in the way of symptoms associated with it.

Modern-day cross-sectional imaging technology is able to give some indication of cerebral and psychological responses to stimuli being conveyed from the lower urinary tract [22]. Functional brain imaging techniques such as functional MRI can look at patterns of brain activation, and definite changes in brain activity have been found in people with LUTS [23,24]. For example, urgency is associated with increased activity in the limbic cortex [25].

Further research is looking at other potential predisposing factors. Wider health issues are recognized, and OAB is associated with obesity, the metabolic syndrome, and insulin resistance [26]. At a genetic level, polymorphism of the ADRB3 gene may be associated with OAB [27], and further advances in this area can be anticipated with the current rapid progress in genetic testing methods.

There is also considerable interest in the role of underlying infections at present (see Chapter 56).

PATIENT ASSESSMENT

Assessment recommended by the International Consultations on Incontinence [28,29] specifies the history and physical examination and minimum investigations, which should include urinalysis (to exclude infection, hematuria, and glucosuria) and a bladder diary. Postvoid residual measurement is particularly indicated when voiding symptoms are present or where impaired bladder emptying is suspected (e.g., coexisting neurological disease).

In addition to characterizing the nature and severity of lower urinary tract symptoms (including associated stress incontinence or voiding symptoms), history should exclude associated visible hematuria or other symptoms suggestive of organic bladder pathology. The differential diagnosis of OAB is extensive (Table 51.1). An account should be taken of the patient's lifestyle including caffeine and alcohol consumption, as alteration of fluid intake may have significant impact on symptoms.

Table 51.1 Differential Diagnosis of Overactive Bladder

- Polyuria due to polydipsia
- Bacterial cystitis
- Bladder cancer
- Bladder stones
- Atrophic vaginitis
- Vaginal prolapse
- Chronic urinary retention
- Interstitial cystitis or painful bladder syndrome
- Nocturnal polyuria
- Drugs (e.g., diuretics)

Symptoms suggesting vaginal wall prolapse, neurological disease, and bowel and sexual dysfunction should be sought specifically, including urinary incontinence related to sexual intercourse. Comorbid conditions should be recorded, in particular a history of diabetes mellitus, congestive cardiac failure, previous pelvic surgery, and neurological disease (e.g., multiple sclerosis or stroke). The possibility of an undiagnosed neurological condition being present should be considered. Coexisting medication may well be relevant, particularly in elderly patients in whom polypharmacy is common (Table 51.2). A cognitive and functional assessment may also be necessary in older women (further details in Chapter 58).

As the adverse effects of OAB relate principally to QoL, an assessment of bother or impact on daily activities has fundamental importance in management decisions. There is a relationship, although not a strong one, between symptom severity and the perception of the degree of bother: 14% of women with mild incontinence have been found to be worried by their storage symptoms, compared with 24% with moderate and 29% with severe incontinence [30]. Sleep interruption due to nocturia and the unpredictable nature of urgency mean that these symptoms impact QoL strongly [5,31].

The most practical and systematic way to capture the crucial information is to use symptom assessment tools (questionnaires). These enable quantification of what symptoms are present, how severe they are, how bothersome, and QoL impact. Several validated condition-specific tools have been developed and continue to emerge, and they serve important roles in research and outcome assessment. Some of the most widely used are from the International Consultation on Incontinence Questionnaires (ICIQ [32]). The total urgency and frequency score (TUFS) is a research tool that weights each void according to its subjective severity on the Patient Perception of Intensity of Urgency Scale and has been validated in patients with OAB [33].

Table 51.2 Drugs Potentially Affecting Continence

- Anticholinergics
- Diuretics
- Alpha- and beta-adrenergic agonists and antagonists
- Calcium channel antagonists
- Antiparkinsonian
- Antidepressants
- Antipsychotics
- Opiates
- Sedatives

Bladder Diary

An invaluable adjunct to patient history, this allows more accurate quantification of daytime urinary frequency and nocturia, functional bladder capacity, nocturnal urine output, and overall urine output. The most simple is the frequency–volume chart (FVC), in which the patient records volume and time of each void and hours of sleep. A minimum of 3 days is suitable for routine assessment [34] and will typically show frequent small volume voids throughout the day and night in patients with OAB. A validated diary has been developed by the ICIQ [35]. Additional parameters can be captured as deemed necessary for the specific circumstances. More detailed charts include incontinence or urgency episodes, and pad usage, though increasing complexity of information captured, or longer duration, is known to reduce patient compliance. Exclusion of nocturnal polyuria (>33% daily urine output voided overnight in patients over the age of 65, or >20% in patients under the age of 65 [36]) is only possible by using FVCs, which are therefore an essential component in the evaluation of nocturia.

Urodynamics

As OAB is a symptomatic diagnosis, the role of urodynamic studies in diagnosis is limited. The majority of uncomplicated patients can begin the management on the basis of clinical assessment alone. In general, cystometry is reserved for those patients who continue to have symptoms despite effective conservative therapy. It provides a means to establish mechanism (such as DO, increased bladder sensations, or inappropriate urethral relaxation), identify any additional relevant mechanisms (such as urodynamic stress incontinence), and look for risk factors that may cause problems with treatment selection (such as impaired voiding). Urodynamic assessment is an interactive test aiming to reproduce symptoms and provide an explanation for them to guide patient management (Figure 51.2). Urodynamic evaluation is appropriate in more complex cases or where invasive treatment is being contemplated. These patients might include those failing to respond to pharmacotherapy and those with suspected bladder outlet obstruction or incomplete bladder emptying, coexisting vaginal prolapse, neurological disease, or previous lower urinary tract surgery. Women with impaired voiding tend to be older, and there is a greater prevalence of diabetes mellitus [37].

Overreliance on urodynamic traces, without referring back to the patient's history or reproduction of symptoms during the test, reduces diagnostic sensitivity of the test and risk of erroneous diagnosis. Failure of cystometry to demonstrate a substantial detrusor pressure rise during an episode of DO incontinence should be interpreted carefully; if the urethral resistance is impaired, then the change in detrusor pressure may be small. Although the symptom of urgency incontinence is suggestive and predictive of the urodynamic observation of DO, a substantial proportion of patients with OAB turn out not to have DO confirmed on UDA. When correlating symptoms and urodynamic results in over 1000 patients, DO was only demonstrated in 44% of women complaining of urgency [38]. Conversely asymptomatic detrusor contractions are frequently seen during filling cystometry in patients without urgency, particularly on ambulatory studies [39].

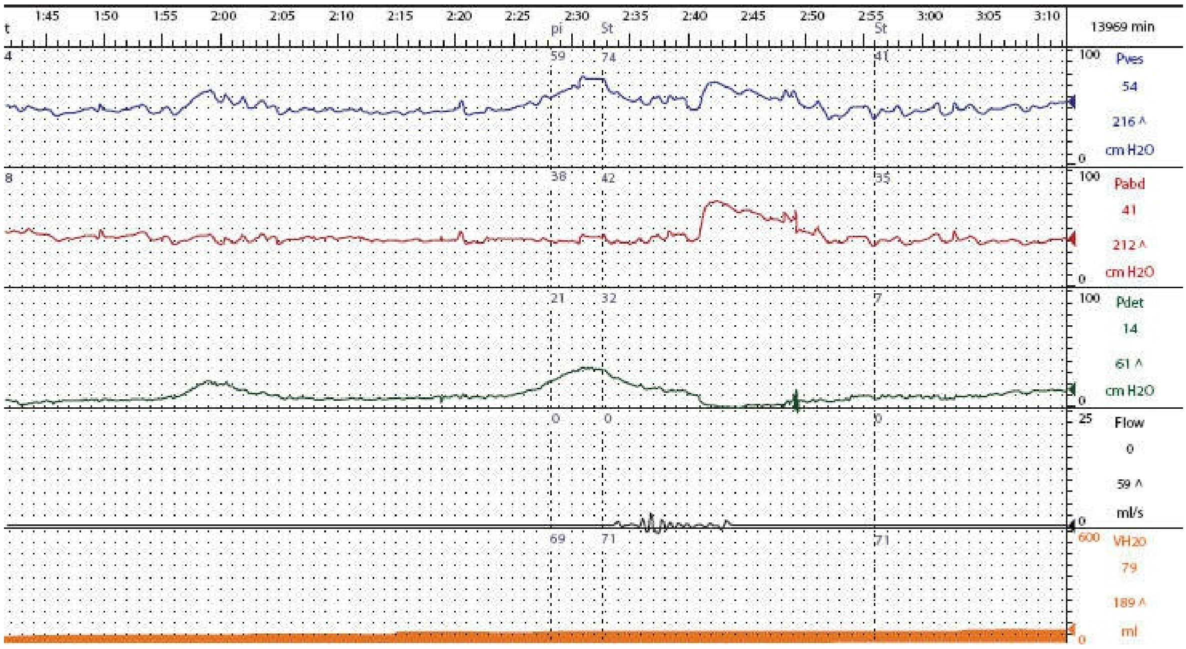

Figure 51.2 Urodynamic trace showing detrusor overactivity incontinence during filling cystometry. The blue trace shows pressure measured in the bladder, and the red line shows that in the rectum (abdominal pressure). The green line represents the difference between the two ("detrusor pressure"), calculated by subtracting red from green. At 2 minutes, the detrusor pressure goes up, signifying DO. At 2 minutes and 30 seconds, it happens again, and this time there is urine flow, i.e., DO incontinence. At 2 minutes and 40 seconds, both bladder and abdominal pressure increase slightly, as the patient contracts her pelvic floor to resist the DO.

TREATMENT

Best results in treatment require good interaction and support from the health-care professional. Explanation is important for compliance and motivation. The Self-Assessment Goal Achievement (SAGA) questionnaire is a patient-completed instrument designed to assess goal attainment in behavioral or pharmacological treatment [40].

Lifestyle Changes

All women with OAB should be managed conservatively in the first instance, and a multidisciplinary approach is important [41]. Many patients benefit greatly from simple advice regarding fluid balance and to minimize tea, coffee, and alcohol intake. Fluid intake can be estimated from the FVC; fluid restriction, including restriction of water-containing foods, may have significant symptomatic benefit [42]. Where caffeine intake is high, a staged reduction in intake may be better tolerated and more realistic for the patient. Significant continence benefits can sometimes be achieved by quite limited weight loss in obese patients, though benefit may relatively greater for those with SUI [43].

Behavioral Therapy

Bladder retraining is considered a first-line therapy in OAB, whether or not patients are incontinent. Bladder retraining involves consistent incremental voiding regimes, aiming to restore central control. Different schedules for bladder retraining include prompted voiding, timed voiding, habit retraining, and bladder drill. Bladder drill has been described using an intensive and regimented protocol performed during an inpatient stay of up to 10 days [44]. Although effective, this may not be compatible with modern health-care systems, and most patients are managed on an outpatient basis with incremental increases in their voiding interval. Focus support groups may be a suitable means to improve compliance. Bladder retraining is often used in combination with antimuscarinic pharmacotherapy [45].

Pelvic floor muscle training may be used successfully by patients with OAB to suppress urgency and UUI episodes [46]. The effectiveness of bladder retraining in combination with pelvic floor muscle training in comparison to either bladder or pelvic floor training alone is as yet unclear, and further investigation is warranted.

Psychological support using various techniques such as cognitive–behavioral therapy may also be helpful. Much of CBT focuses on understanding patterns of behavior and therefore avoiding triggers or conversely trying to accentuate the positives and reduce the influence of negative behavior (Ref CBT for dummies).

PHARMACOTHERAPY

Antimuscarinic Agents

Most women with troublesome OAB will consider drug therapy, and antimuscarinic therapy remains the mainstay of conservative treatment, provided non–drug-based treatment has been tried. All currently available agents are associated with anticholinergic side effects, limiting long-term compliance, such as dry mouth, constipation, blurred vision, and cognitive effects [47,48]. In addition, a significant minority of patients fails to respond adequately. For some of the drugs available, clinical use is based on open studies rather than randomized controlled trials, and the placebo effect in trials of OAB is known to be large [47]. The clinical efficacy and safety of antimuscarinic agents has been reviewed in meta-analyses [47,48]. As the profiles of the agents differ, pharmacotherapy should be individually tailored to each patient according to efficacy, tolerability, comorbidity, and patient lifestyle. Most recently, a paper has shown that the bowel effects of anticholinergics may actually be beneficial [49].

Several antimuscarinic agents are available, with extended-release (ER) formulations and alternative delivery routes, and enhanced bladder or M3 receptor selectivity. Once-daily dosing is considered to improve acceptability to patients. ER formulations have a smoother pharmacokinetic profile and appear to have benefits over immediate-release (IR) formulations in terms of efficacy and tolerability [47]. Other than increasing cystometric capacity, studies with antimuscarinic agents have failed to demonstrate consistent urodynamic effects, yet clear benefit has been demonstrated in terms of frequency, urgency, and incontinence episodes [47]. The International Consultations on Incontinence have produced an expert consensus on available drugs based upon level of evidence and grade of recommendation [29]. Table 51.3 shows currently used antimuscarinic agents receiving high-grade recommendation, based upon good quality evidence. Validated health-related QoL benefits have been demonstrated for several antimuscarinic medications [48].

It is necessary to work with the patient to optimize therapy, including selection of dose and review of dose at follow-up. Dose escalation may be dependent on the extent to which urgency changes at treatment initiation [50]. Adverse effects include dry mouth, constipation, and other effects resulting from the presence of muscarinic receptors in several organs. These effects, and uncertain long-term efficacy, means many patients discontinue treatment. Analysis of the Norwegian prescription database showed that persistence with the initial prescription for new users of antimuscarinic drugs was 38%; 10% switched from the initially prescribed drug to another in the same class, and 52% discontinued altogether [51]. Older people were more likely to persist with the initial prescription, but use of antimuscarinics in older people does carry some risk of cognitive dysfunction [52]. Another situation where caution is needed for antimuscarinic prescription is poorly controlled closed-angle glaucoma.

Table 51.3 Antimuscarinic Agents Recommended for Use in Overactive Bladder

Name	Preparation and dose	Comments
Darifenacin	7.5–15 mg	Highest M3 receptor selectivity (in vitro) Dose escalation possible Once-daily dosing
Fesoterodine	4–8 mg	Active metabolite 5-hydroxymethyltolterodine (5-HMT) Dose escalation possible Once-daily dosing
Oxybutynin	IR 2.5 mg bd–5 mg qds	Most commonly prescribed agent worldwide IR relatively cheap but limited by side effects
	ER 5–20 mg od	ER once-daily dosing
	Transdermal 36 mg twice	Dose escalation possible

	weekly	
		Transdermal avoids metabolite *N*-desethyloxybutynin (reducing side effects) but causes pruritus in 15%.
Propiverine	IR 15 mg od–qds ER 30 mg od	Mixed antimuscarinic (no muscarinic receptor selectivity) and calcium antagonist action
		Most commonly prescribed agent in Germany, Austria, and Japan
Solifenacin	5–10 mg od	M3 receptor selectivity (in vitro)
		Dose escalation possible
		Once-daily dosing
Tolterodine	IR 1–2 mg bd	Bladder selectivity (over salivary gland)
	ER 4 mg od	ER once-daily dosing
Trospium	20 mg bd	Quaternary amine with low lipophilicity, limited CNS side effects
		Low risk of drug interactions
		No muscarinic receptor selectivity

Source: Abrams P et al., *Incontinence. 4th International Consultation on Incontinence*, Health Publications Ltd, Paris, France, 2009.

Abbreviations:IR, immediate release; ER, extended release; od, once daily; bd, twice daily; qds, four times daily.

Beta-3 Adrenergic Agonist

The mechanism of action of mirabegron is through binding of beta-3 adrenergic receptors, which cause detrusor muscle relaxation and which are not widespread on other organs. Mirabegron achieves significant reduction in UUI episodes and voiding frequency [54,55], and benefits can be achieved in patients with symptoms refractory to antimuscarinic drugs [56]. The drug is generally well tolerated, and it does not elicit the common side effects seen with antimuscarinic drugs. In the elderly population, symptomatic improvement can be achieved [57], and the concerns regarding potential cognitive impact for antimuscarinics do not apply.

Desmopressin

Desmopressin, a vasopressin analogue, has an established role in treating pediatric nocturnal enuresis and has also been approved for nocturia in multiple sclerosis and nocturnal polyuria [58]. It may be used off-license to treat nocturia in patients with OAB (bedtime administration). Separately, desmopressin given on demand may allow patients to control daytime OAB symptoms [59], including incontinence [60] (daytime or on-demand administration, which should not be combined with nighttime use). Although generally well tolerated, dose titration may be needed, with checks of sodium levels a few days after initiation or dose adjustment. Hyponatremia is recognized in a minority of patients; this is particularly the case in older women and where baseline sodium is reduced [61,62].

Estrogen

Estrogen has an important physiological effect in the lower urinary tract, and estrogen deficiency has been implicated in the pathogenesis of several conditions, including OAB [63]. Although there is currently no evidence to support the use of estrogen replacement in the management of urinary incontinence [53], some benefit has been claimed for relieving symptoms of OAB. Topical administration may be most appropriate [63]. However, the evidence base is not extensive, and the role of this sort of intervention remains limited [64].

BOTULINUM TOXIN A

Botulinum toxin A (BT-A), a neurotoxin produced by *Clostridium botulinum*, is able to cleave proteins within nerve terminals preventing acetylcholine release at the presynaptic membrane. This effect has been harnessed successfully in the management of refractory DO. BT-A is known to counteract release of acetylcholine from nerve terminals, which effectively prevents nerve-mediated muscle contraction. However, clinical efficacy for LUTS treatment is seen at doses that often maintain bladder contraction, so additional effects of BT-A are probably present at the comparatively low doses used for treating idiopathic DO, for example, release of other neurotransmitters or transmitter release from urothelium

[65,66].

Multiple injections are given into the detrusor muscle throughout the bladder under cystoscopic guidance, generally avoiding the trigone. Phase 3 level 1 evidence underpins the licensing using 100 units of onabotulinumtoxinA in idiopathic DO [67]. Numerous other studies have been published (e.g., References 53,68–70) demonstrating benefit in both clinical and urodynamic outcomes. OnabotulinumtoxinA significantly decreases the number of urinary incontinence episodes per day, the number of micturitions per day, maximum cystometric capacity, and volume voided [71]. There is an increased risk of UTIs and raised postvoid residuals. Urinary retention is the commonest complication of BT-A, and although complete acute retention is uncommon, up to a third of patients with idiopathic DO may need to self-catheterize [72,73]. The development of new nerve terminals and neuromuscular contacts allows recovery of function, so the effect is temporary, in terms of both clinical response and need for self-catheterizing. Repeated injections are required in most patients, and although the duration of response varies between studies, efficacy appears to be maintained for several months [74].

NEUROMODULATION AND NERVE STIMULATION

Stimulation of the S3 nerve root (sacral nerve stimulation [SNS]) by an implanted electrical pulse generator can provide effective relief from DO [75]. A period of temporary percutaneous nerve root stimulation is performed to assess clinical response prior to insertion of a permanent stimulator. The stimulator is a small electrical pulse generator, approximately the same size as a cardiac pacemaker, and is usually implanted in the upper outer quadrant of the buttock. Around 80% of patients with a positive test stimulation experience >50% reduction in incontinence at 6 months [76] though this efficacy may not be maintained in the long term [77]. SNS improves number of incontinent episodes per day and pad usage, and surgical revision rates ranged from 3% to 16%, with some patients having the device removed due to lack of efficacy or infection [78]. Complications most commonly reported are implant site or lead site pain (25%), lead migration (16%), bowel dysfunction (6%), and the need for explantation (9%) [76]. Patients need expert assessment and support, adding to the costs of treatment. Although not suitable for routine management, therefore, sacral neuromodulation appears to be effective and safe for a well-selected minority with refractory DO, and its role may increase in the future as the technological development of generators and implant leads progresses.

Intermittent percutaneous tibial nerve stimulation above the medial malleolus has been described for the management of OAB [79]. The technique shows promise in small uncontrolled studies of patients with refractory DO [79–81], and it can be considered as a primary treatment for OAB. It appears that treatment must be continued for clinical efficacy to be maintained [82]. Response rates quoted in studies vary substantially [83]. There are few adverse effects, but the method is a logistical commitment for the patient and for health-care provision.

SURGERY

Augmentation Cystoplasty

Enterocystoplasty aims to create a low pressure reservoir by increasing bladder capacity and reducing filling pressure [84]. The most commonly used technique is the clam ileocystoplasty [85] in which the bladder is split in a coronal or sagittal plane and a patch of detubularized ileum is sutured into the defect. It is indicated in patients with severe refractory DO with a low functional bladder capacity or in patients with high bladder filling pressures endangering the upper tracts (usually in the presence of neurological disease). Good or moderate long-term outcome has been reported in 92% of patients with neurogenic DO but only 58% of those with idiopathic DO [86]. It is a rare procedure in current practice, particularly since the widespread introduction of botulinum toxin, but it does have a role to play in a small number of highly selected cases [87]. Preoperative consideration should be given to coexisting urethral dysfunction in case additional procedures against stress incontinence may be needed.

Postoperative complications include a significant risk of postoperative difficulty with bladder emptying, secondary to a failure to generate adequate voiding pressures. In the long term, most patients need to self-catheterize to empty their augmented bladder adequately [86]. Creation of a continent catheterizable stoma (using the Mitrofanoff principle) is an option in patients unable or unwilling to catheterize via the urethra. Bowel complications are common [88]. Mucus production by the ileal segment may cause problems, and there is a significant risk of urinary infections and stones. Electrolyte and acid–base balance may become disturbed, resulting in a metabolic acidosis, though this is usually subclinical in adults. Rupture of the augmented bladder is a life-threatening complication that may occur in up to 10% of patients [89]. Malignant change rarely occurs within the ileal segment; many of the reported cases have followed chronic cystitis due to conditions such as tuberculosis [90]. Minimally invasive (laparoscopic and robotic) bladder augmentation has been described in small numbers of patients [91,92]. These initial results and any potential benefits over open surgery need further confirmation before a clear role for the techniques can be established.

Autoaugmentation

Detrusor myectomy was developed in an attempt to reduce the risks associated with augmentation cystoplasty [93]. This procedure involves excising the detrusor muscle over the dome of the bladder, leaving the bladder epithelium intact, thereby creating a pseudodiverticulum and increasing bladder capacity. Around 80% of patients with IDO have successful outcome in the medium term, but nearly half have to self-catheterize [94]. Bladder capacity is increased to a lesser degree compared to augmentation cystoplasty but with the advantage of avoiding bowel complications.

Urinary Diversion

Selected patients with disabling intractable incontinence may be best served by urinary diversion, most commonly via an ileal conduit. This may be appropriate if the bladder becomes severely contracted due to severe long-term DO. In this situation, the management of a urinary stoma may be more acceptable to the patient than constantly changing incontinence pads and washing wet underwear. In addition to the risk of stoma complications, it is now recognized that there is a significant long-term risk to upper tract function following ileal conduit formation, due to renal scarring, infection, and stones [95]; these risks must be weighed up against the potential benefits, particularly in younger patients.

CONCLUSION

OAB is a common disorder affecting the QoL of millions of women worldwide; unfortunately, it is often easier to diagnose than to treat. Management remains unsatisfactory in many patients as behavioral modification is often overlooked and drug therapy with anticholinergic medication may be associated with side effects and poor long-term compliance. Two major recent developments are the introduction of mirabegron and the licensing of onabotulinumtoxinA for idiopathic DO. Surgical intervention is associated with significant morbidity and is only appropriate for a minority of patients refractory to, or intolerant of, conservative therapies. Increasing general awareness and decreased tolerance of urinary incontinence has helped to raise the profile of OAB, and pathophysiological advances have helped develop new therapeutic pathways.

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52 Neurological Disorders

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INTRODUCTION

Neural control of voiding involves complex interactions between the central and peripheral nervous systems, the bladder, and the urethral sphincter. Neurological disorders can affect this system in multiple levels, resulting in a disruption in the bladder's ability to store or empty urine. This chapter will systematically review the characteristic voiding dysfunctions as they relate to various disease states.

VOIDING FUNCTION AND DYSFUNCTION

The bladder's ability to store and empty urine is under neurological control. Therefore, any neurological abnormality can result in voiding dysfunction. In general, neurological lesions either cause loss of function (i.e., detrusor underactivity [DU] or denervation) or result in unopposed reflex "overactivity," i.e., detrusor overactivity (DO). DO can be classified as neurogenic detrusor overactivity (NDO) when a relevant neurological condition is present or idiopathic detrusor activity (IDO) if a cause is not known [1,2]. Neurological lesions that cause underactivity usually result in failure to empty, while those that cause overactivity affect the ability to store urine. Neurological lesions can also affect urethral sphincter function, resulting in loss of the usual coordination between the detrusor and striated sphincter, a condition termed detrusor–sphincter dyssynergia (DSD).

To some extent, the anatomic level of neurological injury can predict the type of dysfunction. The three gross anatomic distinctions that predict effect on voiding function are cerebral (suprapontine), spinal (suprasacral), or peripheral (infrasacral). These levels will serve as a structure by which to examine different neurological disorders and their voiding effects later in this chapter. Table 52.1 summarizes characteristic dysfunctions that result from known levels of injury as adapted from Wein [3].

Voiding dysfunction includes failure to store and/or empty urine and can be categorized by the three broad urodynamic categories listed later. Cerebral lesions above the pons usually result in DO with intact sphincter coordination. Suprasacral spinal (i.e., upper motor neuron) lesions result in DO with a variable effect on sphincter coordination. Injuries involving the sacral cord or cauda equina result in lower motor lesions and DU, with or without sphincter denervation [1]. However, neurological lesions can be multiple or incomplete in nature, resulting in a mixed pattern of voiding dysfunction not predicted by anatomic location [4–6].

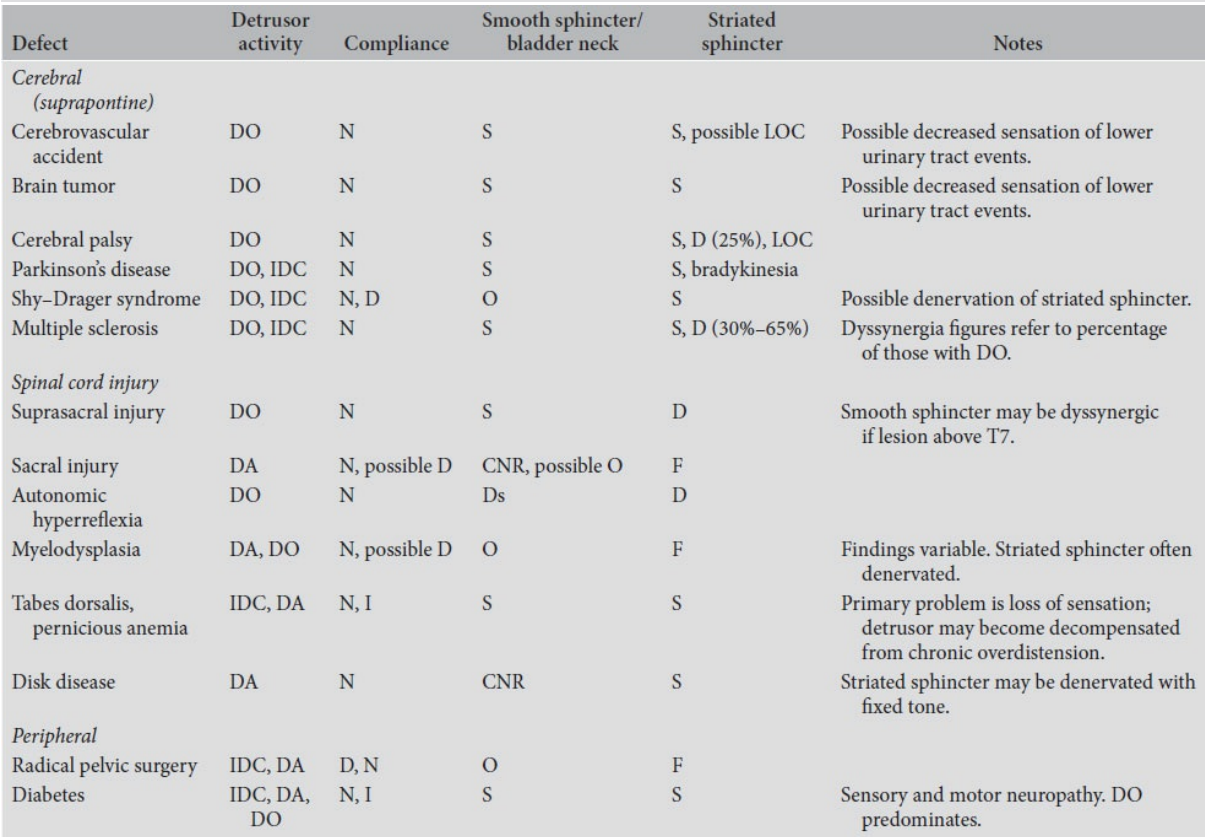
Basic Neurological Control of Micturition

The neural pathways controlling bladder storage and emptying are complex and will only be briefly described in this section. The coordination of bladder emptying involves signaling from parasympathetic, sympathetic, and somatic pathways. The major excitatory signals are from the parasympathetic outflow, originating within the S2–S4 sacral cord segments. Acetylcholine released by postganglionic fibers activates M2 and M3 receptors expressed on the detrusor, to promote activity. Of note, M3 receptors are thought to be the main receptors involved [7]. In addition, parasympathetic nerves release nitric oxide (NO), which inhibits urethral smooth muscle and promotes relaxation [8]. Sympathetic signals arising from the T12 to L2 spinal segments ultimately contribute to the hypogastric and pelvic nerves. Norepinephrine is released from postganglionic fibers and inhibits detrusor activity via β-adrenergic receptors. This same neurotransmitter has excitatory effects on bladder neck and urethra, promoting continence [9]. Finally, somatic motor nerves originating from an area within the lateral ventral horn, known as "Onuf's nucleus," within the S2–S4 sacral spinal cord [10] pass through the pudendal nerve and innervate the striated external sphincter, promoting contraction via cholinergic receptors [9].

The bladder's sensation of fullness is a function of several afferent pathways. Sensory signals from the bladder are sent to the spinal cord via the pelvic and hypogastric nerves, while the bladder neck and urethra send their signals via the pudendal and hypogastric nerves. Two types of fibers within the afferent axons, Aδ (thinly myelinated) and C (unmyelinated) fibers, are involved. Aδ fibers respond to physiological tension, while C fibers remain mostly silent and respond mainly to noxious stimuli. It is important to note that C fibers are widely present in the detrusor and suburothelium and are thought to play a role in urgency and OAB [11].

As the bladder fills, Aδ fibers send signals to lumbosacral spinal tracts and stimulate firing within the sympathetic and somatic efferents to the detrusor and bladder neck, promoting storage. This is known as the "guarding reflex." Signals are also sent to higher centers via pelvic afferents within the spinobulbospinal pathway, reaching the periaqueductal gray (PAG). The PAG sends signals to the pontine micturition center (PMC) and is thought to influence its efferent activity [12]. Within the higher centers, the signal to void or not void is thought to arise from within the medial prefrontal cortex (MPFC) and hypothalamus. During filling, chronic inhibition of the PAG, and thus the PMC, by the MPFC prevents voiding [13].

Table 52.1 Neuromuscular Dysfunction of the Lower Urinary Tract



Defect	Detrusor activity	Compliance	Smooth sphincter/ bladder neck	Striated sphincter	Notes
Cerebral (suprapontine)					
Cerebrovascular accident	DO	N	S	S, possible LOC	Possible decreased sensation of lower urinary tract events.
Brain tumor	DO	N	S	S	Possible decreased sensation of lower urinary tract events.
Cerebral palsy	DO	N	S	S, D (25%), LOC	
Parkinson's disease	DO, IDC	N	S	S, bradykinesia	
Shy–Drager syndrome	DO, IDC	N, D	O	S	Possible denervation of striated sphincter.
Multiple sclerosis	DO, IDC	N	S	S, D (30%–65%)	Dyssynergia figures refer to percentage of those with DO.
Spinal cord injury					
Suprasacral injury	DO	N	S	D	Smooth sphincter may be dyssynergic if lesion above T7.
Sacral injury	DA	N, possible D	CNR, possible O	F	
Autonomic hyperreflexia	DO	N	Ds	D	
Myelodysplasia	DA, DO	N, possible D	O	F	Findings variable. Striated sphincter often denervated.
Tabes dorsalis, pernicious anemia	IDC, DA	N, I	S	S	Primary problem is loss of sensation; detrusor may become decompensated from chronic overdistension.
Disk disease	DA	N	CNR	S	Striated sphincter may be denervated with fixed tone.
Peripheral					
Radical pelvic surgery	IDC, DA	D, N	O	F	
Diabetes	IDC, DA, DO	N, I	S	S	Sensory and motor neuropathy. DO predominates.

Abbreviations:CNR, competent, not relaxing; D, decreased; DA, detrusor areflexia; DO, detrusor overactivity; Ds, dyssynergic; F, fixed tone; I, increased; IDC, impaired detrusor contractility; LOC, loss of (voluntary) control; N, normal; O, open (incompetent at rest); S, synergic.

Several reflexes exist to promote voiding when the sensation of fullness occurs. These are typically held in check until voiding is deemed appropriate. The "bladder–bladder reflex" involves interneurons within the sacral spinal cord, which allow communication between bladder afferent nerves and efferent parasympathetic nerves to the detrusor muscle, promoting bladder emptying. The "bladder–urethral reflex" also involves interneurons between bladder afferent fibers and parasympathetic efferents to the urethral smooth muscle. This promotes smooth muscle relaxation and bladder outlet opening just prior to detrusor contraction [14].

When the decision to void is made, the inhibition by the MPFC is silenced and efferent signals are sent from the PMC to the parasympathetic motor neurons of the detrusor within the spinal cord. Simultaneously, motor neuron activity within Onuf's nucleus is suppressed via inhibitory interneuronal signals. This leads to coordinated contraction of the detrusor along with relaxation of the sphincter, emptying the bladder [15].

Detrusor Overactivity with Synergistic External Sphincteric Function

Incomplete and nontraumatic spinal lesions tend to result in DO with synergistic external sphincter function. Similarly, in patients with lesions above the pons, DO is not typically associated with loss of sphincteric coordination because the lesion is above the level where detrusor contraction is coordinated with reflex urethral relaxation. Typical causes of DO with preserved synergistic sphincteric function include cerebrovascular disease, Parkinson's disease (PD), and some cases of multiple sclerosis (MS) [1,16]. Exaggerated detrusor contractions that occur after suprasacral trauma may be explained by any of the following three mechanisms:

1. Loss of the inhibitory impulse transmission
2. Emergence of primitive alternative micturition pathways
3. Collateral sprouting of new neural pathways [17]

Medical management of DO can usually be achieved with oral or intravesical anticholinergic therapy (see Chapter 41). Newer medications, such as beta-3 receptor agonists, have also been proven effective in the management of DO [18,19]. When DO persists despite medical therapy, intravesical botulinum toxin injection, augmentation cystoplasty, sacral neuromodulation, or percutaneous tibial nerve stimulation (PTNS) may be used to manage DO, resulting in urge incontinence [20–23].

Detrusor Overactivity with Detrusor–Sphincter Dyssynergia

Suprasacral spinal cord injury can disrupt the coordinated voiding reflex between the bladder and external urinary sphincter. This can lead to DO with simultaneous contraction of the striated urethral sphincter [24,25]. This is known as DSD. Typical causes of DSD include suprasacral SCI and MS [26–28]. Identifying DSD is crucial because there is a 50% or greater chance of developing urological complications within 5 years of the onset of DSD [29–31], particularly vesicoureteral reflux and upper tract damage due to the elevation in intravesical pressure (usually when the pressure is chronically above 40 cmH_2O) [32]. Successful management of DO with DSD involves treating both DO and uncoordinated sphincteric contractions. As described earlier, managing DO involves decreasing detrusor activity medically or surgically to allow low-pressure urinary storage. Effective control of intravesical pressure with the anticholinergic therapy can stabilize and even reverse upper tract dilation with DO [33]. Management of DSD includes clean intermittent catheterization (CIC), to bypass the sphincteric obstruction, or by disruption of the urinary sphincter (e.g., pharmacologically with botulinum toxin or mechanically with an intraurethral stent or surgical ablation) [34,35], which may render the patient incontinent. Pharmacological treatments are usually temporary, while mechanical disruption is a more permanent solution. Continuous drainage with an indwelling urethral catheter should be avoided, given the well-characterized complications of infection, urolithiasis, tissue erosion, loss of detrusor compliance, and urothelial cancers. In addition, in those patients with normal sensation, the catheter may be uncomfortable, particularly where there is urethral spasm (DSD). If a long-term catheter is required, then a suprapubic approach is preferable as it reduces the risk of infection and can improve sexual function [36]. It should be noted that DSD is a functional outlet obstruction and therefore cannot be treated safely by condom catheterization or Crede/Valsalva voiding alone.

Detrusor Areflexia (Detrusor Underactivity)

Detrusor areflexia, more recently referred to as detrusor underactivity (DU), is a lower urinary tract dysfunction that may result from a variety of disease processes or injuries. DU was defined by the International Continence Society as a contraction of decreased strength and/or duration resulting in prolonged or incomplete emptying of the bladder (e6). Neurogenic causes of DU include acute CVA, PD, multisystem atrophy, diabetes mellitus, MS, Guillain–Barre syndrome, spinal lumbar disc herniation, infrasacral SCI, and congenital spinal anomalies. DU can also be caused iatrogenically after extensive pelvic surgery [37,38].

In patients with lumbosacral or peripheral nerve lesions, such as myelodysplasia, cauda equina injury, and diabetes mellitus, DU with high or low bladder compliance may develop [1]. Certain upper motor neuron lesions can also result in DU, especially if clinical or subclinical sacral lesions (e.g., coexistent traumatic injury) are present [39]. Examples include acute CVA, cerebellar infarcts, MS, and PD [38]. It has also been noted that hemorrhagic CVAs tend to be more associated with DU when compared to ischemic infarcts [40,41].

Crede/double voiding and/or CIC is the standard treatment for DU [42]. Pharmacological therapies such as alpha blockers may also be used to reduce coexisting urethral outlet resistance. Other available therapies, including muscarinic receptor agonists (bethanechol, carbachol) and acetylcholinesterase inhibitors (distigmine) are used much less commonly due to limited efficacy and unfavorable side effects. Additionally, new therapies such as sacral neuromodulation and stem cell therapy may prove beneficial in the treatment of DU in select patients; however, studies on these modalities remain limited [38]. Because upper tract damage varies directly with increasing time at or above the critical 40 cmH_2O pressure, cases with diminished compliance may also require the use of anticholinergic agents or surgical bladder augmentation to establish urinary storage under acceptable pressure [43].

CONDITIONS OF THE BRAIN AFFECTING THE URINARY TRACT

Cerebrovascular Accident

Cerebrovascular accident (CVA)—stroke—is defined as the acute onset of a focal neurological deficit, usually caused by an occlusive event such as an atherosclerotic thrombus or hemorrhage. Over 800,000 CVAs occur annually in the United States [44]. One-third are fatal, another third necessitate long-term nursing care, and a third allow patients to return home close to their prior level of functioning [45]. The effects of CVA on the function of the lower urinary tract are variable, depending on the location of the neural injury, its size, and etiology [46]. Additionally, because CVAs occur predominantly in the elderly population, evaluation and management are often confounded by coexisting stress incontinence, dementia, and voiding dysfunction from impaired contractility attributable to aging and peripheral neuropathy [45].

Clinical and Urodynamic Features

Clinically, patients may experience a range of voiding complaints from urinary retention, urgency and frequency, and/or incontinence. Neural arcs above the pontine level—where most nonfatal CVAs occur—serve to inhibit micturition. Thus, injury in this area decreases inhibitory control over detrusor function, most often resulting in NDO [47].

While DO is the most common long-term urological problem following a CVA, a significant number of newly affected patients initially develop urinary retention. This retention occurs as a result of "cerebral shock" and may last for a period of several weeks, much like the classic acontractile bladder "spinal shock" phase that immediately follows an SCI [48]. DU is also more commonly seen in cases of hemorrhagic stroke compared to ischemic infarcts [40,41].

Urinary incontinence is common following CVA, with an incidence ranging from 28% to 79%. The etiology of incontinence after CVA is likely multifactorial, with studies linking factors such as depression, impaired cognition, age, dysphagia, hemiparesis, visual field defects, and motor weakness to poststroke incontinence [44]. Limitations in cognitive function and mobility resulting from neural injury may also result in urinary incontinence [49] known as functional incontinence. As recovery ensues, patients most commonly experience urinary urgency. Large studies evaluating the frequencies of the different types of urinary incontinence in the stroke population are limited.

Though most cases of incontinence following CVA are transient, a significant portion of patients will continue to experience incontinence beyond 12 months. Risk factors for persistent incontinence include age, female sex, stroke severity, and prestroke urinary incontinence [44,50].

Although urethral sphincter function is usually preserved, urinary incontinence may result from uninhibited detrusor contractions [51]. Urodynamic testing is useful in differentiating NDO from less commonly seen cases of DU with symptoms of OAB [44,52]. Patients with lesions above the level of the pons characteristically maintain synergetic activity of the sphincter with detrusor contractions [46].

However, patients with suprapontine lesions may purposely increase sphincteric activity during an uninhibited detrusor contraction to avoid urge incontinence. This guarding reflex—termed pseudodyssynergia—may be confused with true dyssynergia by those not familiar with the interpretation of urodynamic studies [53]. As long as urethral sphincter activity remains coordinated with detrusor contraction, intravesical pressure should remain physiological and therefore preserve the function of the urinary tracts.

Evaluation of the stroke patient can be riddled with challenges. Difficulties include obtaining an adequate history, technical difficulty with performing studies, and interpreting urodynamic studies given coexisting findings incidental to aging or comorbidities [45]. However, careful neurological examination and urodynamic evaluation are crucial when assessing the stroke patient who presents for evaluation of voiding dysfunction.

Parkinson's Disease

PD affects men and women equally, primarily in the sixth and seventh decades of life, and it increases in prevalence with advancing age [54]. It occurs with a prevalence of 0.1% in the United States, making it one of the most frequent neurological entities causing voiding dysfunction [55]. Pathologically, the pigmented neurons in the substantia nigra and locus coeruleus in the brainstem degenerate. Systemic clinical features of tremor, bradykinesia, and muscular rigidity are likely due to focal dopamine deficiency in these areas as well as the caudate nucleus, putamen, and globus pallidus [56]. The typical urodynamic findings of patients with PD include DO, sphincter bradykinesia, and impairment of relaxation of the striated muscle component of the urethral sphincter muscle [1,55].

Clinical and Urodynamic Features

Up to 75% of patients with PD experience some degree of voiding dysfunction [57,58]. Nocturia is noted to be one of the most common complaints in patients with PD, reported in >60% of cases [59]. Urgency and frequency were reported in 33%–54% and 16%–36% of patients, respectively [59,60]. Voiding disturbance may also be troublesome, with storage symptoms present in 57%–83% of patients and voiding symptoms reported in 17%–27% [61,62]. Additionally, voiding dysfunction associated with PD in female patients is complex and not always congruent with symptoms [55].

Urodynamic evaluation reveals DO in up to 90% of patients, with sporadic electrical activity of the sphincter during uninhibited detrusor contractions in 61% [16]. In a study of 17 women with PD, stress urinary incontinence was identified in 50% [63]. A unique finding in Parkinson's patients is sphincteric bradykinesia, where there is a delay in relaxation of the external sphincter at the onset of volitional micturition [64]. Additionally, a delayed or incomplete relaxation of the pelvic floor may also be noted [65]. True DSD is a rare finding in PD, seen in <3% of patients [66–68]. Impaired detrusor contractility is also an infrequent urodynamic finding in the patient with Parkinson's [69]. When bladder outlet obstruction due to prostatic enlargement is seen in Parkinson's patients, surgical management may be difficult. In the general population, the risk of incontinence after transurethral prostatectomy is <2%; however, this risk in the Parkinson's patient may be as high as 20% [64].

Care must be taken to differentiate PD from multiple system atrophy (MSA), as the presentation may be similar but urologic management is different. Urinary incontinence, elevated PVR, DSD, urgency, and frequency are all more common in MSA compared to PD [67–70]. In addition, response to surgical treatments is worse in MSA, with incontinence rates after TURP reported as high as 100% [61,71]. Urodynamic evaluation and sphincter electromyography can aid in differentiating MSA from PD. Findings such as an open bladder neck at rest and striated sphincter dysfunction are more commonly seen in MSA than PD [65,72].

More recent attempts to correlate clinical disease states with urodynamic findings have revealed that increasing PD stage results in worsening urge incontinence, DO, and decreasing bladder capacity [73]. Holligar et al. [73] studied 37 idiopathic parkinsonian patients with a mean age of 65 years. Symptoms were classified as mild, moderate, or severe; mild symptoms were unilateral in nature, moderate involved exacerbated bilateral symptoms and deteriorating balance, and severe symptoms required the use of assistance with daily activities and/or ambulation. Table 52.2 summarizes the significant findings. As parkinsonian symptoms worsen, so do clinical and urodynamic parameters. This suggests that bladder function may worsen progressively with advancing disease.

Table 52.2 Clinical and Urodynamic Features of Parkinson's Patients by Severity of Symptoms

Parkinson's severity	Urge	Urge incontinence	Detrusor overactivity	Bladder capacity (mL)
Mild	5/14	0	6/14	380
Moderate	14/14	2	10/14	290
Severe	9/9	4	9/9	260

Source: Holligar S et al., *J Urol*, 157, 1378, 1997.

Neurological evaluation is crucial to evaluate bladder function and to guide appropriate therapy. Urodynamics with simultaneous electromyography is the most sensitive available tool to investigate the nature of voiding dysfunction [55]. The goals of proper management are to improve symptoms and protect the upper urinary tracts. Treatment of the patient with l-dopa can significantly improve symptoms; however, anticholinergic therapy can be added to suppress uninhibited detrusor contractions. Newer pharmacological agents, such as beta-3 receptor agonists, may also be considered. Studies investigating the efficacy of these medications in the Parkinson's patient are needed. Modalities such as deep brain stimulation (DBS) of the subthalamic nucleus have been shown to decrease urinary symptoms, but effects on urodynamic parameters are conflicting [74–76]. Sacral neuromodulation has been shown to significantly improve incontinence, nocturia, and pad usage in patients with neurogenic bladder dysfunction. However, long-term efficacy in patients with progressive neurological diseases, such as PD, has yet to be determined [77].

Cauda Equina Syndrome

Latin for "horse's tail," the term cauda equina is used to describe the caudal end of the spinal cord, known as the conus medullaris, as well as the spinal nerves and nerve roots beginning at the root of the first lumbar nerve. Cauda equina syndrome (CES) is an uncommon, but serious, condition associated with compression of some or all of these nerves, typically by a large, space-occupying lesion located within the lumbosacral canal [1,78,79]. The constellation of symptoms seen may include lower back or groin pain, perineal pain or anesthesia ("saddle anesthesia"), unilateral or bilateral sciatica with varying degrees of lower extremity weakness and/or sensory loss, as well as bladder and bowel dysfunction. Occasionally, a physical exam will also reveal decreased rectal tone [1,3,4]. A high index of suspicion is needed for prompt diagnosis as these changes may progress or become permanent if not treated appropriately with urgent surgical decompression [4,80,81].

Bladder dysfunction, a key element of CES, typically results from an interruption of the complex reflex arcs that control bladder filling and emptying. Both sensory and motor innervations to the bladder are affected. The detrusor muscle is unable to contract appropriately, and patients are often unable to sense that they are full. Additionally, patients may be unable to fully relax their external sphincter, worsening urinary retention and eventually presenting as overflow incontinence [6,82]. Bladder symptoms often resolve if CES is treated in a timely fashion. Prolonged urinary dysfunction has been associated with decompression done beyond 48 hours of diagnosis as well as with the presence of saddle anesthesia, preoperative chronic back pain, and/or rectal dysfunction [5,16,83].

Common causes of CES include lumbar disk herniation, spinal stenosis, tumors, trauma, epidural hematomas/abscesses, as well as iatrogenic causes and postoperative complications such as hematomas after spinal anesthesia or spinal surgery. Interestingly, the use of Gelfoam (Pfizer, New York) in spinal surgeries has also been associated with CES [1].

A detailed history in patients with suspected CES is extremely important and should include questions about changes in bowel/bladder habits. Physical exam should include evaluation of the sacral nerve roots. Palpation of the suprapubic area may reveal a distended bladder, requiring drainage via a Foley catheter. Pin-prick testing of the perineal dermatomes (S2–S4) is important, as patients with CES may often have intact sensation to pressure and light touch. A rectal exam should be done to assess rectal tone and voluntary sphincter contraction. An anal wink test and evaluation of the bulbocavernosus reflex (S1–S3) should also be performed. The reflex involves contraction of the anal sphincter with pressure to the glans/clitoris or traction on the patient's Foley catheter [1,17,84]. If imaging is needed, MRI is the preferred modality [24,85]. This should be done rapidly to avoid delay in treatment.

If one suspects CES in any patient, an immediate neurosurgical consult should be placed. Once CES is diagnosed, urgent decompression should be performed within 48 hours of the diagnosis [1]. Worsened outcomes in sensory, motor, bowel, and bladder function have been demonstrated when surgery is done after 48 hours [5]. Patients should be counseled on the fact that certain genitourinary symptoms may persist, despite decompression within 48 hours, including decreased penile sensation with or without erectile dysfunction in men and decreased sensation and urinary incontinence during intercourse in women [5,25,26,86,87].

Shy–Drager Syndrome (Multiple System Atrophy)

Shy and Drager described a neurological syndrome of autonomic nervous system dysfunction characterized by orthostatic hypotension, anhidrosis, erectile dysfunction, extrapyramidal symptoms, and poor urinary and fecal control [88]. Shy–Drager syndrome is also known as multiple system atrophy (MSA), and it is considered one of the "Parkinson-plus" syndromes of movement disorders [5]. The mean age of onset is 55 years, with a male predominance of 2 or 3:1 [89]. MSA results in the symmetrical degeneration of neurons and associated fibers of motor and extrapyramidal systems, including the cerebellum and brainstem [90]. Disease progression usually results in death 7–20 years after the onset of neurological symptoms [89].

The difference in neuropathological lesion location and number between patients explains the variance in urodynamic findings between Parkinson's patients and those with MSA. Unlike Parkinson's patients, MSA patients tend to have worse lower urinary tract dysfunction, characterized by poor bladder contractility and pelvic floor EMG findings, suggesting that almost 50% demonstrate peripheral denervation [55]. The resulting incontinence is probably caused by DO and some element of paralysis of the external sphincter [91]. Blaivas has demonstrated an open bladder neck during cystography, further indicative of peripheral sympathetic dysfunction [91]. Thus, MSA affects sympathetic, parasympathetic, and somatic nervous systems—compared to the relatively more defined idiopathic PD—and thorough neurological evaluation is invaluable in separating and characterizing these different disease entities [55]. The combination of detrusor dysfunction and sphincter denervation does *not* support the surgical management of symptoms; currently recommended treatment is therefore that of a combination of intermittent catheterization and medical therapy, including anticholinergics and desmopressin [88,92].

Brain Neoplasms

The majority of patients with intracranial neoplasms often maintain control over urinary tract function [1]. Similar to CVAs, alterations in lower urinary tract function will tend to relate directly to the area of the brain affected, rather than the type of neoplasm. For example, compression by tumor or degeneration of neural arcs above the pontine level—such as the superior aspects of the frontal lobe [93] and frontoparietal areas [94] that inhibit detrusor activity—would induce DO with synergetic sphincter function [46,95].

Dementia

Dementia is the loss of thought and reason that results from deterioration and atrophy of both gray and white matter in the brain, particularly of the frontal lobes [1]. Although usually associated with conditions such as head injury, hydrocephalus, encephalitis, syphilis, and Alzheimer's, Pick's, and Creutzfeldt–Jakob diseases, the etiology of neuronal degeneration associated with dementia is poorly understood [56].

The most common urinary symptom is incontinence, with a reported prevalence as high as 90% [96]. However, the cause of incontinence remains unclear; it is not known whether detrusor dysfunction or, more likely, a defect in cognitive function (functional incontinence) is responsible for the lack of social continence in patients with dementia. In one report, 71% of elderly patients with cognitive impairment showed DO; however, 65% of those with no impairment demonstrated DO by the same criteria. Therefore, the incontinence associated with dementia is not likely due to DO [97]. It has been demonstrated that neurogenic incontinence (DO) is more common in multi-infarct and Lewy body disease dementia, while functional incontinence is more prevalent in Alzheimer's disease due to cognitive decline and decreased motivation [98].

Aging, Cognitive Decline, and Conflicting Medication Effects

In both men and women, the prevalence of overactive bladder (OAB) and incontinence increases significantly with advancing age [99]. The impact of OAB can adversely impact quality of life. This includes psychological burden, and an increased risk of falls, fractures, skin infections, and UTIs. In fact, the onset of bladder symptoms is often the deciding factor in transitioning from community to residential-based care. The mainstay of treatment for OAB is antimuscarinic therapy; however, caution is warranted in the elderly population when using these drugs. Anticholinergic side effects include both peripheral nervous system symptoms like dry mouth and constipation and central nervous system symptoms like cognitive impairment, blurry vision, and sleep disturbances. The central nervous system interactions can be the rate-limiting step in treatment if the patient is already beginning to experience cognitive decline. In a population of patients who have had a lifetime to accrue lengthy medication regimens, consideration should also be given to drug–drug interactions. With regard to side effect profiles and pharmacokinetics in the elderly, trospium chloride may be better tolerated than other antimuscarinics including oxybutynin, tolterodine, and solifenacin [100].

The mainstay of treatment for cognitive decline in the aging patient is central cholinergic stimulation [101]. Cholinesterase inhibitors slow the breakdown of synaptic acetylcholine and prolong its ability to stimulate postsynaptic receptors. The three drugs commonly used are rivastigmine, donepezil, and galantamine. While these drugs are designed to target central nervous system cholinergic pathways, associated peripheral nervous system effects include muscle cramps, weakness, cardiorespiratory events, and urinary incontinence. Cholinergic treatment increases OAB symptoms and has even been shown to lead to an incidence of 8% of urge urinary incontinence in those on donepezil [101]. Studies have demonstrated less peripheral cholinergic side effects and less drug–drug interactions in rivastigmine compared to donepezil and galantamine [102].

Clearly, there is a delicate balance when managing OAB and risking cognitive side effects as well as when treating dementia and risking OAB side effects. In cognitively vulnerable populations like the elderly and demented, medical management should consider the use of selective agents with the safest side effect profile and least pharmacokinetic interactions. Newer agents, such as the recently approved beta-3 adrenoreceptor agonist, mirabegron, may be particularly useful in this patient population. Mirabegron was shown to significantly reduce incontinence episodes and micturition frequency, while maintaining a treatment-emergent adverse event profile similar to placebo [18]. Newer studies suggest that combinations of mirabegron and solifenacin may achieve increased efficacy with virtually no change in safety profile compared to solifenacin monotherapy [19].

Multiple Sclerosis

MS is the most common disabling neurological disorder affecting people between 20 and 50 years of age [103]. It is characterized by focal inflammatory and demyelinating lesions of the nervous system, affecting mainly those living in the temperate climates. Prevalence is estimated at 1/1000 in Americans, 2/1000 in Northern Europeans, and 20 to 40/1000 in first-degree relatives of patients with MS [103–105]. In approximately 60% of patients, the disease is initially manifested by exacerbations and remissions. The clinical course of MS can be acute, progressive, chronic, and/or benign [106].

Neurological dysfunction is caused by demyelinating plaques of the white matter of the brain and spinal cord, especially the posterior and lateral columns of the cervical cord, which serve as pathways for neurological control over vesical and urethral function [107]. These plaques are caused by an autoimmune response and attach to the central nervous system myelin, leading to a loss of salutatory conduction and conduction velocity in axonal pathways [103].

Clinical and Urodynamic Features

Voiding dysfunction is experienced by 90% of patients with MS [108]. Interestingly, a change in bladder function is the presenting complaint in at least 10% of MS patients [109]. These include not only frequency, urgency, and urge incontinence but also urinary hesitancy, intermittency, and poor urinary stream. The nature of voiding dysfunction is most dependent on the location of the plaque formation, such as intracranial, suprasacral, or sacral cord plaques.

Urodynamically, the most frequent pattern seen is DO, which is observed in 50%–99% of patients [103,108,110,111]. DSD is also documented in up to 50% of patients with DO [28,112,113]. Of patients with symptoms suggestive of obstruction, 73% had DU [114]. DU is seen in 20%–30% of patients, most of whom usually strain to void [115]. Hypocontractility may be related to cerebellar plaque involvement, lack of cortical facilitatory input, or sacral cord involvement. Some evidence suggests that DU is a temporary condition that may progress to DO in 57%–100% [114]. Although these patients may be managed effectively with an intermittent catheterization program, periodic urodynamic reevaluation is essential to ensure protection of the upper urinary tract [116]. Given the waxing and waning nature of MS, reevaluation is especially important because the neurourological status of the patient with MS may change over time. Having said that, DSD revealed on urodynamic evaluation rarely remits [114].

Optimal management of lower urinary tract dysfunction is based on the avoidance of indwelling catheters and minimizing intravesical storage pressure while assuring low-pressure urinary drainage [116]. Urinary storage pressure is minimized with anticholinergic medications or augmentation cystoplasty if medical therapy is ineffective [117]. Unfortunately, sphincterotomy is not an option for women, and many women with neuropathic bladder dysfunction are treated in the community with indwelling urethral or suprapubic catheters [1]. However, early experience using botulinum toxin injections into the sphincter for the treatment of DSD is limited but growing and may eventually prove to be a therapeutic option [118,119]. A randomized, double-blind, placebo-controlled study investigating botulinum toxin's effect on DSD in MS patients showed that botulinum toxin significantly increased voiding volume and decreased premicturition and maximal detrusor pressures. It failed, however, to decrease postvoid residual volume [120].

CONDITIONS OF THE SPINAL CORD AFFECTING THE URINARY TRACT

The degree of voiding dysfunction associated with spinal cord conditions is related to the process of the condition itself, the area of the spinal cord affected, the severity of neurological impairment, and the coexisting pelvic floor pathology. Neurological injury, which can involve parasympathetic, sympathetic, and somatic nerve fibers, can result in a complex array of signs and symptoms. Urodynamic investigation of those with neurological impairment is essential as it provides objective information regarding the nature and extent of the effect on lower urinary tract function. Such information is invaluable in adequate patient management.

Spinal Cord Injury

Neurogenic lower urinary tract dysfunction resulting from spinal cord injury (SCI) is an excellent model for understanding neurourological dysfunction. The principles of urological evaluation and management of traumatic SCI patients are applicable to those with other spinal cord pathologies [34]. The estimated annual incidence of SCI reaches 40 new injuries per million population in the United States, or approximately 11,000 new cases per year—with a prevalence of approximately 247,000 persons [121]. With 85% of injuries occurring at or above the T12 level [122], the reported neurological level and the extent of the lesion of SCI at hospital discharge reveal 34.3% of patients with incomplete quadriplegia and 25.1% with complete paraplegia; 22.1% of patients develop complete quadriplegia and 17.5% incomplete paraplegia [121]. Historically, the most common cause of death in SCI patients had been secondary renal failure; however, improved medical assessment and management has led to dramatic shifts in the causes of death [1]. Nonetheless, lower urinary tract dysfunction following SCI is frequent and may result in infection, urolithiasis, upper tract failure, and lower urinary tract symptoms.

Clinical and Urodynamic Features

Characteristics of voiding dysfunction after SCI are dependent on the stage of recovery, i.e., spinal shock, recovery, and stable phases [1].

Immediately following spinal cord trauma, *spinal shock* occurs. This phase characteristically presents with flaccid paralysis and absence of reflex activity below the level of the lesion. Voiding symptoms typically include urinary retention due to DU that may last for months. The DU usually resolves weeks to a few months following the SCI with resumption of reflex detrusor activity. While in acute retention, patients should be managed with a regime of intermittent catheterization.

The *recovery* phase follows spinal shock and is marked by the return of reflex detrusor activity. This phase is noted clinically by the appearance of new incontinence, autonomic dysreflexia (AD), or lower extremity spasticity. The neurological level of the SCI often corresponds to the resulting type of lower urinary tract dysfunction (Figures 52.1 and 52.2). Performing urodynamic testing at this time is key to understand the pathophysiology of each patient's condition [123,124]. With cervical or thoracic spinal cord lesions, the most common outcome will be DO with DSD. Sacral spinal cord injuries are commonly associated with DU, although this may also be seen with higher-level lesions. Injuries of the lumbar spine are more difficult to predict, with lower urinary tract dysfunction ranging from DO with DSD, or DO with sphincter deficiency, to DU.

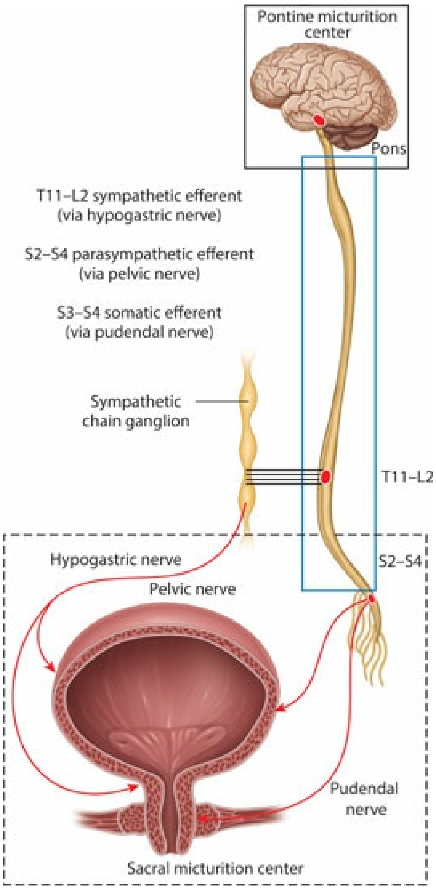

Pontine micturition center
Pons
T11–L2 sympathetic efferent (via hypogastric nerve)
S2–S4 parasympathetic efferent (via pelvic nerve)
S3–S4 somatic efferent (via pudendal nerve)
Sympathetic chain ganglion
T11–L2
Hypogastric nerve
S2–S4
Pelvic nerve
Pudendal nerve
Sacral micturition center

Figure 52.1 Innervation of the lower urinary tract. The control of micturition and continence arise at three levels: suprapontine (thin line box), spinal (thick line box), and peripheral/infrasacral (dashed box). Each level contains distinct nerve fibers with complex interplay between all levels.

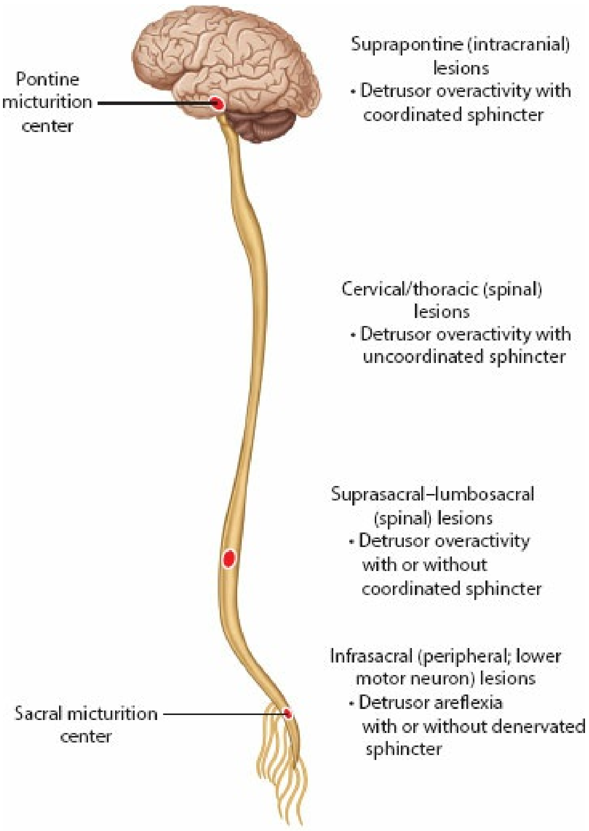

Pontine micturition center
Suprapontine (intracranial) lesions
• Detrusor overactivity with coordinated sphincter
Cervical/thoracic (spinal) lesions
• Detrusor overactivity with uncoordinated sphincter
Suprasacral–lumbosacral (spinal) lesions
• Detrusor overactivity with or without coordinated sphincter
Infrasacral (peripheral; lower motor neuron) lesions
• Detrusor areflexia with or without denervated sphincter
Sacral micturition center

Figure 52.2 Urodynamic outcome following complete denervating injury. Outcomes are dependent on level and extent of injury. Incomplete or partial lesions may lead to variation in urodynamic findings.

The final phase following SCI is labeled the *stable* phase and by definition is the period characterized by the absence of additional neurological recovery or change in urodynamic pattern [1]. Although the pattern of voiding pathology remains stable, there can be an increase in the severity of the dysfunction and/or a continued loss of compliance. Therefore, it is critical to continue periodic evaluation of lower urinary tract function and surveillance of the upper urinary tract for further sequelae.

The level of spinal lesion and its relationship to lower urinary tract dysfunction have been documented and evaluated in 489 consecutive patients presenting with SCI [123]. In 104 patients with cervical SCI, 15% (16 patients) had DU. In the remaining 85% (88 patients), involuntary detrusor contractions (IDC) were documented, with 65% (57 of 88) exhibiting concurrent DSD. All 87 thoracic SCI patients were found to have DO, and 90% of them exhibited concurrent DSD. Lumbar SCI was found to have the least predictable urodynamic patterns, with 40% having DU, 30% with DO, and 30% with DO with DSD. In the sacral SCI cohort, 12% of patients had normal urodynamic studies, while 64% of patients had DU.

Urological management of patients with SCI should focus on allowing low-pressure storage and efficient bladder drainage at low detrusor pressures. DU may be managed with CIC. If hand function is poor, other methods of urinary drainage may be utilized, including placement of a suprapubic catheter or urinary diversion. Long-term urethral catheters should be avoided due to the risk of infection, urolithiasis, erosion, and urothelial metaplasia and cancer. DO may be managed with a variety of treatment modalities including anticholinergic medications, beta-3 receptor agonists, and intravesical injections of botulinum toxin. If safe bladder pressures are unable to be achieved with conservative methods, patients may ultimately require augmentation cystoplasty or urinary diversion. In patients experiencing DSD, CIC remains the gold standard. Sphincteric injection of botulinum toxin has also shown promise; however, large, randomized trials are lacking. Other treatments include sphincterotomy and urethral stenting; however, these may be associated with significant complications and increased morbidity. In addition, the usual need for an external collecting device precludes their use in females [125].

Brown–Sequard Syndrome

Hemitransection of the spinal cord results in this rare, but well-documented condition with pathognomonic findings for a spinal cord injury [126,127]. The classic presentation of this syndrome—provided that it results from a single spinal lesion—is ipsilateral hemiparesis (pyramidal tract) of the leg with contralateral loss of superficial sensation (spinothalamic tract) and ipsilateral loss of deep sensation (dorsal tract). The variable presentation that results in either motor or sensory symptoms depends upon the plane of the lesion.

Clinical and Urodynamic Features

Voiding symptoms are variable among these patients. Those presenting with more severe motor deficits (i.e., intramedullary diseases) are more likely to have symptoms ranging from urinary retention to filling phase symptoms such as frequency and urge incontinence [128]. However, there is no relationship between voiding symptoms and the laterality of the lesion or concurrent sensory disturbances [128–130]. There is also a paucity of publications reporting urodynamic studies in these patients with findings that are concordant with voiding symptom severity. The most frequent urodynamic findings in symptomatic patients tend to be DO and areflexia [123,128]. Because the relationship between the spinal lesion and resulting voiding symptoms is variable, thorough neurological examination paired with urodynamic evaluation are key in managing symptoms and protecting the upper tracts of each patient.

Autonomic Dysreflexia

AD is a well-defined syndrome of acute excessive sympathetic output that occurs in patients with spinal cord injuries, most commonly above the T6 level. This condition is associated with an uncontrolled spinal reflex mechanism from afferent visceral (or other noxious) stimulus below the level of the lesion, resulting in, if not managed appropriately, a life-threatening hypertension. The most common cause is stimulation of the lower urinary tract, with 75%–85% of cases precipitated by bladder distension [131]. Other triggers include infection, urethral distension, instrumentation, stones, decubiti, gastrointestinal pathology, long bone fracture, sexual activity, and testicular torsion [125].

At presentation, the symptoms associated with AD generally include a bilateral pounding headache, with diaphoresis above the level of the spinal lesion, nasal congestion, malaise, nausea, and visual blurring. The signs observed commonly are flushed sweaty skin above the level of the lesion with cool, pale skin below that level. The main finding is elevation of the blood pressure with reflex bradycardia—which in a post-SCI patient may mean that readings of 120/80 mmHg are elevated, as base pressures in these patients are often in the 90/60 mmHg range [1]. Less commonly, tachycardia or arrhythmia may also be noted [125]. The labile hypertension associated with the AD response can result in intracranial hemorrhage and death [132]. Early recognition of the syndrome is critical, with initiation of management immediately [133]. If AD does not reverse with bladder decompression, pharmacological management with oral nifedipine, nitroglycerine ointment, or IV nitroprusside should be initiated.

Several studies have reported success with prophylactic use of selective α-adrenergic blockers, such as terazosin, for long-term management [134,135]. Even if prophylaxis is utilized, careful monitoring during procedures remains an absolute necessity. Any endoscopic procedure in susceptible patients should ideally be done under spinal anesthesia or general anesthesia with close monitoring [125].

Intervertebral Disk Disease

Voiding dysfunction is a well-established complication of lumbar intervertebral disk herniation, resulting from displacement of any intervertebral disks into the spinal canal. Herniated disks occur in a variety of disease processes including degenerative disease and trauma. The symptoms resulting from the displacement will be dependent on the level of the lesion, the extent of the displacement, and the type of neural injury, which may involve parasympathetic, sympathetic, and/or somatic nerve fibers (Table 52.3). The combination of these factors will result in a complex combination of signs and symptoms.

Nerve conduction will be compromised in cases of acute compression. At the level of the sacrum, this can result in DU from impaired autonomic outflow to the detrusor. If there is additional interference of somatic outflow at the pudendal nerve, concomitant intrinsic sphincteric deficiency may occur [136].

The most frequent site of lumbar disk herniation is the L4–L5 and L5–S1 intervertebral spaces, which can result in CES [83,137]. The characteristic symptoms and signs in this syndrome include lower back pain, obstructive voiding symptoms with or without incontinence, sensory loss at the perineum, sensory loss of the lateral foot (S1–S2 dermatome), and absence of the bulbocavernosus reflex [138]. Disruption from gradual degenerative disk displacement may result in hyperexcitability of sensory and motor fibers, with symptoms including irritative urinary frequency and urgency with DO [139]. Urodynamic testing should be an integral part of the evaluation of all patients with incomplete lumbosacral spinal injuries [1].

Table 52.3 Innervation of the Lower Urinary Tract

	Spinal cord level	**Function**
Afferent		
Nociceptors	S2–S4	Initiation of micturition
Sensory	S2–S3	Perineal sensation
Efferent (autonomic)		
Sympathetic (hypogastric nerve)	T11–L2	Sphincter contraction, bladder relaxation
Parasympathetic (pelvic nerve)	S2–S4	Bladder contraction
Somatic (pudendal nerve)	S3–S4	External sphincter contraction

Ankylosing Spondylitis

A rare inflammatory disease of the spine, ankylosing spondylitis results in fusion of the joints and ligamentous calcification. This disease predominantly affects men, with deleterious effects on neurological function generally occurring following spinal cord compression, caused by either atlantoaxial subluxation or trauma to the rigid spine [140–142].

The most common neurogenic lower urinary tract dysfunction caused by ankylosing spondylitis results in a CES with impaired detrusor contractility [140]. More severe cases may result in DU, and sphincteric activity may also be compromised as neuropathy progresses. Surgical decompression following neurological impairment has met with varying success [143].

Guillain–Barré Syndrome

Guillain–Barré syndrome is an inflammatory demyelinating polyneuropathy, usually arising following an infectious episode that primarily affects the peripheral nervous system, with some effect on the nerve roots [144–146]. Although recovery is a hallmark of Guillain–Barré syndrome, 85% of patients sustain persistent neurological deficits [147]. In severe cases, progression continues to affect central nervous, respiratory, and autonomic function, often including urinary retention [148].

Lower urinary tract dysfunction is present in 6%–40% of patients diagnosed with Guillain–Barré syndrome [149]. Symptoms include detrusor and sphincter motor and sensory deficits consistent with variation in the combination of nerves affected during the course of Guillain–Barré syndrome [150,151]. Urodynamic studies on patients with Guillain–Barré syndrome have revealed DU, impaired bladder sensation, and occasionally DO; it is not known whether these findings are accounted for by either central nervous system involvement or the timing of the urodynamic study [151,152].

Tabes Dorsalis

Tabes dorsalis (locomotor ataxia) is an uncommon form of neurosyphilis affecting less than 5% of people with syphilis. This condition results in a demyelination of the dorsal columns in the spinal cord [153–155]. Progression of sacral root and dorsal column degeneration results in advancing stages of disease and ultimately is manifested urologically with the development of urinary retention [156].

Classic descriptions of the effects of tabes dorsalis on voiding discuss the prevalence of DU; however, more recent studies suggest that DO may occur [154]. It is postulated that involvement of the conus medullaris or cauda equina predisposes to a poorly compliant areflexic bladder and that suprasacral lesions are responsible for the DO in these cases [157]. These patients can be managed effectively with the treatment of the primary infection with antibiotics and an intermittent catheterization program [158].

Human Immunodeficiency Virus

Voiding dysfunction in patients with human immunodeficiency virus (HIV) of variable etiologies has been documented in recent studies [159–161]. A common cause of lower urinary tract symptoms is urinary tract infection. HIV-infected patients experience a greater number of urinary tract infections compared to the general population and are particularly vulnerable when CD4 counts fall below 500/mm^3. Etiology may include common uropathogens, but one should consider less common causes of infection such as fungi, parasites, mycobacteria, and viruses when disseminated infection occurs [162].

A complete urological assessment is critical in the evaluation of any complaints suggesting voiding dysfunction, especially as up to 40% of patients with AIDS have associated neurological dysfunction [163,164]. Neurological pathologies in AIDS patients, which can lead to voiding dysfunctions, include toxoplasmosis (reported in 14% of AIDS patients with neurological disease [164]), neoplasms of the central nervous system, lymphoma, systemic lymphoma with central nervous system involvement, and Kaposi's sarcoma [165–167].

Urodynamic Evaluation

Findings following urodynamic evaluation in patients with AIDS are variable and may include DU, DO, DO with DSD, or nonneurological bladder outlet obstruction [160,164]. In the study by Hermieu et al., the onset of lower urinary tract disturbance represented a poor prognostic indicator, as 44% of these patients died within 24 months of evaluation [160].

Tropical Spastic Paraparesis

Tropical spastic paraparesis is a condition of progressive paraparesis and back pain, most likely induced by infection with the retrovirus human T-cell lymphotropic virus type 1 (HTLV 1) [168]. This clinical entity is caused by meningomyelitis with demyelinization and axonal loss, which can involve the corticospinal tracts [169]. There is significant voiding dysfunction associated with this syndrome, with urinary hesitancy, urgency, and incontinence found in up to 60% of patients [168].

Urodynamic Evaluation

Studies of affected patients have revealed a predominance of DO, often with impaired contractility at voiding and less frequently DU [170,171]. Despite variable presentations, the lower urinary tract dysfunction can precipitate upper tract deterioration; therefore, urodynamic evaluation is recommended in all patients with acquired immune deficiency syndromes with voiding symptoms [163].

Transverse Myelitis

Transverse myelitis is a rare inflammatory condition of the spinal cord, which may affect children or adults in an acute or progressive fashion [172,173]. The entire thickness of the cord is involved, including both the gray and white matter, with the diagnosis made following elimination of spinal cord compression and the absence of other neurological diseases [174]. Affected individuals may suffer from persistent neurological deficits, most commonly urologic, although complete recovery may occur within 3–18 months [174,175].

Urodynamic Evaluation

Lower urinary tract dysfunction in these patients usually presents as either urinary retention or incontinence. A recent study showed the outcomes with predominant DO, DO with DSD, and less frequently DU [176]. These urodynamic findings often persisted despite complete neurological recovery.

Lyme Disease

Lyme borreliosis is caused by the spirochete *Borrelia burgdorferi*, which has demonstrated the ability to invade numerous body tissues, including the central and peripheral nervous systems and the bladder [1]. Although initially associated with urinary retention, symptoms of urinary urgency, urge incontinence, and nocturia may occur at any time during the disease process [177]. Patients with Lyme disease may present with DU or DO [178]. Although the disease may respond to a 2-week course of antimicrobial therapy [179], those with relapsing and remitting symptoms may require long-term administration of antimicrobials [180].

Herpes Zoster

Reactivation of persistent varicella virus from a dorsal root ganglion will result in episodes of herpes zoster [181]. During such episodes, symptoms primarily include sensory disturbances such as pain and paresthesia, although paralytic complications do rarely occur [182].

Infrequently, the virus reactivation includes the autonomic nerves of the bladder, with resultant irritative voiding symptoms such as dysuria and frequency. In cases involving the afferent neurons of the sacral micturition reflex arc, somatic and visceral motor neuropathy can occur, and urinary retention may ensue [183,184]. The course of the viral infection is usually self-limiting, with spontaneous recovery typically occurring within several months [1,185].

Poliomyelitis

Following a World Health Organization resolution in 1988, great strides have been made in the eradication of poliomyelitis worldwide, with only 11 countries currently affected with endemic polio [186]. Poliomyelitis results in destruction of the gray matter of the anterior horn cells and selective destruction of large-diameter fast-conducting motor neurons [187]. Polio is essentially a pure motor neuropathy with sensory function usually preserved [188]. Urinary retention may occur in up to 40% of patients, depending on disease severity. Patients with post-polio syndrome may manifest an increased incidence of irritative lower urinary tract symptoms, although studies on this issue are incomplete [1].

Urodynamic evaluation reveals DU when testing affected individuals, with bladder sensation and anal sphincter function remaining intact [189].

Tethered Cord Syndrome and Short Filum Terminale

The tethered cord syndrome results from impediment of the cephalad migration of the conus medullaris and may result from a short filum terminale, intraspinal lipoma, or fibrous adhesions resulting from the surgical repair of spinal dysraphism [190,191]. The syndrome is classically diagnosed in children, especially during adolescence, but rarely, the process may occur in adulthood [192,193]. Lower urinary tract dysfunction is common in this syndrome, and, in otherwise asymptomatic children, urodynamic abnormalities may be the basis for surgical intervention [194].

Urodynamic Evaluation

Detrusor areflexia has been reported in 60% of patients, although recovery of lower tract function approached 60% with surgical release of the cord [192]. Similarly, DO has also been reported [195]. In another series, 22% of patients with tethered cords had DO; all improved following spinal surgery [196]. Early and aggressive neurosurgical correction is therefore indicated [197].

CONDITIONS OF THE PERIPHERAL NERVOUS SYSTEM AFFECTING THE URINARY TRACT

Pelvic Plexus Injury

The major sympathetic and parasympathetic innervation of the lower urinary tract follows the branching array of the pelvic plexus. These nerve fibers can be disrupted during complicated pelvic surgical procedures, or following pelvic fracture, with resultant lower urinary tract dysfunction. Sympathetic (thoracolumbar) nerves promote urine storage by relaxing the detrusor muscle and relaxing the bladder outlet. Parasympathetic (sacral) nerves stimulate detrusor contraction. If the primary injury affects the parasympathetic nerve fibers, generally there is impaired detrusor contractility, although DU may occur in severe instances [1]. Similarly, in cases involving predominately sympathetic innervation, the resultant symptoms usually include intrinsic sphincter deficiency with stress urinary incontinence. Study of patients with voiding dysfunction following major pelvic surgery has shown resolution of symptoms in 6 months for up to 80% of affected patients [198].

Abdominoperineal Resection

Abdominoperineal resection (APR) for rectal cancer almost invariably results in the disruption of the pelvic plexus, with both cadaveric and operative dissections of the plexus pathway demonstrating its susceptible nature during rectal resection [199,200]. The courses of the pelvic nerves are as follows:

From the inferior hypogastric plexus, it has multiple branches forming a weblike complex within the endopelvic fascial sleeve, some of which innervate the bladder detrusor.
A main branch traveling inferolateral to the rectum remains deep to the fascia of the levator ani muscle and courses to the external urinary sphincter.
At the level of the bladder neck in females, this pelvic nerve branch sends direct branches to the urinary sphincter [201].

As a result of this course, this has been associated with significant lower urinary tract dysfunction as an operative complication [202]. The reported rate of urinary retention following APR ranges from 25% to 90%, with urinary tract infection frequently being associated [202,203].

Prior studies reveal evidence of sympathetic denervation in 100%, parasympathetic denervation in 38%, and pudendal denervation in 54% of patients postoperatively [1]. The postoperative voiding dysfunction is usually transitory, although sphincteric insufficiency may be permanent [204]. Post-APR urinary retention is best managed by clean intermittent self-catheterization.

Radical Hysterectomy

A similar effect on the lower urinary tract is seen from radical hysterectomy as in APR due to the similar dissection necessitated during the operation and bilateral pelvic lymphadenectomy. However, the location of the plexus inferolateral to the rectum reduces the disruption of the parasympathetic nerve fibers during hysterectomy, and the extent of pericervical dissection (e.g., “nerve-sparing” approach) does not appear to affect the postoperative urinary symptom complex [205]. Persistent postoperative lower urinary tract dysfunction is best managed with a combination of anticholinergic therapy to decrease intravesical storage pressure and catheterization for retention, with most oncologists leaving the patients catheterized for a minimum of 1 week postoperatively. The incidence of fistula is also increased by the radical dissection compared to those hysterectomies for benign indications.

Diabetic Cystopathy

Diabetes mellitus is the most prevalent medical condition resulting in sensory neurogenic lower urinary tract dysfunction affecting 2% of the U.S. population [1,206,207]. Voiding symptoms generally develop at least 10 years after the onset of the disease, as a result of one of three types of neuropathy: peripheral neuropathy, mononeuritis multiplex, and autonomic neuropathy [91,208]. Metabolic abnormalities of Schwann cell function result in segmental demyelinization and subsequent axonal degeneration, impairing nerve conduction [209,210].

Clinical and Urodynamic Features

Diabetes contributes significantly to voiding dysfunction in women [211]. Gradual development of impaired bladder sensation is the first sign, usually associated with other sensory impairments consistent with peripheral neuropathy. Decreased sensation leads to increased intervoiding intervals, which cause an increase in bladder capacity. Eventually, the bladder may become progressively overdistended, impairing contractility and leading to incomplete emptying [212]. Subsequently, symptoms associated with traditional “diabetic cystopathy” may include urinary hesitancy, slowing of the urine stream, and decreasing urinary frequency [211,213]. These symptoms may progress to include a sensation of incomplete emptying or even urinary dribbling from overflow incontinence [211,214].

When questioned, up to 50% of unselected diabetes mellitus patients have subjective evidence of traditional diabetic cystopathy. The urodynamic evaluation, however, suggests alterations in lower urinary tract function in only 27%–85% of these patients [214,215]. Urodynamic studies frequently reveal impaired bladder sensation, increased cystometric bladder capacity, decreased detrusor contractility, an impaired urine flow, and an elevated postvoid residual urine volume [91]. However, more recent studies suggest that DO rather than the “traditional diabetic cystopathy” may be the most common observed voiding dysfunction in patients with diabetes. Kaplan and Te reported on another group of patients with diabetes referred because of voiding symptoms. Of this group, 55% were found to have DO, 23% impaired detrusor contractility, 10% detrusor areflexia, and 11% “indeterminate findings.” In the 42 patients in this group with sacral cord neurological signs, 50% had impaired detrusor contractility and 24% had detrusor areflexia [216]. In addition, poor diabetic control will contribute to urgency and frequency as a result of decreased warning time from impaired sensation and polyuria from the elevated glucose.

Upper tract changes depend upon the duration and severity of the disease process as well as the effect on intravesical pressure. The effect of diabetes-induced lower urinary tract dysfunction on the upper urinary tract is difficult to determine because of the other effects of diabetes on renal function [1]. When managing patients with diabetic cystopathy, preservation of renal function is paramount. A direct effect of diabetes on renal microvasculature, combined with upper tract obstructive changes resulting from diabetic cystopathy, put the diabetic kidneys at great risk. A timed voiding schedule is effective in those with impaired contractility, while intermittent catheterization is reserved for those who experience greater difficulty with emptying. Anticholinergic therapy may be effective for those with DO or impaired bladder compliance [207].

CONCLUSIONS

While neurological conditions are frequently associated with lower urinary tract dysfunction, clinicians often overlook neurological etiologies during workup and treatment of voiding dysfunctions. A high index of suspicion should be maintained where the severity of symptoms is disproportionately high or in rapid onset of symptoms. A brief neurological examination at the time of presentation of new patients —or during urodynamic—should be considered as a standard for good practice. Management of voiding dysfunction in patients with neurological comorbidities requires consideration of functional disabilities and other medications.

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53 Nonneurogenic Voiding Dysfunction and Urinary Retention

Bernard T. Haylen

INTRODUCTION

One of the core aims of the clinical and urodynamic assessment of women with symptoms of pelvic floor dysfunction is to screen for the presence of voiding dysfunction (VD), i.e., abnormally slow and/or incomplete micturition [1]. Clinical assessment may provide limited, generally nonspecific information with two screening urodynamic tests, uroflowmetry and a postvoid residual (PVR) measurement of much greater value. Uroflowmetry, or the measure of urine flow over time, allows the simple and noninvasive analysis of the normality or otherwise of urine flow while the complementary measurement of PVR will indicate the completeness or otherwise of micturition.

Abnormal urine flow rates or patterns or high PVRs in women will generally require the further investigation of voiding cystometry in order to determine the cause. Pressure and flow analysis will assist the discrimination between the presence of one of the two main causes of abnormally slow urine flow, i.e., bladder outflow obstruction and a hypotonic or atonic bladder.

It is important clinically to diagnose or eliminate the diagnosis of VD in women presenting for assessment of symptoms of pelvic floor dysfunction. Surgical treatment of urodynamic stress incontinence (USI) and drug treatment of detrusor overactivity (DO) both have the potential to cause VD. Preexisting VD will prejudice these treatments, leading to the possibility of acute or chronic retention.

The subsequent discussion will focus on women not presenting with existing neurological disorders known to be associated with VD.

CLINICAL ASSESSMENT

Symptoms of VD should be included in a comprehensive history in women presenting with symptoms of pelvic floor dysfunction. The Standardization and Terminology Committees of the International Continence Society (ICS) and the International Urogynecological Association [1] have suggested the following definitions for “voiding and postmicturition symptoms”:

Voiding and postmicturition symptoms: A departure from normal sensation or function experienced by the patient during or following the act of micturition.

Hesitancy: Complaint of a delay in initiating micturition.

Slow stream: Complaint of a urinary stream perceived as slower compared to previous performance or in comparison with others.

Intermittency: Complaint of urine flow that stops and starts on one or more occasions during voiding.

Straining to void: Complaint of the need to make an intensive effort (by abdominal straining, Valsalva, or suprapubic pressure) to either initiate, maintain, or improve the urinary stream.

Spraying (splitting) of urinary stream: Complaint that the urine passage is a spray or split rather than a single discrete stream.

Feeling of incomplete (bladder) emptying: Complaint that the bladder does not feel empty after micturition.

Need to immediately revoid: Complaint that further micturition is necessary soon after passing urine.

Postmicturition leakage: Complaint of a further involuntary passage of urine following the completion of micturition.

Position-dependent micturition: Complaint of having to take specific positions to be able to micturate spontaneously or to improve bladder emptying, e.g., leaning forward or backward on the toilet seat or voiding in the semistanding position.

Dysuria: Complaint of burning or other discomfort during micturition. Discomfort may be intrinsic to the lower urinary tract or external (vulvar dysuria).
Urinary retention: Complaint of inability to pass urine despite persistent effort.

These symptoms are mostly nonspecific and not diagnostic in themselves though the symptoms of hesitancy, a poor stream, and straining to void have been more commonly linked to an abnormally slow urine flow rate or a high PVR [2].

Of the various clinical signs, that of uterine and/or vaginal prolapse, particularly if higher stage, can be associated with a diagnosis of VD by a urethral "kinking effect." Atrophic vaginal changes might be an indicator that atrophic urethral changes might be present causing a possible "stenotic" effect.

HISTORY OF UROFLOWMETRY

The first attempt to obtain an objective measurement of the urine flow rate was made in 1897 by Rehfisch [3] (Ryall and Marshall [4]) using a poorly detailed method employing an air displacement principle. Ballenger et al. [5] felt that the cast distance of urinary stream (voiding distance) might be a useful clinical guide to the presence of prostatic disease.

Drake [6] made the first accurate measurements of urine flow. He used a spring balance; a pen that wrote on a kymograph was attached to one end, and a receptacle for the voided volume was attached to the other end. By rotating the kymograph drawn at a known speed, Drake obtained a trace of voided urine volume against time. He calculated the maximum urine flow rate by a measurement of the steepest part of the volume–time curve. It is evident from his description that the apparatus was relatively crude and difficult to use. Furthermore, urine flow rates had to be calculated from volume–time data. Drake's flowmeter was never produced commercially. Kaufman [7] commercially produced a modification of Drake's flowmeter that was more refined but similarly made no direct recording of flow rate.

The advent of electronics in medical instrumentation allowed the mass production of accurate and reliable recording devices. Von Garrelts [8] designed the first of the electronic urine flowmeters, which consisted of a tall urine-collecting cylinder with a pressure transducer in the base. The pressure transducer measured the pressure exerted by an increasing column of urine as the patient voided. Since a direct relationship existed between the volume voided and the pressure recorded, von Garrelts was able to produce a direct recording of urine flow rate by electronic differentiation with time.

In 2016, it is 39 years since it was determined that uroflowmeters of acceptable accuracy were available [9]. The current accuracy of modern uroflowmeters is around ±2%–5%, despite the fact that a variety of different physical principles are currently used. Regular calibration of the uroflowmeter is required to maintain accuracy.

DEFINITION OF URINE FLOW RATE MEASUREMENTS

In any field of scientific measurement, it is important that all workers use standardized terminology. Urine flow rates are measured in milliliters per second (mL/s). Figure 53.1 denotes the definitions for urine flow rate measurements as suggested by the Standardization and Terminology Committees of ICS and IUGA [1]:

Urine flow: Voluntary urethral passage of urine, which may be
Continuous: No interruption to flow.
Intermittent: Flow is interrupted.
Flow rate: Volume of urine expelled via the urethra per unit time. It is expressed in mL/s.
Voided volume (*mL*): Total volume of urine expelled via the urethra.
Maximum flow rate (*MUFR–mL/s*)–Q_{max}: Maximum measured value of the flow rate correcting for artifacts.
Flow time (*second*): The time over which measurable flow actually occurs.
Average (urine) flow rate (*AUFR–mL/s*)–Q_{ave}: Voided volume divided by the flow time. It may be calculated from the area beneath the flow time curve.
Voiding time (*second*): This is the total duration of micturition, which includes interruptions. When voiding is completed without interruption, voiding time is equal to flow time.
Time to maximum flow (*second*): This is the elapsed time from the onset of urine flow to maximum

urine flow.

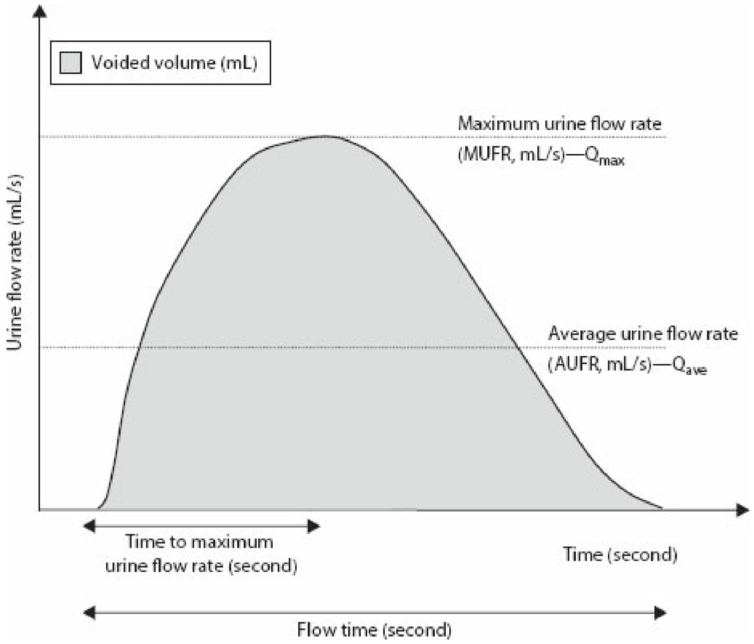

Figure 53.1 A schematic representation of urine flow over time.

Figure 53.1 shows a schematic representation of urine flow over time.

METHODS OF URINE FLOW RATE MEASUREMENT

Numerous physical principles have been employed over the years in an attempt to develop what Backman [10] and Von Garrelts and Strandell [11] would see as an ideal uroflowmeter:

1. High level of accuracy at different voided volumes and urine flow rates
2. Easy to read and rapidly available permanent tracings
3. Unobtrusive and not distracting to the patient by appearance or sound
4. Easy to clean

There have been many methods used for urine flow measurement, from measuring the time to void a given volume through audiometric and radioisotopic methods to even include high-speed cinematography. The most common method has been that of Drake [6] modified by von Garrelts and Strandell [11]—the measurement of urine weight.

In addition, flowmeters have been produced that use the principles of air displacement, differential resistance to gas flow, electromagnetism, photoelectricity, electrical capacitance, and a rotating disc.

Flowmeters employing the principles of weight transduction, a rotating disc, and a capacitance transducer are the best known and the most completely tested and validated of the flowmeters available.

The weight transducer type of flowmeter weighs the voided urine and by differentiation with time produces an “online” recording of urine flow rate:

$$FR = dVdT$$

where dV is the change in volume of urine over change in time, dt.

The rotating disc flowmeter depends on a servometer maintaining the rotation of the disc at a constant speed. Urine hits the disc, and the extra power required to maintain the speed is electronically converted into a measurement of flow rate.

The capacitance flowmeter is the simplest of the three flowmeters. This flowmeter consists of a funnel leading urine into a collecting vessel. The transducer is in the form of a dipstick made of plastic and coated with metal, which dips into the vessel containing the voided urine.

All three types of flowmeter perform accurately and efficiently. For clinical purposes, the measured and indicated flow rate should be accurate to within ±5% more than the clinically significant flow rate range [12]. The capacitance (dipstick) flowmeter is the least expensive to buy and has the advantage of no moving parts, which means mechanical breakdowns are eliminated. Rotating disc flowmeters have the advantage of not requiring priming with fluid. Automatic start and stop facilities in some modern flowmeters assist by minimizing patient and staff involvement during the uroflowmetry (Figure 53.2).

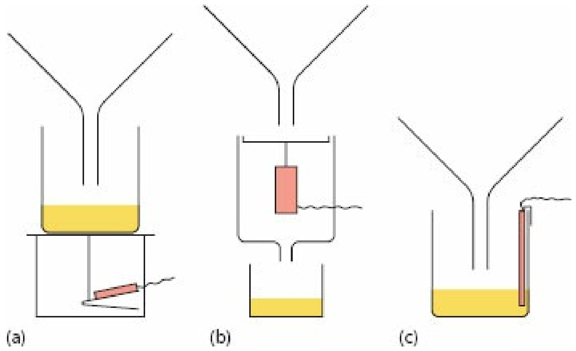

Figure 53.2 Urine flowmeters: (a) weight transducer, (b) rotating disc, and (c) capacitance (dipstick).

CLINICAL MEASUREMENT OF URINE FLOW RATES

The environment for patient flow rate recording is of considerable importance. Female patients usually void in circumstances of almost complete privacy. It is essential in the clinical situation that every effort is made to make the patient feel comfortable and relaxed. If these requirements are ignored, psychological factors are introduced and a higher proportion of patients will fail to void in a representative way. Ideally, all free uroflowmetry studies should be performed in a completely private uroflowmetry room/toilet, lockable from the inside, and out of hearing range of other staff and patients. As crouching over a toilet seat causes a 21% reduction in the average urine flow rate [13], patients should be encouraged to sit to void. When video studies are combined with pressure–flow recordings in a radiology department, up to 30% of women may fail to void.

Patients should be encouraged to attend for uroflowmetry with their bladder comfortably full. It is desirable that the measured urine flow rates should be for a voided volume within the patient’s normal range. This range can be determined if, in the week before the flow study, the patient completes a frequency–volume chart (urinary diary). On this chart, the patient enters the volumes of fluid consumed and the volumes of urine voided. Recent nomograms, however, provide normal reference ranges for urinary flow rates over a wide range of voided volumes. There is generally no need for multiple uroflowmetry in most women. Abnormal or unusual flow curves and urinary flow rates, however, merit repeating the study.

URINE FLOW RATES IN NORMAL (ASYMPTOMATIC) WOMEN

The maximum and average urinary flow rates are the two most important uroflowmetry parameters. They are both numerical representations of the urine flow curve. The clinical usefulness of flow rates had been attenuated by the lack of absolute values defining normal limits [14]. As urinary flow rates are known to have a strong dependence on voided volume [6,15], these normal limits need to be over a wide range of voided volumes, ideally in the form of nomograms.

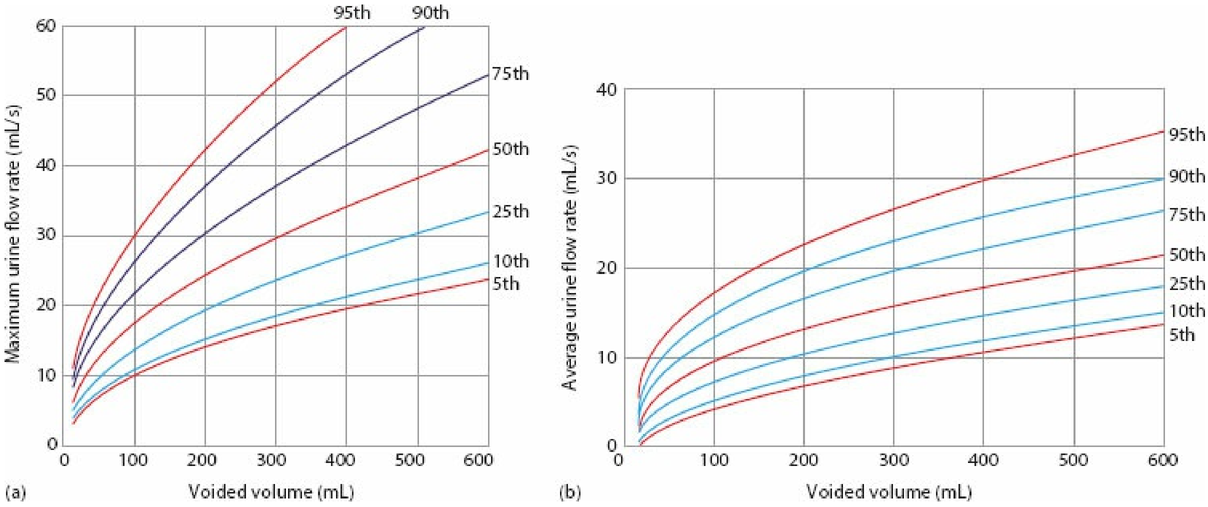

Figure 53.3 (a) Liverpool nomogram for maximum urine flow rate in women. (b) Liverpool nomogram for average urine flow rate in women.

Studies on normal values for urinary flow rates in women include those of Peter and Drake [16], Scott and McIhlaney [17], Backman [18], Susset et al. [19], Walter et al. [20], Drach et al. [15], Bottacini and Gleason [21], Fantl et al. [22], and Rollema [23]. Data and/or statistical analysis in these studies has not allowed effective nomogram construction. Study restrictions have included small patient numbers [19–23]; the use of outmoded or less well-evaluated equipment [15–16] and the incompleteness of data at lower voided volumes [15,18] due in part to the inaccuracy of some equipment at lower voided volumes [15].

In a 1989 study, Haylen et al. [24] studied 249 female volunteers (aged 16–63 years), all of whom were deemed normal by denying specific urinary symptomatology, underwent uroflowmetry studies. Each woman voided once in a completely private environment over a calibrated rotating disc-type uroflowmeter; 46 voided on a second occasion. The maximum and average flow rates of the first voids were compared with the respective voided volumes. By using statistical transformations of both voided volumes and urine flow rates, relationships between the two variables were obtained. This allowed the construction of nomograms, which, for ease of interpretation, have been displayed in centile form (Figure 53.3):

$$\text{Ln(MUFR)} = 0.511 + 0.505 \times \text{Ln(voided volume)}$$

$$\text{Root mean square error} = 0.340^{*}$$

More recently, Barapatre et al. [25] produced nomograms using the data of 343 healthy Indian women. The results, after elimination of “abnormal” data, were much slower urine flow rates overall than those in the Liverpool nomograms and an age dependency of urine flow rates, not normally noted in asymptomatic women [15,22,24,26]. As noted later, their median centiles in asymptomatic women were slower than the studies using the Liverpool nomograms in symptomatic women:

$$\text{Square root(AUFR)} = -0.921 + 0.869 \times \text{Ln(Voided Volume)}$$

$$\text{Root mean square error} = 0.640^{\dagger}$$

Traditional “cutoff” values for normal urine flow rates have been used with due scientific analysis of their accuracy or value. The maximum urine flow rate has been most studied. Recommended lower limits of normality range between 12 and 20 mL/s. Most commonly, a minimum rate of 15 mL per second is quoted for the same parameter if at least 150 mL (or sometimes 200 mL) has been voided. The practice of artificially imposing minimum limits for the voided volume is difficult to justify [27] and very often impractical. Women with certain states of lower urinary tract dysfunction, those in whom the flow rate might be most important, may not be able to hold 200 mL. It has been demonstrated that only 45% of voided volumes are more than 200 mL and 55% are more than 150 mL, making interpretation of fixed urine flow rates valid [28]. Because of the strong dependency of urine flow rates on a voided volume, a normal urine flow rate at 200 mL may not also be normal at 400 mL.

CLINICAL FACTORS INFLUENCING URINE FLOW RATES IN NORMAL (ASYMPTOMATIC) WOMEN

Voided Volume

The use of nomograms overcomes the dangers of referencing flow rates to any one voided volume. A maximum flow rate of 15 mL/s might fall just within the fifth centile curve at 200 mL voided volume, though well below the same curve at 400 mL. The median voided volume of 171 and 175 mL in the aforementioned series [24,28] again highlights the need for normal reference ranges to include data at lower voided volumes.

Both the maximum and average urine flow rates in the aforementioned study were found to have a strong and essentially equal dependence on voided volume. The clinical use of either flow rate is equally valid. However, the centile lines onto which the maximum and average urine flow rates respectively fall for the same voided volume (centile rankings) are not interchangeable in an individual instance due to wide variations in urine flow patterns. The closer the urine flow pattern comes to the "ideal" flow time curve seen in Figure 53.1, the more chance there will be that the centile rankings for the maximum and average urine flow rates are the same.

No systematic deterioration of either flow rate at higher voided volumes was discernible from this population study. The same may not be true for an individual.

Age and Parity

Drach et al. [15], Fantl et al. [22], and Haylen et al. [24] found no significant age dependence of urinary flow rates in normal women, unlike the findings of Barapatre et al. [25]. The same studies also found that there was no significant effect of parity on urine flow rates in normal women. This was not tested by Barapatre et al. [25].

Repeated Voiding

There was a remarkable consistency in the centile rankings of the paired first and second voids in the study of Haylen et al. [24]. This consistency is further witnessed in the multiple voids from a single 25-year-old normal female volunteer (Figure 53.4). Fantl et al. [22] found no significant difference between the first and up to the sixth void in the 60 women they tested. This was not tested by Barapatre et al. [25]. Clinically, in the majority of normal women, the centile rankings of successive voids will not differ widely. It is uncertain, at present, whether this is also true for women with lower urinary tract dysfunction. As suggested previously, abnormal or unusual flow rates or curves merit repeating the study.

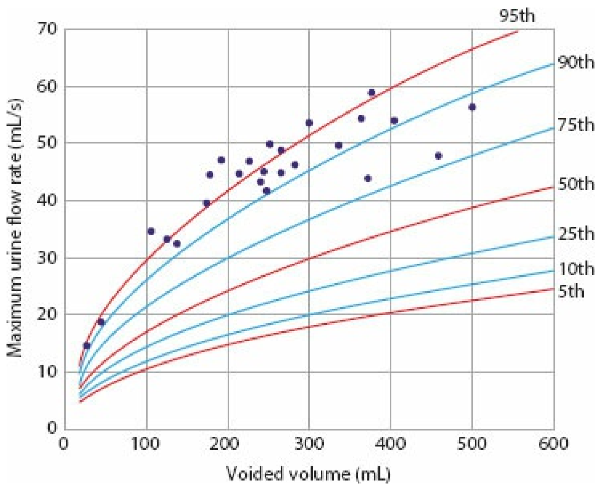

Figure 53.4 The maximum flow rates from a large number of voids by a single 25-year-old female volunteer superimposed on the respective Liverpool nomogram.

Presence of a Catheter

The aforementioned nomograms refer to free flowmetry voids; they are not applicable where pressure of another catheter is present in the urethra. All urethral catheters can be expected to have the effect of decreasing urinary flow rates for the equivalent voided volume. Part of this reduction is physical obstruction with pressure catheters varying from 6 FG (microtranducer) to 10 FG (water-filled). By necessity, potentially unfavorable environmental and psychological factors are introduced when catheterization flowmetry is performed. Ryall and Marshall [29] suggested that the reduction is maximum urinary flow rate caused by the fine (diameter = 2 mm) urethral catheter used in their study of 147 symptomatic men was of the order of several mL/sec. Though small, this reduction was enough to change the diagnostic categorization of one-third of their subjects.

Normal Male vs. Normal Female Urine Flow Rates

Female urine flow rates are higher than those of men [10,15,24]. Female maximum urine flow rates are on average 0.19 times greater than those of young men and 0.39 times greater than the older men [24]. Urethral length (4 cm vs. 20 cm) should account for all the intersex difference [10,24].

URINE FLOW RATES IN WOMEN WITH SYMPTOMS OF PELVIC FLOOR DYSFUNCTION

Between 1958 and 1990, there were four studies on urine flow rates in symptomatic women (those with symptoms of pelvic floor dysfunction), three of which were small [15,16,21]. The other study [30] was limited to the effect of final urodynamic diagnosis on urine flow rates. Three studies indicated that symptomatic women had slower urine flow rates than normal women with one study [15] showing no difference. In 1995, Haylen et al. [31] completed a study of 250 women who were consecutive referrals for urogynecological assessment with symptoms of pelvic floor dysfunction. The flow data for these women were converted to centiles from the Liverpool Nomograms for the following analyses of their median values:

A Comparison of the Urine Flow Rates of Symptomatic and Asymptomatic Women

Table 53.1 shows that the median centiles of the maximum and average urine flow rates of the urogynecology (symptomatic) patients were significantly reduced from those of the asymptomatic population. There was a close agreement between the studies with the 1990 study [30] performed in a different country to the 1995 study [31].

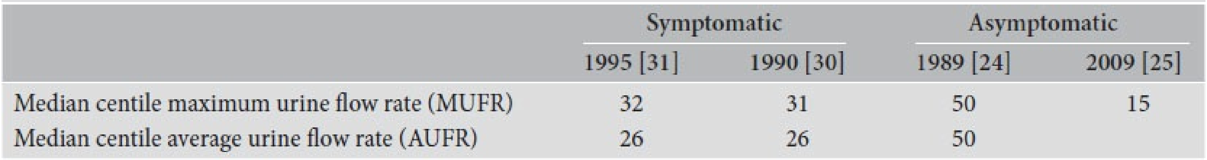

Table 53.1 Comparison of Urine Flow Rates of Symptomatic and Asymptomatic Women

	Symptomatic		Asymptomatic	
	1995 [31]	1990 [30]	1989 [24]	2009 [25]
Median centile maximum urine flow rate (MUFR)	32	31	50	15
Median centile average urine flow rate (AUFR)	26	26	50	

As noted, Barapatre et al.'s [25] 2009 study gives results for urine flow rate centiles in asymptomatic women far slower than equivalent studies in symptomatic women.

Effect of the Presence of Genital Prolapse on Urine Flow Rates in Symptomatic Women

A generally progressive decline in the maximum and average urine flow rates (median centiles) of symptomatic women [31] with increasing grades of genital prolapse was noted. The most significant decline occurred in the presence of uterine prolapse closely followed by cystocoele and enterocoele. More recent data [32], however, would suggest the significance of this may be lost in multivariate analysis of a much larger cohort of symptomatic women.

Effect of Prior Hysterectomy on Urine Flow Rates in Symptomatic Women

A significant decline in the urine flow rates [31] of symptomatic women (median centiles) in the presence of a prior hysterectomy. The effect was the same with both vaginal and abdominal hysterectomy. The flow rates for those symptomatic women without prior hysterectomy was found to be the same as that for the asymptomatic female population. Further analysis suggests that in women with both prior hysterectomy and intercurrent genital prolapse, there is a cumulative decline in urine flow. More recent data [32], however, would suggest the significance of this may be lost in multivariate analysis of a much larger cohort of symptomatic women.

Effect of Age and Parity on Urine Flow Rates in Symptomatic Women

Unlike asymptomatic women, there is a significant effect of age on the maximum and average urine flow rates [30,31]. More recent data [32] suggest that age is the main association of abnormally slow urine flow rates in a large cohort of symptomatic women. Parity was not found to be a significant factor in either this or the 1999 study [31].

Effect of Final Urodynamic Diagnosis on the Urine Flow Rates of Symptomatic Women

Median urine flow rate centiles of the urogynecology patients separated according to the final urodynamic diagnosis are given in Table 53.2.

All categories of diagnoses have their median centiles under those for the normal female population (50 by definition).

VD appears to be the diagnosis for which urine flow rates might have the best discriminatory ability. Further analysis shows that the *10th centile of the Liverpool nomogram* [28,30,31] for the maximum urine flow rate has the best discriminatory ability (sensitivity 81%, specificity 92%) with respect to diagnosing the presence or absence of the final diagnosis of VD either as a solitary or a mixed diagnosis.

Table 53.2 Effect of Final Urodynamic Diagnosis on the Urine Flow Rates of Symptomatic Women

Diagnosis	**Number**	**MUFR**	**AUFR**
USI	107	48	40
DO	14	38	32
VD	7	1	6
USI plus DO	39	34	32
USI plus VD	22	3	2
DO plus VD	14	3	2
USI plus VD plus DO	10	4	7
Normal	7	70	52

More recent data [32] on a large cohort of symptomatic women again showed the highest urine flow rate centiles in women with USI and DO and the lowest in women with VD.

OTHER FACTORS INFLUENCING URINE FLOW RATES

Urine flow depends on the relationship between the bladder and urethra during voiding. The situation during voiding is the antithesis of the situation required for continence. Continence depends on intraurethral pressure being higher than intravesical pressure. For voiding to occur, intravesical pressure must exceed intraurethral pressure.

Einhorning [33] and later Asmusen and Ulmsten [34] showed clearly that before any rise in intravesical pressure, a fall in intraurethral pressure occurred. This suggests that the urethra actively relaxes during voiding rather than being passively “blown open” by the detrusor contraction. Soon after the urethra has relaxed and pelvic floor descent has occurred, the detrusor contracts. The detrusor normally contrives to contract until the bladder is empty, producing a continuous flow curve. Many women void by urethral relaxation alone with minimal or no detrusor involvement. This method of voiding is common in women with USI.

Changes in intra-abdominal pressure also influence urine flow. Some women appear to void entirely by increasing intra-abdominal pressure, that is, by contraction of the diaphragm and anterior abdominal wall muscles.

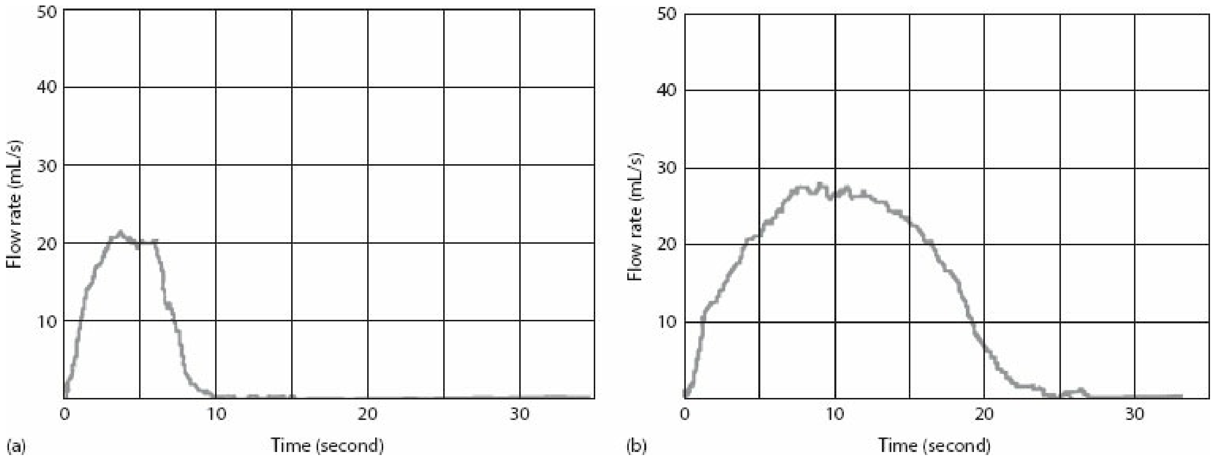

Figure 53.5 Normal flow curves for voided volumes of (a) 121 mL and (b) 345 mL.

It follows from this discussion that the urine flow may differ from normal as a result of abnormalities of the urethra or the detrusor.

Urethral Factors

Anatomical factors

The urethra may be abnormally narrow or the urethra may not be straight. The narrowest part of the urethra, as shown by video studies of voiding, is usually the midzone. However, the urethra may become narrowed and the most common site is at the external meatus associated with estrogen deficiency in the postmenopausal women. Bladder neck obstruction in the female had been thought to be extremely rare [35]. The female urethra is usually straight, and deviation from this state is most common in anterior vaginal wall prolapse and higher degrees of uterine and vaginal vault prolapse. Data earlier point to a possible adverse effect of such prolapse on urine flow rates. The prolapse and urethral effects make bladder outflow obstruction not that uncommon in women.

Pathological Factors

Unusual congenital conditions such as urethral duplications, urethral diverticula, or urethral cysts may obstruct voiding. Infective lesions as in urethritis or infected paraurethral cysts may lead to voiding difficulties. Post-traumatic strictures and urethral neoplasms will have a similar effect. Intravaginal abnormalities, such as prolapse or foreign bodies, may also obstruct micturition.

Functional Factors

Abnormal urethral behavior during voiding may lead to alteration in the urine flow rate recording. Urethral closure may be due to contraction of the intraurethral striated muscle or to contraction of the pelvic floor. In the neurologically abnormal patient, contraction of the intraurethral striated muscle with or without the pelvic floor is known as detrusor sphincter dyssynergia. In the nervous and anxious but neurologically normal patient, the urethra may be closed by pelvic floor contraction.

Detrusor Factors

Contractility

It is well known that when neurological disease occurs, bladder behavior may be altered. However, in patients with no neurological disease, poor detrusor contractility may be responsible for a slow flow rate. Such patients may have UTIs or urinary retention. These patients have normal urethral function as judged by urethral pressure profilometry or radiology. Their reduced flow rates are secondary to a weak and poorly sustained detrusor contraction. A proportion of this clinical group goes on to demonstrate classical neurological diseases such as multiple sclerosis.

Innervation

Normal detrusor behavior depends on normal innervation. Bladder contractions are preserved if the sacral reflex arc is intact even when the upper motor neurons are damaged. However, if the sacral reflex arc is damaged, bladder contractions are generally absent. The only form of contractile activity possible when the lower motor neuron is damaged is locally mediated—the “autonomous” bladder. The urine flow rates produced by the abnormally innervated bladder are usually reduced and interrupted.

Pathological Factors

Although little specific literature on the subject exists, it is evident that gross disease of the detrusor will result in abnormal urine flow rates. The fibrosis resulting from irradiation, tuberculosis, cystitis, or interstitial cystitis is likely to impair detrusor contractility

URINARY FLOW PATTERNS

Urine flow curves are complementary to flow rates in the assessment of voiding. Because flow curves cannot be numerically represented (except by urine flow rates), they are less useful for clinical comparisons than flow rates. Several patterns of flow curves can however be recognized.

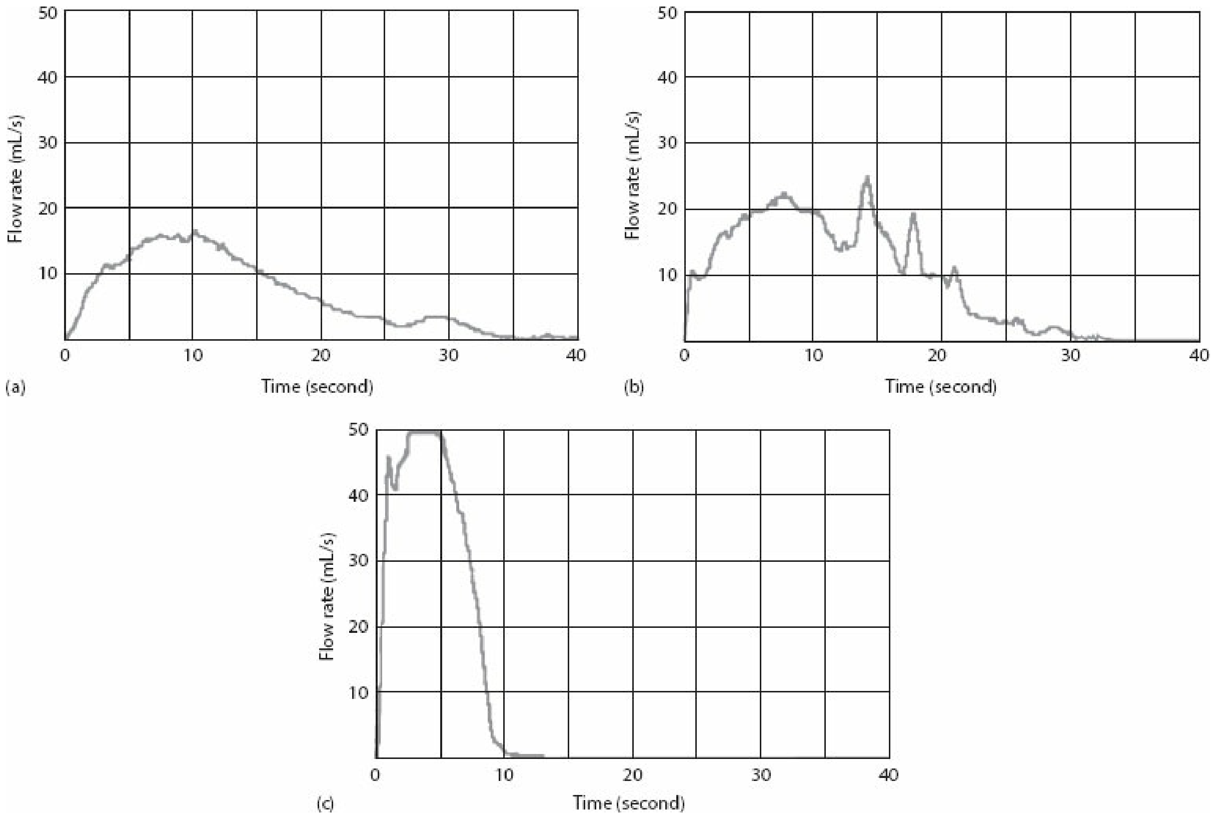

Figure 53.6 (a) low normal (suboptimal) flow curve (voided volume 261 mL), (b) abdominal strain pattern (voided volume 353 mL), (c) high takeoff flow pattern (voided volume 336 mL).

Normal

The normal flow trace (Figure 53.5a and b) shows a symmetrical peak with a maximum flow rate generally achieved within 5 seconds of the beginning of voiding. The maximum flow rate is generally 1.5–2 times the average flow rate.

A low normal (suboptimal) flow trace (Figure 53.6a) shows no symmetrical peak. Maximum flow rate, somewhere between the 5th and 25th centile, occurs early, and then the flow trails off. An abdominal strain pattern (Figure 53.6b) shows the influence of generally intermittent abdominal strain during the void. It is manifested by irregular moderately fast accelerations in maximum urine flow. A high takeoff pattern (Figure 53.6c) shows a very rapid acceleration to a high maximum flow rate. A higher incidence of such traces has been noted in both men and women with DO.

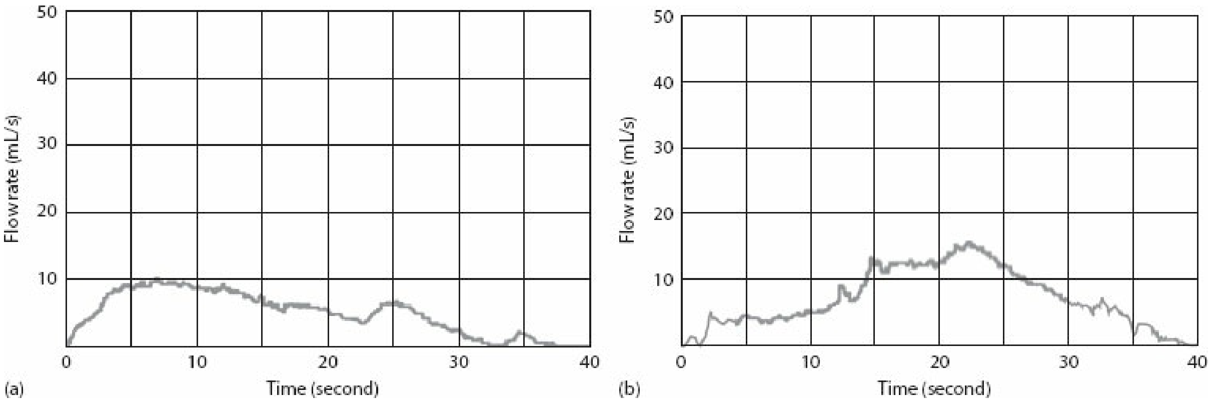

Figure 53.7 Reduced urine flow trace caused by (a) bladder outflow obstruction (maximum detrusor voiding pressure 54 cmH_2O) and (b) detrusor underactivity (maximum detrusor voiding pressure 15 cmH_2O).

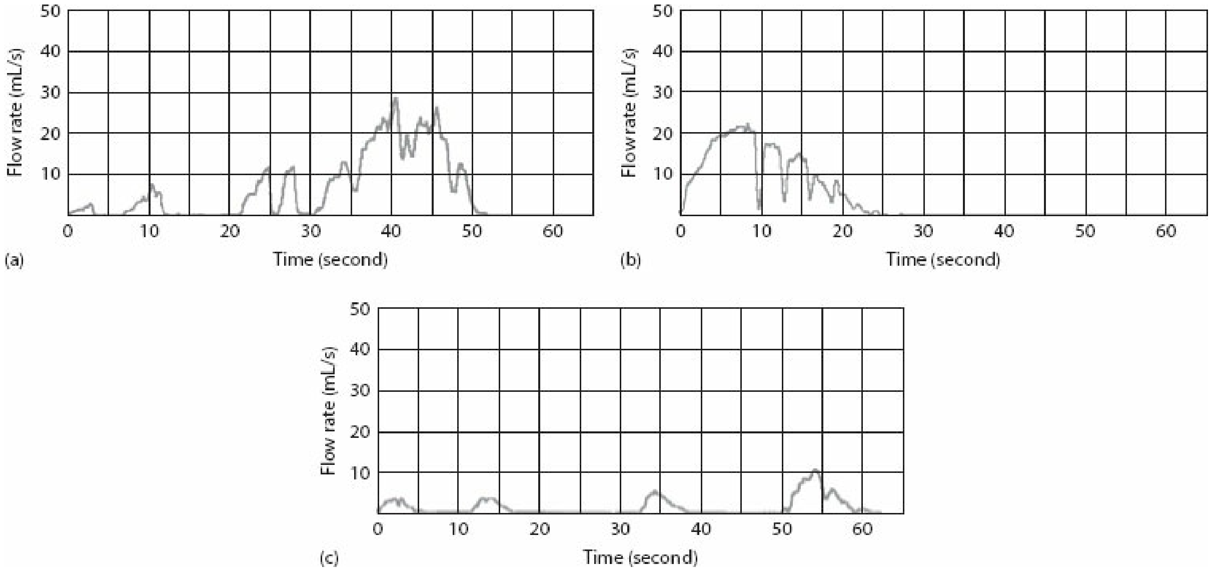

Figure 53.8 (a) Abdominal pressure voiding pattern, (b) voluntary sphincter contraction urine flow pattern, and (c) detrusor sphincter dyssynergia flow pattern.

Abnormal–Continuous Flow

Urine flow curves reflected in flow rates below the 5th centile may generally be regarded as abnormal; abnormality can be suspected in those curves with flow rates between the 5th and 10th centile.

A reduced flow rate may be due either to a urethral obstruction or to a poor detrusor contraction (Figure 53.7a and b). It is necessary to perform full pressure flow studies to demonstrate the cause of a reduced urine flow rate.

Abnormal–Interrupted Flow

An abdominal pressure voiding pattern (Figure 53.8a) is where abdominal straining provides the pressure behind the voiding. Little detrusor activity is present. Irregular interrupted peaks of flow are the result. Maximum urine flow rate is more than twice the average urine flow rate.

A voluntary sphincter contraction urine flow pattern (Figure 53.8b) occurs as the anxious nervous patient closes her distal urethral sphincter mechanism. Flow rate may decrease or stop. Characteristically, the rate of change of flow rate is rapid, indicating sphincter closure. The fluctuations due to detrusor underactivity would be much slower than those seen here.

Detrusor sphincter dyssynergia is an involuntary phenomenon in which the expected coordination of the detrusor contraction and urethral relaxation is lost. Despite an effective detrusor contraction, the urethral mechanism remains closed for longer periods of time (up to several minutes). Detrusor sphincter dyssynergia may result in a large residual urine together with upper tract dilatation and renal failure and is often associated with repeated infection. Detrusor sphincter dyssynergia only occurs in neurologically abnormal patients, most classically in high spinal cord trauma. The flow rate produced by detrusor sphincter dyssynergia (Figure 53.8c) is usually reduced and always interrupted.

POSTVOID RESIDUAL MEASUREMENT

Definition

The PVR is defined as the volume of urine remaining in the bladder at the completion of micturition [1].

Clinical Relevance

The PVR is a key marker of bladder function in terms of emptying ability. An abnormally high PVR, if confirmed by repeat measurement, confirms the presence of VD. Voiding cystometry is needed to assist in determining the cause.

Accuracy of PVR Measurement

The accuracy of PVR measurement has not matched other urodynamic variables such as pressure and flow. Subsequent discussion will show that the best accuracies are around ±25% for methodologies, usually ultrasound, involving immediacy (within 60 seconds). Those techniques (usually catheterization) involving delayed measurement can lead to errors, generally overestimation by, at times, very significant percentages.

Diuresis Factor

The main source of error in PVR measurement is the additional renal input into bladder volume from the delay in PVR measurement following micturition leading to an overestimation. Two factors can be multiplied to determine this input: (1) the diuresis (mL/min) occurring at the time (this can be 1–14 mL/min) [36,37] and (2) the duration of the delay (min) between completion of micturition and PVR measurement (if the latter is by urethral catheterization, the end point of the delay is the completion of bladder drainage). If both are excessive, the overestimation can be marked.

PVR Measurement by Catheterization

Urethral catheterization, the traditional approach to PVR measurement, is most vulnerable to the *diuresis factor*, as it takes 4.5 minutes minimum in studies [36,37] from the completion of micturition to the completion of bladder drainage using a catheter. Other factors are relevant:

Catheter Factor

For PVR measurement by urethral catheterization, the use of a catheter, which incompletely drains the bladder, will lead to an underestimation of the true PVR. A short plastic catheter (particularly a 14 FG though a 12 FG is probably also adequate) will make sure [37,38] that whatever PVR present will be completely drained (under 1 mL postcatheterization bladder volume). A 14 FG Foley urethral catheter will leave, on average, 77 mL of postcatheterization bladder volume [38,39]. Smaller Foley catheters than 14 FG can be expected to have an even higher postcatheterization bladder volume.

It is a quoted practice to enhance the drainage of a Foley catheter by suction drainage using a syringe. While there is weak evidence that this might be helpful [39], the efficacy of this technique has not been proven. Similarly, small-bore urodynamic filling catheters have been used to drain the bladder, though this may be relatively slow, thus increasing the delay in collection. There are no published data to confirm their efficacy in bladder drainage.

Measurement Apparatus Factor

Presuming the PVR collection occurs without delay, a catheter with known efficacy in bladder drainage is used and there is no PVR spillage; one has to rely on the accuracy of the measuring apparatus used, which might have variable and often inappropriate (for the volume) and inaccurate calibration.

PVR Measurement by Ultrasound

Accuracy

Ultrasound techniques of known accuracy offer the best prospects of minimizing the aforementioned inaccuracies in PVR measurement, allowing cost considerations. The benefits of ultrasound for PVR measurement (known accuracy, reduced time, and patient trauma) need to be added to the increasing array of other indications for ultrasound in urogynecology (bladder neck assessment and intercurrent lower urinary tract and pelvic floor pathology [40]) when equipment costs are being considered. With ultrasound, all women with any PVR have the opportunity of a second attempt to reduce or clear this volume. This might avoid the need for subsequent repeat PVR measurements if surgery was being contemplated in a patient with an abnormally high PVR measured using urethral catheterization.

Abdominal Ultrasound

The use of this modality to measure bladder volumes dates back to 1967 [41]. Different formulae have been used generally, using three bladder dimensions, height, width, and depth (generally multiplied by a constant, with 0.625 commonly used [42]). Results have been variable and conflicting [42] with accuracies limited by the variability in bladder shape and filling [43]. Accuracies in most published series are around 21%–25% [41–43]. The key limitation of transabdominal ultrasound is the distance between the abdominal wall and the bladder, with fat (obesity), gas, and bone (shadowing of the pubis) potential impediments to the transmission of the sound beam. Smaller bladder volumes (under 100 mL) have been cited as more difficult to quantify with false negatives occurring under 50 mL [42]. Advances in ultrasound technology will have improved visualization over time.

Transvaginal Ultrasound

This modality, first reported in 1989 [44], involves the calculation of bladder volumes using two bladder dimensions in the sagittal plane. It has been shown to provide accurate and validated [45] measurements of PVRs from 0 to 175 mL with superior visualization of PVR under 30 mL, where around 80% to 90% of PVR appear likely to occur [46,47]. Accuracy is 24% (overall) and 15% (volumes 50 mL and over). Under 50 mL, the accuracy rises to 55%. Transrectal ultrasound was also reported in 1989 [48], using similar methodology to that for transvaginal ultrasound with a mean accuracy of 16%. Although its calibration was done only in men, it is possible to measure PVRs in women accurately using this modality. The accuracy of transperineal (translabial) ultrasound in PVR measurement [49] has been researched and found to be almost identical to that of transvaginal ultrasound [44]. This modality is already used widely in urogynecology [40], with perhaps less specialized probes than what is used with transvaginal or transrectal ultrasound.

Doppler Planimetry

This alternate form of abdominal ultrasound has gained popularity in measuring PVRs. Commercial application had started in 1986 [50] with an early report in 1996 [51]. The systems are small and portable with the technique for use quickly learned. Cross-sectional planes of the bladder are measured at 15° angular increments with a computer software constructing a 3D model of the bladder from which volume is determined. This form of PVR assessment has been shown to be accurate within 15% of bladder volumes as measured by a urethral catheter within the range of 0–999 mL [50,51]. Reported limitations on its use are serious abdominal scars, uterine prolapse, and pregnancy [51,52] with false positives in cases of pelvic cysts [50] and at times hematomas.

Overall correlation of more recent models of Doppler planimetry the BME-150A (S & D Medicare Co., Seoul, Korea) and BladderScan BVI 3000 (Diagnostic Ultrasound Co., Bothell, WA) with catheterized bladder volumes (12 FG latex rubber urethral catheter) were 0.92 and 0.94, respectively, with a mean difference from true residual volume of 7.8 and 3.6 mL [53]. While both scanners were reported [53] to have good accuracy at low bladder volumes, like previous studies, exact sensitivities and accuracies for volumes under 100 mL have not been reported. Both types of bladder scanners do not have the other applications of conventional transabdominal, transvaginal, and transperineal ultrasound.

PVR Measurement by Other Methods

Not discussed here are those other possible methods of PVR assessment such as abdominal palpation and bimanual pelvic examination, which are imprecise. Radiology and radionucleotide scans have not gained favor as these techniques are more invasive, carry additional risks, and are also impractical in the settings outlined.

NORMAL AND ABNORMAL POSTVOID RESIDUALS AND URINARY RETENTION

PVRs in Asymptomatic Women

Using transvaginal ultrasound [46] within 60 seconds of micturition, the upper limit of normal PVR (95th centile) is 30 mL. In a study with measurement delayed to up to 10 minutes, an upper limit of normal of 100 mL has been quoted [54].

PVRs in Symptomatic Women

Using transvaginal ultrasound [31,47], the upper limit of normal (87th centile) is 30 mL. Other studies quote higher figures of 50 mL [55], 100 mL [56], and 150 mL [57]. All of the latter studies [55–57] used urethral catheterization with the postmicturitional delay (1) of up to 10 minutes or (2) untimed [55,57] in PVR measurement.

Prevalence of Immediate PVRs in Symptomatic Women

In a recent study of 1140 women presenting with symptoms of pelvic floor dysfunction [47], Haylen et al. showed that the prevalence of the different immediate (measured by transvaginal ultrasound within 60 seconds of voiding) PVRs were *0–10 mL, 76%; 11–30 mL, 5%; 31–50 mL, 15%; 51–100 mL, 8%; >100 mL, 6%; and >200 mL, 2%.*

Combining the data from studies [31] and [47], *an upper limit of normal for PVRs in symptomatic women of 30 mL*, is suggested.

Associations of Immediate PVRs in Symptomatic Women [47]

The prevalence of PVRs more than 30 mL was shown to increase significantly with *age* ($p < 0.001$) and *higher grades of prolapse* ($p < 0.001$). A PVR more than 30 mL is associated with a significantly higher risk of *recurrent urinary tract infections* (UTI—$p < 0.001$). There is an inverse relationship between a PVR more than 30 mL and the symptom of stress incontinence ($p = 0.018$) and the final diagnosis of USI ($p < 0.001$).

Acute Retention of Urine

This is defined as a generally (but certainly not always) painful, palpable, or percussable bladder when the patient is unable to pass any urine when the bladder is full [1].

Chronic Retention of Urine

This is defined as a nonpainful bladder, where there is a chronic high PVR. From Haylen et al.'s study [32], 200 mL might be a reasonable "cutoff" for chronic retention.

FINAL DIAGNOSIS OF VOIDING DYSFUNCTION

Diagnosis of VD

As stated in the introduction, VD is defined as an abnormally slow and/or incomplete micturition. This implies an abnormally slow urine flow rate and/or an abnormally high PVR. There should be confirmation by repeat measurement. Pressure–flow studies are indicated to evaluate the cause of any VD. Some possible causes are (1) *detrusor underactivity, (2) acontractile detrusor, and (3) bladder outflow obstruction* [1].

Prevalence of VD

Depending on definition, VD has a prevalence of 14% [58] to 39% [59] and more than 40% [60] the middle figure, making it either the third or fourth most common urodynamic diagnosis (after USI, pelvic organ prolapse, and possibly DO).

Criteria for Diagnosis of Voiding Dysfunction

The only validated criteria to date are (1) a urine flow rate under the 10th centile of the Liverpool nomogram and/or (2) an immediate PVR more than 30 mL. Alternate suggested criteria of a PVR more than 50 mL and a maximum urine flow rate under 15 mL/min require validation. More studies are required employing PVR criteria by urethral catheterization.

Associations of the Diagnosis of Voiding Dysfunction

The study of Haylen et al. [59] determined the following associations using the validated criteria in the earlier section. VD-1 uses the maximum urine flow rate; VD-2 uses the average urine flow rate.

- *Age*: There was a significant increase in the prevalence of VD with age (VD-1, VD-2: $p < 0.001$).
- *Parity*: There was a lesser but still significant increase with parity (VD-1, $p = 0.010$; VD-2, $p = 0.014$).
- *Presenting symptoms*: Symptoms of VD ($p < 0.001$) and prolapse ($p < 0.001$) were significantly linked to VD-1, VD-2 with the symptom ($p < 0.001$) and sign ($p < 0.001$) of stress incontinence significantly linked to NON VD-1, NON VD-2 (absence of VD).
- *Prior hysterectomy*: There was a significant relationship of VD to prior hysterectomy (VD-1, $p = 0.006$; VD-2, $p = 0.053$) and prior continence surgery (VD-1, $p = 0.008$; VD-2, $p = 0.010$) respectively. There was a greater increase in VD-1, VD-2 with vaginal hysterectomy compared with abdominal hysterectomy but the difference didn't reach significance.

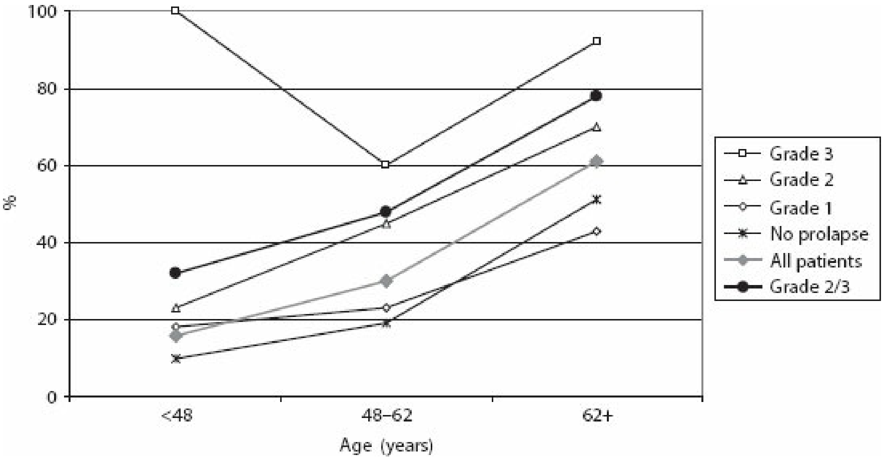

Figure 53.9 The relationship of VD-1 to age for (1) all patients, (2) patients with grade 0 prolapse (final diagnosis), (3) patients with grade 1 prolapse, (4) patients with grade 2 prolapse, and (5) patients with grade 3 prolapse.

- *Menopause*: Data initially showed that menopausal women on combined estrogen/progesterone therapy had significantly less VD than those not taking HRT. However, this effect was lost when age was taken into account.
- *Prolapse*: There is a significant relationship of VD to increasing grades of uterine prolapse, anterior vaginal wall (cystocoele), posterior vaginal wall (rectocele), and vaginal vault (enterocoele), respectively ($p < 0.001$ for VD-1 and VD-2 for all types of prolapse). Much of the relationship would be due to a PVR rather than a urine flow rate effect.
- *Retroverted uterus*: The relationship between the retroverted uterus and VD was nonsignificant ($p = 0.250$).

Figure 53.9 shows the relationship of VD-1 to age for (1) all patients, (2) patients with grade 0 prolapse (final diagnosis), (3) patients with grade 1 prolapse, (4) patients with grade 2 prolapse, and (5) patients with grade 3 (3–4) prolapse.

- *Recurrent UTIs*: There was no significant relationship between voiding difficulty (VD-1 [$p = 0.213$], VD-2 [$p = 0.213$]) and recurrent UTI. The strong relationship of PVRs and recurrent UTI noted earlier is not continued when urine flow rates are added to make the diagnosis of VD (urine flow rates appearing to have no significant association with recurrent UTI).

INDICATIONS TO SCREEN FOR VOIDING DYSFUNCTION

Uroflowmetry and PVR measurement should be regarded as an appropriate screening test for VD in all women with symptoms of pelvic floor dysfunction.

Abnormal urine flow studies in female patients are less common than in male patients. This is because in the male patient a high proportion of lower urinary tract problems are related to outflow obstruction. In the female, the incidence of outflow obstruction is low, whereas the incidence of incontinence and associated abnormalities of bladder behavior is high.

Urine flow studies and PVR are preliminary to cystometry that is necessary to define the urodynamic abnormality responsible for the symptom complex of frequency, nocturia, urgency, and urge incontinence. Anticholinergic medications will exacerbate any tendency toward urinary retention in patients with the combined diagnoses of DO and VD.

Urine flow studies and a PVR are an important preoperative investigation in women awaiting surgery USI. Assuming USI has been urodynamically proven, a normal urine flow rate and PVR reassure the surgeon that long-term VD is much less likely to follow the operation to cure the stress incontinence. Since effective surgery usually results in an increase in urethral resistance, in women with poor preoperative flow rates, incomplete emptying or even persistent failure to void may follow surgery [60]. Therefore, urine flow studies, with or without pressure flow studies, are to be recommended before surgery. An interrupted flow is associated with delayed postoperative voiding after suburethral tapes [61]. Voiding cystometry, as noted, is required to definitively diagnose bladder outflow obstruction.

Voiding problems in patients with neuropathic lower urinary tract dysfunction consists of three main types. Patients may experience incontinence as a result of bladder overactivity. The main problem may be the failure to empty the bladder because of a poorly sustained detrusor contraction. Detrusor sphincter dyssynergia may prevent an effective detrusor contraction from emptying the bladder with the consequent possible complications of recurrent infections or renal failure. Urine flow studies may suggest the origin of the problems experienced by this group of patients, although video–pressure–flow studies are desirable in almost every case.

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54 Pathophysiological Mechanisms of Chronic Pelvic Pain

Ursula Wesselmann

INTRODUCTION

Chronic pelvic pain syndromes belong to the category of visceral pain. Pelvic pain is a debilitating problem that can significantly impair the quality of life of a woman. Patients with chronic pelvic pain are usually evaluated and treated by gynecologists, urologists, gastroenterologists, and internists. Although these patients seek medical care because they are looking for help to alleviate their pelvic discomfort and pain, in clinical practice, much emphasis has been placed on finding a specific etiology and specific pathological markers for pelvic disease. These patients typically undergo many diagnostic tests and procedures. However, often the examination and workup remain unrevealing and no specific cause of the pain can be identified. In these cases, it is important to recognize not only that pain is a symptom of pelvic disease but also that the patient is suffering from a chronic pelvic pain syndrome, where "pain" is the prominent symptom of the chronic visceral pain syndrome.

This chapter will focus on the neurobiology of chronic nonmalignant pelvic pain, a chronic visceral pain syndrome. Knowledge of the neurophysiological characteristics of visceral pain will guide the physician in making a diagnosis of chronic pelvic pain and in differentiating it from the lump diagnosis of idiopathic pain [1]. A basic understanding of neurobiology is paramount to gain further insights into the mechanisms of the pelvic pain disorders and to develop effective clinical management strategies for patients presenting with these syndromes.

DEFINITIONS AND TAXONOMY OF CHRONIC PELVIC PAIN

Definitions are important if a body of reliable information, which will eventually lead to a better understanding of the pathophysiology of chronic pelvic pain, is to be built up in scientific literature [2]. At present, one of the major problems of research into chronic pelvic pain is the lack of agreed definitions, which would allow comparison between studies. On the other hand, the lack of understanding of the pathophysiological mechanisms of the pelvic pain syndromes makes it difficult to decide on criteria to define chronic pelvic pain conditions.

There is no generally accepted definition of chronic pelvic pain. Much debate over the classification of chronic pelvic pain has occurred, is ongoing, and will occur in the future. The International Association for the Study of Pain (IASP) initially defined chronic pelvic pain without obvious pathology as chronic or recurrent pelvic pain that apparently has a gynecological origin but for which no definitive lesion or cause is found [3]. However, this IASP definition for pelvic pain has not been widely used in the literature [4]. This definition implied the absence of pathology, which might not necessarily be the case, and it also excluded cases where pathology is present although not necessarily the cause of pain. In fact, the relationship of pain to the presence of pathology is often unclear in women with chronic pelvic pain.

The IASP has recently introduced an updated visceral pain taxonomy.*

The new IASP taxonomy defines chronic pelvic pain as chronic or persistent pain perceived in structures related to the pelvis of either men or women and explicitly recognizes that chronic pelvic pain is often associated with negative cognitive, behavioral, sexual, and emotional consequences as well as with symptoms suggestive of lower urinary tract, sexual, bowel, pelvic floor, or gynecological dysfunction.

Several medical societies have taken a lead in revising the taxonomy of chronic pelvic pain. The International Continence Society (ICS) has defined "pelvic pain syndrome" as the occurrence of persistent or recurrent episodic pelvic pain associated with symptoms suggestive of lower urinary tract, sexual, bowel, or gynecological dysfunction in the absence of proven infection or other obvious pathology in their 2002 consensus publication [5]. The ICS is currently preparing an updated consensus document regarding the ICS standards of terminology for symptoms, signs, diagnostic tests, and overall evaluation related to the nine domains of chronic pelvic pain in women and men: the lower urinary tract, female genital tract, male genital tract, gastrointestinal tract, musculoskeletal system, peripheral and central nervous system (CNS), psychological aspects, sexual dysfunction, and comorbidities.[†] The European Association of Urology has emphasized to move away from an organ-centered understanding of pain located in the pelvis to an understanding based on the mechanism of pain and integrating, as far as possible, psychological, social, and sexual dimensions of the problem [6]. In the gynecological literature, chronic pelvic pain is often referred to as pelvic pain in the same location for at least 6 months. The American College of Obstetricians and Gynecologists has proposed the following definition [7]: “Chronic pelvic pain is non-cyclic pelvic pain of 6 or more months’ duration that localizes to the anatomic pelvis, anterior abdominal wall at or below the umbilicus, the lumbosacral back, or the buttocks and is of sufficient severity to cause functional disability or lead to medical care. A lack of physical findings does not negate the significance of a patient’s pain, and normal examination results do not preclude the possibility of finding pelvic pathology.”

EPIDEMIOLOGY OF CHRONIC PELVIC PAIN

Chronic pelvic pain is a common condition. Epidemiological data from the United States showed that 14.7% of women in their reproductive years reported chronic pelvic pain [8]. Extrapolating to the total female population gave an estimated 9.2 million chronic pelvic pain sufferers in the United States alone. Analysis of a large primary care database from the United Kingdom demonstrated that the annual prevalence rate of chronic pelvic pain in women is 38/1000, which is comparable to the prevalence rate of asthma [9]. Diagnoses related to the urinary or gastrointestinal tracts were more common than gynecological causes [10]. Irritable bowel syndrome (IBS) accounts for 12% of primary care visits and 28% of gastroenterological practice [11]. While prevalence estimates vary widely, it has been suggested that somewhere between 450,000 [12] and one million people [13] in the United States suffer from interstitial cystitis/bladder pain syndrome (IC/BPS). Using the Nurses’ Health Study (NHS) I and II cohort as a study population, the prevalence of IC/BPS in NHS II was reported as 67/100,000 and in NHS I as 52/100,000 [14]. The Rand IC/BPS Epidemiology Study, a population-based symptom prevalence estimate study in adult females in the United States, concluded that there are 3.3–7.9 million women age 18 and older in the United States with IC/BPS; however, only 9.7% of these women reported being assigned a diagnosis of IC/BPS [15]. Female predominance of IC/BPS of about 5:1 or greater has been reported in previous studies, but a recent study showed that the prevalence of IC/BPS symptoms in men approaches that in women [16], raising the concern that this condition may be underdiagnosed and undertreated in men.

A recent WHO systematic review of the prevalence of chronic pelvic pain assessing the worldwide literature found that the rate for dysmenorrhea was 16.8%–81%, for dyspareunia 8%–21.8%, and for noncyclic pelvic pain 2.1%–24% [17]. Not surprisingly, the study found that there were few studies on chronic pelvic pain from less developed countries and the variation of rates of chronic pelvic pain worldwide was due to variable study quality. Importantly, wherever valid data were available, a high disease burden of pelvic pain was documented. Despite a high prevalence of pain, many women never had the condition diagnosed [18]. Populations at risk of having chronic pelvic pain seem to be women with a history of pelvic inflammatory disease, endometriosis, IC, IBS, obstetric history, previous abdominopelvic surgery, musculoskeletal disorders, and physical and sexual abuse [7].

INNERVATION OF THE PELVIS

Over the last 20 years, the basic neurobiology of the pelvis, despite the complexity of this region of the body, has come to be a reasonably well-developed discipline [19,20]. This section provides an overview of the innervation of the pelvis, which is a prerequisite to understanding the functional mechanisms that might play a role in the neuropathology of chronic pelvic pain. It is important to note that this summary attempts to derive as much information as possible from investigations involving humans although some generalizations are necessarily taken from animal studies, recognizing that much research in this field is in its infancy.

In general, the pelvis and the pelvic floor are innervated by both divisions of the autonomic nervous system (the sympathetic and parasympathetic), as well as by the somatic and sensory nervous systems.

In a discrete broad anatomic view, dual projections from the thoracolumbar and sacral segments of the spinal cord carry out this innervation, converging primarily into peripheral neuronal plexuses before distributing nerve fibers throughout the pelvis (Figure 54.1). Interactive neuronal pathways routing from higher origins in the brain through the spinal cord add to the complexity of neuronal regulation in the pelvis.

The nomenclature of the various plexuses, ganglia, and nerves in the pelvic cavity [21] is varied and sometimes confusing, presenting designations from both Nomina Anatomica (1977) and clinical usage [22]. In this chapter, the anatomic nomenclature is provided, and the clinical usage is given in brackets: superior hypogastric plexus (presacral nerve), hypogastric plexus (hypogastric nerve), inferior hypogastric plexus (pelvic plexus), and pelvic splanchnic nerve (pelvic nerve).

Within the pelvis, the inferior hypogastric plexus (pelvic plexus) is regarded as the major neuronal integrative center. This plexus is located retroperitoneally adjacent to each lateral aspect of the rectum, with interconnections between the left and right inferior hypogastric plexuses at the posterior aspect of the rectum. It innervates multiple pelvic organs, including the urinary bladder, proximal urethra, distal ureter, rectum, and internal anal sphincter, as well as genital and reproductive tract structures [23]. The anterior part of the inferior hypogastric plexus, associated with the distal extent of the hypogastric plexus (hypogastric nerve), is referred to as the paracervical ganglia in females [24].

The inferior hypogastric plexus receives sympathetic and parasympathetic input. Sympathetic nerves originate in the thoracolumbar segments of the spinal cord (T10–L2) and condense into the superior hypogastric plexus (presacral nerve) located just inferior to the aortic bifurcation. Preganglionic efferents originate largely in the intermediolateral cell column, whereas afferents have their cell bodies located in the dorsal root ganglia of these segments. Nerve fibers project from the superior hypogastric plexus as paired hypogastric plexuses (hypogastric nerves) and fuse distally before diverging bilaterally into branches destined for the inferior hypogastric plexuses. Additional sympathetic innervation to pelvic organs may involve preganglionic nerves, which synapse on postganglionic nerves originating in sympathetic chain ganglia; these postganglionic nerves join sacral nerves and course to their destinations via pelvic somatic neuronal pathways [25]. Parasympathetic preganglionic nerve efferents are thought to arise from cell bodies of the sacral parasympathetic nucleus located in the sacral spinal cord (S2–S4) and fuse as the pelvic splanchnic nerve (pelvic nerve) before entering the inferior hypogastric plexus [26]. Parasympathetic afferents have cell bodies located in the S2–S4 dorsal root ganglia and course also within the pelvic splanchnic nerve. In addition to its parasympathetic efferent and afferent component, the pelvic splanchnic nerve also receives postganglionic axons from the caudal sympathetic chain ganglia [27].

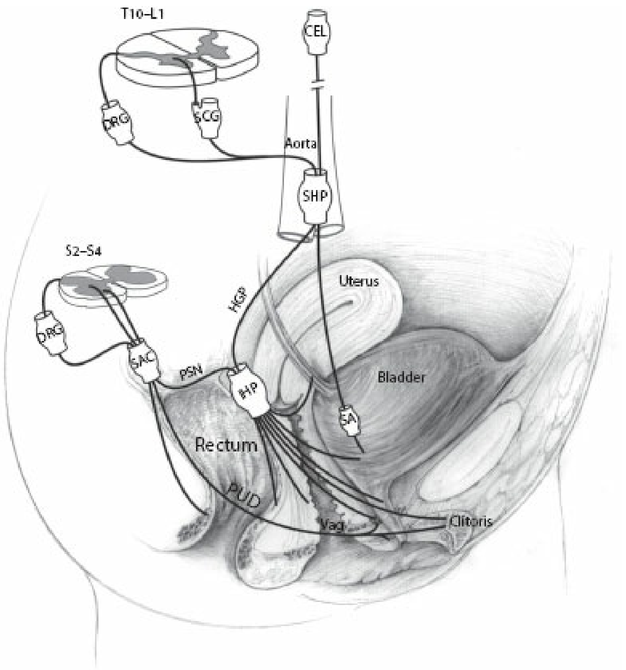

Figure 54.1 Innervation of the pelvic area in females. Although this diagram attempts to show the innervation in humans, much of the anatomic information is derived from animal data. *Abbreviations*: CEL, celiac plexus; DRG, dorsal root ganglion; HGP, hypogastric plexus; IHP, inferior hypogastric plexus; PSN, pelvic splanchnic nerve; PUD, pudendal nerve; SA, short adrenergic projections; SAC, sacral plexus; SCG, sympathetic chain ganglion; SHP, superior hypogastric plexus. (Reproduced from Wesselmann U et al., *Pain*, 73, 269, 1997. With permission of the International Association for the Study of Pain® (IASP). The figure may not be reproduced for any other purpose without permission.)

Somatic efferent and afferent innervation to the pelvis is generally understood to involve the sacral nerve roots (S2–S4) and their ramifications. Somatic efferents arise within Onuf's nucleus situated in the ventral horn of the S2–S4 spinal cord, and afferents reach the dorsal horn with their cell bodies in the dorsal root ganglia of these segments [28]. Central projections of somatic afferents overlap with pelvic nerve afferents within the spinal cord, which theoretically allows coordination of somatic and visceral motor activity [25]. The sacral nerve roots emerge from the spinal cord forming the sacral plexus, from which the pudendal nerve diverges (S2–S3). The pudendal nerve also receives postganglionic axons from the caudal sympathetic chain ganglia.

Nociception and pain arising from within the pelvis and pelvic floor involve diverse neuronal mechanisms. In general, sensations from the pelvic viscera are conveyed within the sacral afferent parasympathetic system, with a far lesser afferent supply from thoracolumbar sympathetic origins [29]. Receptive fields in the perineum are understood to be carried out primarily by sensory–motor discharges associated with pudendal nerve afferents [29,30]. While the interactions of sensory afferents are quite complex, likely possibilities by which these pathways exert effects on autonomic efferent function include mediatory effects on spinal cord reflexes and modulatory effects on efferent release in peripheral autonomic ganglia and in peripheral organs. These neural structures in the periphery comprise the first of numerous relays of sensory neurons, which transmit painful sensations from the abdominal/pelvic cavity to the brain.

Traditionally, it was thought that ascending pathways for visceral and other types of pain were mainly the spinothalamic and spinoreticular tracts. However, three previously undescribed pathways that carry visceral nociceptive information have been discovered: the dorsal column pathway, the spino(trigemino)-parabrachio-amygdaloid pathway, and the spinohypothalamic pathway [31]. Specifically, the dorsal column pathways play a key role in the processing of pelvic pain, and neurosurgeons have successfully used punctate midline myelotomy to relieve pelvic pain due to cancer [32]. In addition, descending facilitatory influences may contribute to the development of maintenance of hyperalgesia, thus contributing to the development of chronic pelvic pain [33].

DIFFERENCES BETWEEN VISCERAL AND SOMATIC PAIN

Persistent pain of visceral origin is a much greater clinical problem than that from the skin, but the overwhelming focus of experimental work on pain mechanisms relates to cutaneous sensation. Until relatively recently, it was often assumed that concepts derived from cutaneous studies could be transferred to the visceral domain. However, there are several reasons to believe that the neural mechanisms involved in pain and hyperalgesia of the skin are different from the mechanisms involved in painful sensations from the viscera [34,35]. In contrast to somatic pain, visceral pain cannot be evoked from all viscera and is not always linked to visceral tissue injury (see the "Visceral Nociceptors and Sensitization" section). In addition, visceral pain tends to be diffused and poorly localized, whereas somatic pain can be localized very precisely. This is due to the fact that the visceral innervation is not as dense as the somatic innervation and that there is an extensive divergence in the CNS. Further, visceral pain can be referred to other visceral structures and somatic structures of the same segmental level (see "Referred Visceral Pain Mechanisms").

Visceral Nociceptors and Sensitization

The existence of visceral nociceptors has been debated for a long time. This is partially due to the difficulty of defining and applying physiologically relevant noxious stimuli to the viscera. Research in animal models of visceral pain has shown that several types of sensory receptor exist in most internal organs and that different pain states are mediated by different neurophysiological mechanisms [36]. Acute, brief visceral pain appears to be triggered initially by the activation of high-threshold visceral afferents and by the high-frequency bursts that these stimuli evoke in intensity-coding afferent fibers, which are afferents with a range of responsiveness in the innocuous and noxious ranges. However, more prolonged forms of visceral stimulation, including those leading to hypoxia and inflammation of the tissue, result in sensitization of high-threshold receptors and the bringing into play of previously unresponsive afferent fibers (silent nociceptors; see below). This increased afferent activity enhances the excitability of central neurons and leads to the development of persistent pain states. In addition, a special class of C-fiber nociceptors—mechano-insensitive or "silent" nociceptors—has been found in nearly all tissues. They were first described in an animal model of experimental arthritis [37] and subsequently in animal models of visceral pain [38]. Silent afferents are activated only in the presence of tissue damage or inflammation. Following release of injury products, these previously silent receptors are activated by a wide range of thermal and mechanical stimuli and may also have a background discharge.

Referred Visceral Pain Mechanisms

There are two components of visceral pain, both of which were described more than 100 years ago [39]: "true visceral pain" (deep visceral pain arising from inside the body) and "referred visceral pain" (pain that is referred to segmentally related somatic and also other visceral structures). Secondary hyperalgesia usually develops at the referred site [40]. A number of explanations have been offered for the existence of referred pain [35]. An initial model for interpreting referred pain was based on the idea of viscerosomatic convergence occurring in primary afferent fibers, with multiple branches innervating both viscera and somatic structures. This hypothesis is unlikely since few branching axons have been found in animal studies. In addition, the hypothesis does not explain the time delay in the evolution of referred pain.

Another suggested mechanism for referred pain is that visceral and somatic primary neurons converge onto common spinal neurons. This is the convergence–projection theory. There is considerable experimental evidence for this hypothesis. It offers a ready explanation for the segmental nature of referred pain but does not address explicitly the issue of hyperalgesia in the referred zone. To interpret "referred pain with hyperalgesia," two main theories have been proposed, which are not mutually exclusive. The first is known as the convergence–facilitation theory. It proposes that the abnormal visceral input would produce an irritable focus in the relative spinal cord segment, thus facilitating messages from somatic structures. The second theory postulates that the visceral afferent barrage induces the activation of a reflex arc whose afferent branch is presented by visceral afferent fibers and the efferent branch by somatic efferents and sympathetic efferents toward the somatic structures (muscle, subcutis, and skin). The efferent impulses toward the periphery would then sensitize nociceptors in the parietal tissues of the referred area, thus resulting in the phenomenon of hyperalgesia.

When examining and treating a woman with chronic pelvic pain, it is important to consider both aspects of the pain syndrome (true and referred pain), including the pain deep in the pelvic cavity and pain referred to somatic structures (lower back and legs) and other visceral organs. Considering the concept of referred visceral pain will allow the physician to look at the global picture of visceral dysfunction, rather than "chasing" one aspect of the visceral pain syndrome out of context.

COMORBIDITIES AND PELVIC PAIN

Careful clinical history and examination show that patients with pelvic pain often suffer from "more than one pain." These clinical observations are supported by epidemiological studies. Data from the Interstitial Cystitis Data Base Study [41] show that 93.6% of the patients enrolled with a diagnosis of IC reported having some pain in some part of their body. Of the patients having pain, 80.4%, 73.8%, 65.7%, and 51.5% reported having pain in their lower abdomen, urethra, lower back, and vaginal area, respectively. There is substantial overlap observed between chronic pelvic pain and other abdominal and urogenital symptoms [18,42,43]. These observations could be explained pathophysiologically by referred visceral pain mechanisms to other visceral and somatic areas with overlapping spinal cord projections. In addition, there is increasing clinical and epidemiological evidence of the co-occurrence of chronic pelvic pain conditions with chronic pain syndromes in other "nonpelvic" body areas (e.g., fibromyalgia), raising the question of systemic alterations of pain modulatory mechanisms in this patient population [44].

These epidemiological studies to assess comorbidities of chronic pelvic pain conditions require validated case definitions to identify the comorbid conditions in large populations, and the results of these studies depend on the range of comorbidities that are screened for. For example, vulvodynia in women is a pain comorbidity, which has only more recently been included in such efforts, probably because this body area is considered taboo [45–47].

Patients with IC/BPS typically present with fibromyalgia, chronic fatigue syndrome, IBS, temporomandibular disorder, migraine, chronic pelvic pain, vulvodynia, low back pain, sicca syndrome, allergies, asthma, depression, and anxiety [48]. Several studies have recently also confirmed the coexistence of endometriosis and IC/BPS, ranging from 16% to 78% [49]. Epidemiological studies have demonstrated that the odds ratios for IC/BPS increases with increasing numbers of antecedent nonbladder syndromes [48,50]. The distribution of nonbladder syndrome types was skewed, with allergy overrepresented in those with few nonbladder syndromes, and the classic functional somatic syndromes of fibromyalgia, chronic fatigue syndrome, and IBS were overrepresented in those with many nonbladder syndromes [50]. A common theme to this group of comorbid disorders could be related to the autonomic nervous system, and indeed a recent study [51] identified a high level of autonomic dysfunction in subjects with IC/BPS including poor sleep function, Raynaud's-like symptoms, and orthostatic symptoms.

Thus, research efforts to elucidate the pathophysiological mechanisms of pelvic pain have recently shifted from an organ-based approach to a more global approach (http://www3.niddk.nih.gov/fund/other/ http://www.mappnetwork.org/).

PHARMACOLOGICAL ASPECTS

Despite the fact that it is a very common chronic pain syndrome, very little is known about effective pharmacological treatment for chronic pelvic pain [52–55]. Pharmacological pain management is empirical only. Often, drugs are used to alleviate chronic pelvic pain, which have shown efficacy for the treatment of chronic neuropathic pain states [54]. Very few drugs have been specifically approved for the treatment of chronic pelvic pain syndromes. An example is Elmiron (pentosan polysulfate sodium), which is indicated for the relief of bladder pain or discomfort associated with IC/BPS. Controlled clinical trials are desperately needed to design improved pharmacological treatment strategies.

The principal guidelines for pharmacological pain management for chronic pelvic pain are similar to the pharmacological treatment of other chronic pain states. Although clinical trials and case reports on the pharmacological management of chronic pain syndromes provide general guidelines as to which drug to choose, currently we have no method to predict which drug is most likely to alleviate pain in a given patient. The goal of pharmacotherapy is to find a medication that provides significant pain relief with minimal side effects. It is important that the patient understands the limitations of this “trial-and-error” method of prescribing drugs. Adequate trials should be performed for each drug prescribed and only one drug should be titrated at a time, otherwise it is not possible to assess the effects of a certain drug on pain scores. The starting dose should always be the smallest available and titration should occur at frequent intervals, guided by pain scores, and side effects. This requires frequent contact between the patient and the pain clinic during the titration period. It is important for the patient and the physician to understand that some side effects actually improve as the patient continues to take the drug for several weeks. If these side effects are not intolerable, the patient should be guided through this period.

Since epidemiological data have confirmed the widespread existence of chronic pelvic pain in the female population in the last 20 years, there is growing interest in the pharmaceutical industry to expand basic science and clinical research efforts for this underserved patient population. Realizing the sometimes marked differences in the expression and function of receptors in visceral and somatic pathways has led to new pharmacological research explorations of both new and previously overlooked potential therapeutic targets [55,56], which might provide new avenues for treating chronic pelvic pain in the future.

Several receptor targets have been identified in the pelvis and urogenital tract, which might play a role in pelvic pain [56]. The mammalian transient receptor potential channels play a role in sensing mechanisms throughout the body, including the pelvis. Pharmacological interventions targeting these ion channels might provide a new opportunity for painful bladder syndrome and other chronic pelvic pain syndromes [55,57–61]. Prostaglandins are synthesized in response to tissue injury by cyclooxygenase. They sensitize sensory fibers to mechanical and thermal stimuli and contribute to spinal processing of visceral pain [62]. Cytokines and other neuroactive substances associated with inflammation also have a clear role in visceral inflammatory pain states. *N*-methyl-d-aspartate (NMDA) receptors are expressed in primary afferents and in dorsal horn neurons. Intrathecal application of NMDA and non-NMDA receptor antagonists significantly attenuate visceral hypersensitivity in behavioral models, and spinal application of NMDA agonists increases the magnitude and duration of visceral pain responses [63,64]. ATP is released from all tissue types when there is tissue damage. In visceral tissue, ATP binds ionotropic purinergic (P2X) receptors. P2X3 receptors are specific for nociceptors and P2X receptor antagonists attenuate colonic afferent activity [65–67]. ATP, released from the bladder urothelium, binds P2X3 receptors on bladder afferents increasing bladder contraction and micturition [68,69]. This also increases bladder afferent activity resulting in pain. P2X3 knockout mice have urinary bladder hyporeflexia with increased voiding volume and decreased voiding frequency and decreased inflammatory pain [70,71]. The corticotropin-releasing factor (CRF) receptor is involved in the stress response, activating the hypothalamic–pituitary–adrenal (HPA) and sympathoadrenal axes. Women with chronic pelvic pain demonstrate HPA axis alterations similar to patients with other stress-related bodily disorders [72]. Enhanced pelvic responses to stressors have been demonstrated in CRF-overexpressing mice [73]. Opioids constitute a major class of analgesics to treat visceral pain. Nociceptin–orphanin receptor agonists have been used in preclinical models of pelvic pain with promising potential for therapeutic effects. This antihyperalgesic effect does not involve a CNS site of action [74]. In summary, modulation of visceral nociceptive pathways can occur at peripheral, spinal, and supraspinal sites. There is a concerted effort underway to develop target-specific visceral analgesics for the treatment of chronic pelvic pain [75]. However, based on the recognition that chronic pelvic is a heterogeneous group of conditions and learning from previously failed clinical trials, the discovery of a single target for the treatment of chronic pelvic pain is unlikely. A key issue for the success of future clinical trials will be improved patient phenotyping to identify subgroups of patients with chronic pelvic pain, based on aspects such as clinical symptoms, quantitative sensory testing parameters, biomarkers, and comorbid conditions.

CLINICAL IMPLICATIONS

Treating patients with chronic pelvic pain remains a significant clinical challenge. Given the many comorbidities observed in this patient population, it will be important to identify which patients will be at risk to develop other chronic pain syndromes and to design strategies for early intervention. As the pathophysiological mechanisms of visceral pain explored in basic science research provide an explanation for some of the clinical phenomena observed in patients, additional, revived, and new concepts of chronic pelvic pain have emerged:

1. A spectrum of different insults might lead to chronic pelvic pain.
2. Different underlying pathogenic pain mechanisms may require different pain treatment strategies for patients presenting with pelvic pain.
3. Multiple different pathogenic pain mechanisms may coexist in the same patient presenting with chronic pelvic pain, requiring several different pain treatment strategies (perhaps concomitantly) to treat visceral pain successfully [53].

These are the very exciting times for the field of pelvic pain, since pelvic nociceptive pathways are being identified and pharmacological compounds are being discovered to modulate visceral nociceptive pathways. Clinical guidelines have been developed in several countries over the last 15 years proposing an integrated approach to chronic pelvic pain syndromes by a multidisciplinary team of health-care providers [6,56,76,77]. The need for a multidisciplinary team approach to pelvic pain syndromes will require changes in the health-care system to allow a coordinated involvement of multiple teams, beyond the historic boundaries of medical subspecialties and of primary and secondary care. This has recently been address in the British Pain Society's pelvic pain patient pathway map [78] and in the pain report of the Institute of Medicine in the United States, issued at the request of the Congress as part of President Obama's health reform legislation [79].

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55 Bladder Pain Syndrome/Interstitial Cystitis

Amina Douglas, Matthew Parsons, and Philip Toozs-Hobson

INTRODUCTION

Bladder pain syndrome/interstitial cystitis (BPS/IC) is a debilitating, chronic disease that has a negative impact on patient's quality of life. The etiology of the disease is unknown and it remains a diagnosis of exclusion. It is characterized by pelvic, bladder, and urethral pain associated with irritative voiding symptoms including urinary frequency, urgency, and nocturia.

The nomenclature and definition of the disease has changed over the years. The symptomatology of the BPS was first described in 1808 by Philip Physick, an American physician from Philadelphia. He described a disease of bladder pain not associated with the finding of bladder stones. In 1915, Guy Hunner reported Hunner's ulcers. On cystoscopy, he described seeing scarred-looking areas surrounded by one or more areas of hyperemia that bleed on touch in the bladders of women with a long history of bladder symptoms for which no cause had been found [15]. The term "interstitial cystitis" was used to describe patients with bladder pain and typical cystoscopic findings such as glomerulations and Hunner's ulcers. In 1987, the National Institute of Diabetes and Digestive and Kidney Disease (NIDDK) published criteria for research purposes to define IC [11]. These criteria have little clinical application. They are restrictive and when applied clinically can lead to missed diagnoses of IC in many patients. The International Continence Society later developed the term "painful bladder syndrome" to describe the clinical condition. Its definition did not include abnormal cystoscopic findings [2]. The condition was renamed "bladder pain syndrome" in 2008 by the European Society for the Study of Interstitial Cystitis. More recently, the International Consultation on Incontinence [14] revised the definition of BPS. It now defines the condition as chronic pelvic pain, pressure, or discomfort perceived to be related to the urinary bladder accompanied by at least one other urinary symptom: persistent urgency or urinary frequency.

INCIDENCE

Women between the ages of 40 and 60 years are the most commonly affected. The condition occurs in both females and males but has a 9:1 female predominance. It occurs most frequently in Caucasians. The reported prevalence of BPS/IC varies between populations and has changed with time. Berry et al. [5] reported the prevalence of BPS/IC to between 2.7% and 6.5% in American women. Nickel [24] reported prevalence ranging from 8 out of 100,000 in the Netherlands to 500 out of 100,000 in some parts of the United States. This variation is in part due to the lack of standardized diagnostic criteria for BPS/IC and the changes in the definition of the disease over time.

ETIOLOGY

Despite being first described over 100 years ago, the cause of BPS/IC remains unknown. The disease process is probably multifactorial with patients having one or more causative factors. Over the years, investigators have demonstrated specific pathologies that may contribute to the symptoms of the disease. As a result, several theories of the pathogenesis have been postulated and some are listed in the following texts.

Infection

Even when it was first described, infection was suspected as the cause of BPS/IC. BPS/IC has many hallmark symptoms of bacterial cystitis; however, urine analyses and urine culture demonstrate no evidence of infection [22]. It has been postulated that an initial bacterial infection may have been the cause of bladder damage causing the lasting symptoms of BPS/IC [9,54]. However, to date, no consistent organism has been isolated in the urine or bladder biopsy specimens of patients with BPS/IC.

Indeed, the NIDDK criteria and the International Consultation on Incontinence (ICI) [14] require infection to be excluded before a diagnosis of BPS/IC can be made.

Autoimmune Disorder

Studies have shown an association between BPS/IC and autoimmune disorders including Sjogren's syndrome [51], systemic lupus erythematosus [3], and also allergies. The evidence for this, however, has not always been consistent.

Mast Cells

Mast cells are multifunctional immune cells. They contain numerous vasoactive and proinflammatory substances such as histamine, prostaglandins, and tryptase. Many of these substances are contained within cytoplasmic granules. Mast cells are found within the bladder mucosa and detrusor muscle. Neuroimmune interaction involving mast cells in the bladder may explain the neuropathic pain seen in BPS/IC. Mast cells have a close spatial relation with nerves in the bladder. Activation of mast cells results in the release of mast cell granules. The release of inflammatory mediators from these granules results in neuronal sensitization, sensory nerve upregulation, neuropathic pain, and the release of neurotransmitters that further simulate mast cells. This vicious circle contributes to the chronic and painful symptoms associated with BPS/IC [46]. The increased number of mast cells and activation has been shown in some patients with BPS/IC [47,49]. However, increased numbers of mast cells have also been reported in patients with other diseases including endometriosis and irritable bowel syndrome [4,30]. The role of mast cells in the etiology of BPS/IC is still not clearly understood.

Vascular Abnormalities and Hypoxia

Abnormality in the bladder vasculature resulting in relative ischemia of the bladder has been suggested to be partly responsible for some of the symptoms of BPS/IC [42,44].

Dysfunctional Bladder Epithelium and Potassium Cycling

Parsons et al. [32] suggested that dysfunctional bladder epithelium resulting in abnormal (increased) bladder epithelial permeability is the cause of the symptoms of BPS/IC. In a healthy bladder, the transitional epithelium is relatively impermeable. A protective layer composed of glycosaminoglycans (GAGs) lines the urothelium. The GAG layer acts as a barrier rending the bladder epithelium impermeable to urinary solutes, which may be toxic to the bladder. Damage to this protective layer results in toxic solutes in particular potassium diffusing into the bladder, affecting the sensory nerves and injuring tissue. The theory of potassium cycling, developed from this, suggests that potassium diffuses into the bladder interstitium once the epithelium permeability is impaired. It depolarizes sensory nerve endings and muscles and leads to tissue injury. Parsons suggests that this pathophysiological process is responsible for the generation of symptoms of urgency and pain in patients with BPS/IC.

Parsons developed the potassium sensitivity test (PST) as an office-based diagnostic tool for BPS/IC in patients in whom the diagnosis was not clear on history alone. The test involved instillation of two separate solutions, sterile water and potassium chloride in the bladder of patients suspected of having BPS/IC. The PST is positive when a patient reacts preferentially to potassium versus water. PST tests for both the presence of bladder epithelial dysfunction and the hypothesis of potassium cycling. A patient with no symptoms who has a normal bladder epithelium would not be experiencing any symptoms when potassium is instilled, while a patient with impaired bladder epithelium will experience symptoms with potassium instillation [32]. The usefulness of PST has been debated and it is thought to be of low specificity and of questionable value in routine clinical practice [12].

CLINICAL FEATURES

Patients with BPS/IC typically complain of chronic pelvic pain. This may be associated with daytime as well as nighttime frequency, nocturia, and urgency. These symptoms occur in the absence of urinary tract infection. It is often said that suprapubic pain aggravated by bladder filling and relieved by voiding is classic of BPS/IC. However, this is not always the case. In some patients, the pain may be in the perineum, urethra, or vagina. The nature of the pain is also variable. It may be experienced as a sharp pain, as pressure, or as burning. The disease may be progressive but often presents in cycles of flares and remission. Flares may be provoked by a number of factors including sexual activity, hormonal fluctuations, and physical and emotional stress [31,37].

BPS/IC is a debilitating disease. It impairs quality of life and causes depression, sleep deprivation, and difficulties with sexual intercourse [25,50]. A close association has been reported between BPS/IC and other chronic conditions including irritable bowel syndrome, chronic fatigue syndrome, and fibromyalgia [1].

INVESTIGATION AND ASSESSMENT

BPS/IC remains a diagnosis of exclusion. Investigations performed are done to exclude other diseases that may account for the patient’s symptoms and assess the severity of BPS/IC.

A history should be taken to establish the duration of symptoms and elucidate if there are other associated symptoms that would suggest an alternative diagnosis. A previous history of bladder disease, pelvic surgery, or other medical illnesses including irritable bowel syndrome and autoimmune disease should also be established.

Pelvic Examination

Pelvic examination is often unhelpful in making the diagnosis of BPS/IC. The abdomen should be palpated to assess for bladder tenderness. Examination is often more helpful in excluding other conditions that can cause similar symptoms. Women who complain of vaginal or vulval pain should be examined with pain mapping of the vulval region and for tenderness in the urethra, bladder, and levator and adductor muscles of the pelvic floor [53].

Urine Studies

Urine culture is essential to exclude simple urinary tract infection as well as atypical infections caused by *Ureaplasma urealyticum*, *Mycoplasma hominis*, or *Chlamydia trachomatis*.

Cytology is recommended if hematuria is present or if there are risk factors for bladder cancer (smoking, age, family history, and occupational exposure to certain industrial chemicals such as aromatic amines). If there is sterile pyuria, culture for tuberculosis and fastidious organisms should be performed.

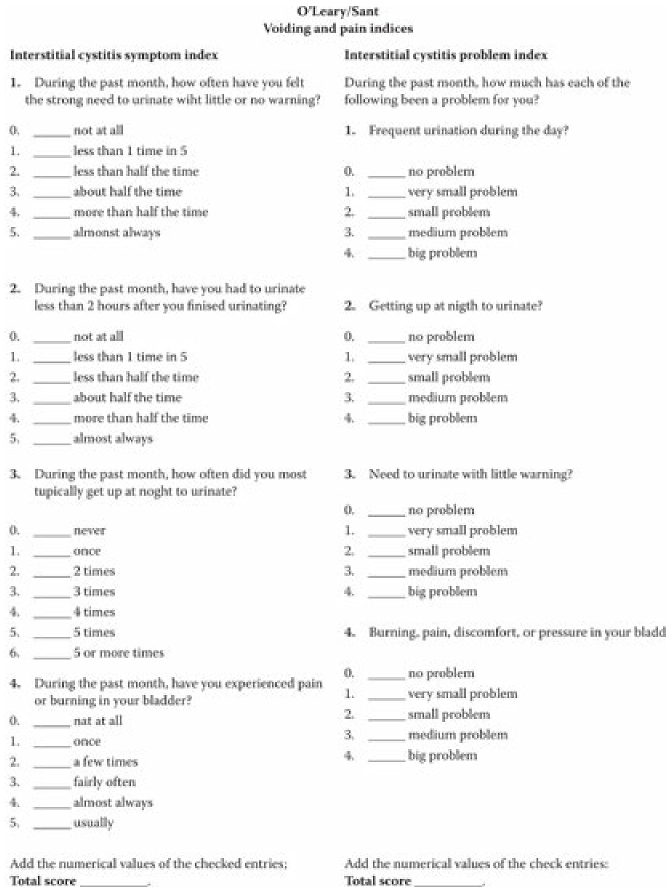
Questionnaires and Symptom Scales

Questionnaires are widely used for the evaluation of the severity of the patient’s symptoms and also to assess their progress. The ideal questionnaire is one which is brief and reliably distinguishes BPS/IC from other causes of the patient’s symptoms. There are three IC symptom questionnaires:

1. The University of Wisconsin IC scale
2. O’Leary–Sant symptom and problem index
3. Pelvic pain and urgency/frequency patient symptom scale (PUF questionnaire)

The University of Wisconsin IC scale has not been validated for use in identifying and diagnosing IC. It does, however, address some quality of life issues unlike the other two questionnaires and could therefore prove to be clinically useful.

The O’Leary–Sant and PUF questionnaires (Figures 55.1 and 55.2) are validated questionnaires completed by patients and are used to help identify patients with BPS/IC from those without the disorder. The O’Leary–Sant questionnaire was developed by focus groups and validated by administration to patients with IC and asymptomatic controls [18,28]. The O’Leary–Sant questionnaire focuses questions on symptoms of urgency and frequency and bladder-related pain. It does not, however, address the relationship between these symptoms and sexual activity or more general issues.



O'Leary/Sant
Voiding and pain indices

Interstitial cystitis symptom index

1. During the past month, how often have you felt the strong need to urinate wiht little or no warning?

0. ______ not at all
1. ______ less than 1 time in 5
2. ______ less than half the time
3. ______ about half the time
4. ______ more than half the time
5. ______ almonst always

2. During the past month, have you had to urinate less than 2 hours after you finised urinating?

0. ______ not at all
1. ______ less than 1 time in 5
2. ______ less than half the time
3. ______ about half the time
4. ______ more than half the time
5. ______ almost always

3. During the past month, how often did you most tupically get up at noght to urinate?

0. ______ never
1. ______ once
2. ______ 2 times
3. ______ 3 times
4. ______ 4 times
5. ______ 5 times
6. ______ 5 or more times

4. During the past month, have you experienced pain or burning in your bladder?

0. ______ nat at all
1. ______ once
2. ______ a few times
3. ______ fairly often
4. ______ almost always
5. ______ usually

Add the numerical values of the checked entries;
Total score __________.

Interstitial cystitis problem index

During the past month, how much has each of the following been a problem for you?

1. Frequent urination during the day?

0. ______ no problem
1. ______ very small problem
2. ______ small problem
3. ______ medium problem
4. ______ big problem

2. Getting up at nigth to urinate?

0. ______ no problem
1. ______ very small problem
2. ______ small problem
3. ______ medium problem
4. ______ big problem

3. Need to urinate with little warning?

0. ______ no problem
1. ______ very small problem
2. ______ small problem
3. ______ medium problem
4. ______ big problem

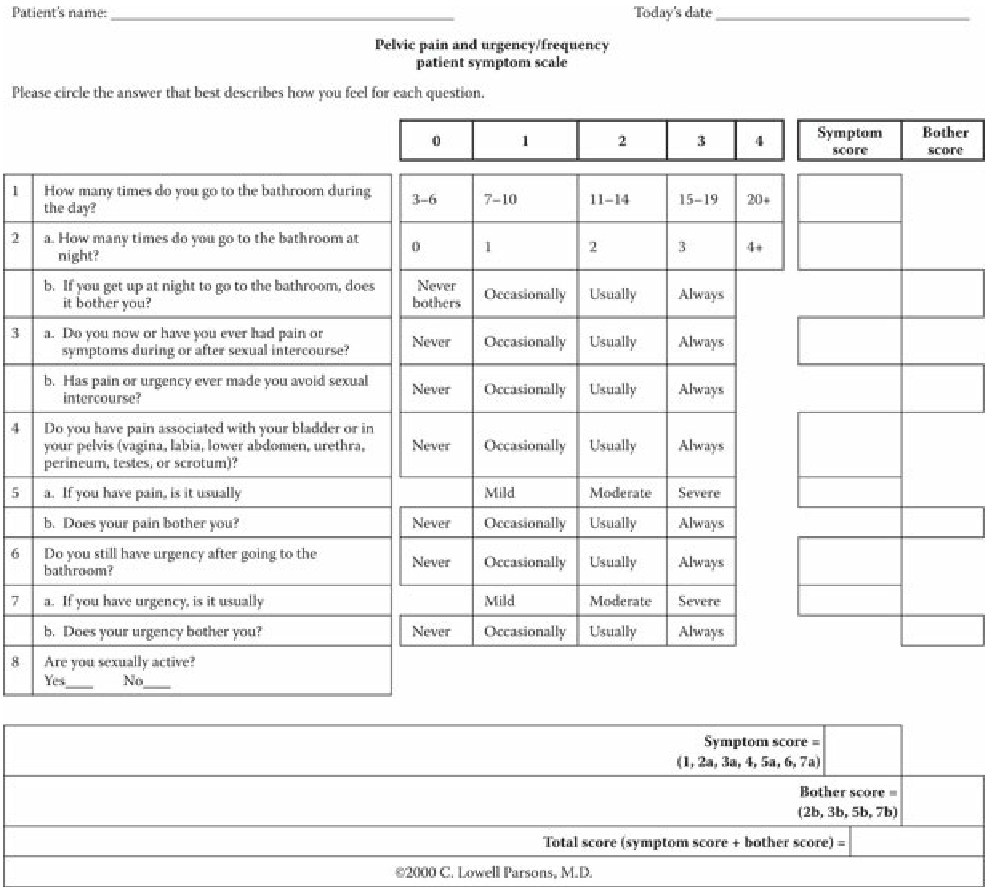
4. Burning, pain, discomfort, or pressure in your bladd

0. ______ no problem
1. ______ very small problem
2. ______ small problem
3. ______ medium problem
4. ______ big problem

Add the numerical values of the check entries:
Total score __________.

Figure 55.1 O'Leary–Sant questionnaire.

The PUF questionnaire was published more recently and was studied in large population of both gynecologic and urological patients [35]. The PUF questionnaire includes questions that address the wide range of symptoms that patients with this disorder may experience. It includes questions on frequency, urgency, and pain in both the bladder and pelvis and tries to assess the amount of bother caused to the patient by these symptoms. A study by Ref. [35], which utilized the PUF questionnaire, concluded that 23% of American females were affected by IC, and this has made many experts wary of its use.



Patient's name: ______________________ Today's date ______________

Pelvic pain and urgency/frequency
patient symptom scale

Please circle the answer that best describes how you feel for each question.

		0	1	2	3	4	Symptom score	Bother score
1	How many times do you go to the bathroom during the day?	3–6	7–10	11–14	15–19	20+		
2	a. How many times do you go to the bathroom at night?	0	1	2	3	4+		
	b. If you get up at night to go to the bathroom, does it bother you?	Never bothers	Occasionally	Usually	Always			
3	a. Do you now or have you ever had pain or symptoms during or after sexual intercourse?	Never	Occasionally	Usually	Always			
	b. Has pain or urgency ever made you avoid sexual intercourse?	Never	Occasionally	Usually	Always			
4	Do you have pain associated with your bladder or in your pelvis (vagina, labia, lower abdomen, urethra, perineum, testes, or scrotum)?	Never	Occasionally	Usually	Always			
5	a. If you have pain, is it usually		Mild	Moderate	Severe			
	b. Does your pain bother you?	Never	Occasionally	Usually	Always			
6	Do you still have urgency after going to the bathroom?	Never	Occasionally	Usually	Always			
7	a. If you have urgency, is it usually		Mild	Moderate	Severe			
	b. Does your urgency bother you?	Never	Occasionally	Usually	Always			
8	Are you sexually active? Yes____ No____							

Symptom score =
(1, 2a, 3a, 4, 5a, 6, 7a)

Bother score =
(2b, 3b, 5b, 7b)

Total score (symptom score + bother score) =

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Figure 55.2 Pelvic pain and urgency/frequency scale.

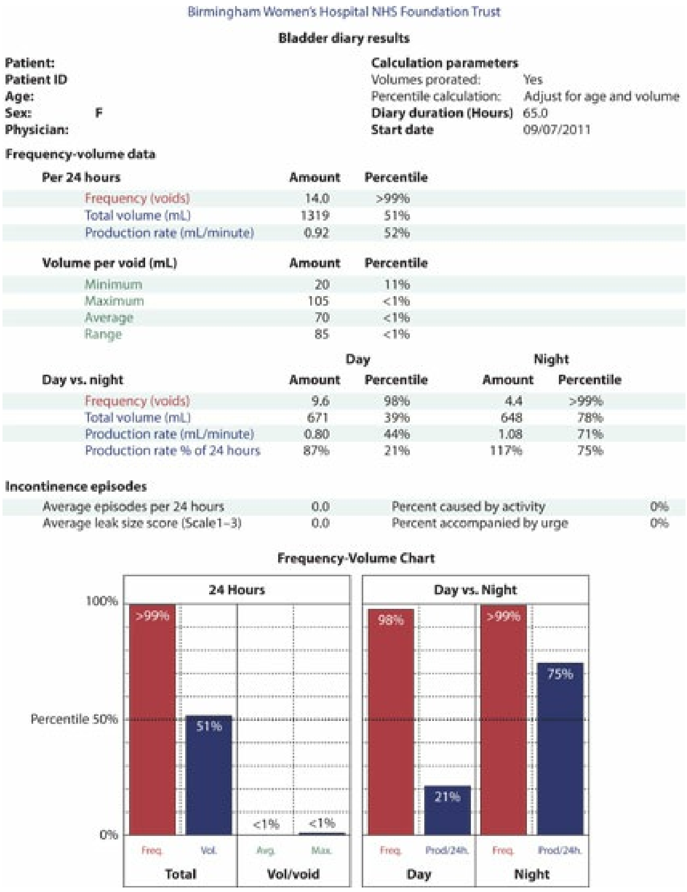
As yet, none of the questionnaires has been shown to be of value in terms of diagnosis [21]. They are used to screen patients with urinary tract symptoms to identify those who should be further examined for IC or to follow those who have already been diagnosed [17]. The questionnaires help evaluate patient's response to treatment and follow the course of the disorder.

Voiding Diary

The voiding diary (Figure 55.3) is a useful tool in the investigation of lower urinary tract symptoms. Fluid intake and output is recorded by the patient in the diary for initial evaluation. Voiding diaries help to assess the degree of frequency, nocturia, and volumes voided at each episode. They are also useful in the identification of polydipsia and polyuria, which cause urinary frequency. They help to ascertain the highest functional capacity, which is usually the maximum voided amount and patient sensation at each void. Patients with BPS/IC have lower volumes at time of sensation to void and lower functional capacity than those without the condition [16]. It is therefore usual to see women with BPS/IC having frequent voids of small volume.

Urodynamics

Urodynamics has no role in the diagnosis of BPS/IC as there are no existing urodynamic findings specific for BPS/IC. Its use is to exclude confusable diseases such as detrusor overactivity or obstructed voiding that may be the cause of the patient's symptoms. It is not performed routinely if the diagnosis is certain from the history but is reserved for select cases where the diagnosis is uncertain.



Birmingham Women's Hospital NHS Foundation Trust

Bladder diary results

Patient:		**Calculation parameters**	
Patient ID		Volumes prorated:	Yes
Age:		Percentile calculation:	Adjust for age and volume
Sex:	F	**Diary duration (Hours)**	65.0
Physician:		**Start date**	09/07/2011

Frequency-volume data

Per 24 hours	**Amount**	**Percentile**
Frequency (voids)	14.0	>99%
Total volume (mL)	1319	51%
Production rate (mL/minute)	0.92	52%

Volume per void (mL)	**Amount**	**Percentile**
Minimum	20	11%
Maximum	105	<1%
Average	70	<1%
Range	85	<1%

	Day		**Night**	
Day vs. night	**Amount**	**Percentile**	**Amount**	**Percentile**
Frequency (voids)	9.6	98%	4.4	>99%
Total volume (mL)	671	39%	648	78%
Production rate (mL/minute)	0.80	44%	1.08	71%
Production rate % of 24 hours	87%	21%	117%	75%

Incontinence episodes

Average episodes per 24 hours	0.0	Percent caused by activity	0%
Average leak size score (Scale1–3)	0.0	Percent accompanied by urge	0%

Frequency-Volume Chart

Figure 55.3 Results of analysed voiding diary.

Cystoscopy

Cystoscopy and biopsy is used to exclude diagnosis of bladder cancer or urethral diverticulum in those with risk factors or suggestive symptoms.

It is also used for the identification of Hunner's ulcers (Figure 55.4). The presence of Hunner's ulcers was previously thought to be pathognomonic of what was defined as IC. Cystoscopy with hydrodistension during general or regional anesthesia is required to substantiate the occurrence of Hunner's ulcers. During rigid cystoscopy, the bladder is filled at a pressure of 80 cmH_2O above the patient's bladder until the flow ceases and maximum capacity is reached. The bladder is emptied and then refilled to approximately 20%–50% of capacity inspecting for lesions and hemorrhages (Figure 55.5) that are evident on the second filling. Hunner's ulcers typically involve the dome and posterior and lateral walls of the bladder and spare the trigone [27]. Biopsy may be necessary to confirm that it is such a lesion. Hunner's ulcers are rare findings. Glomerulations are the most common cystoscopic abnormality following hydrodistension in patients with BPS/IC [20,26]. Glomerulations are areas of submucosal bleeding. They are not specific to BPS/IC and as such their identification at time of cystoscopy is not diagnostic of BPS/IC. Glomerulations have been identified in the bladders of patients without bladder disease or bladder pain [10,55].

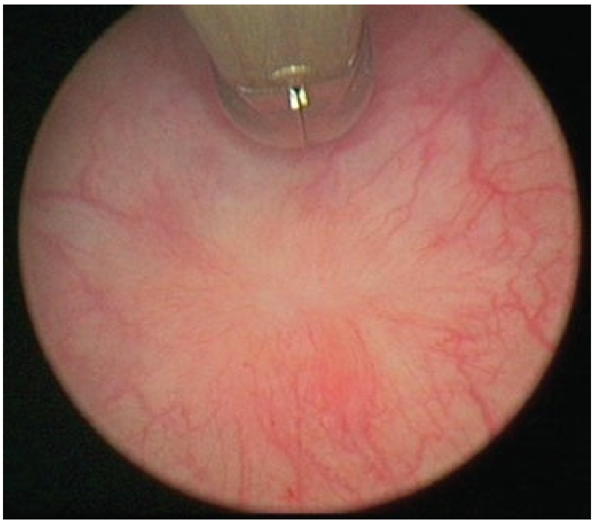


Figure 55.4 Cystoscopic appearance of Hunner’s ulcer.

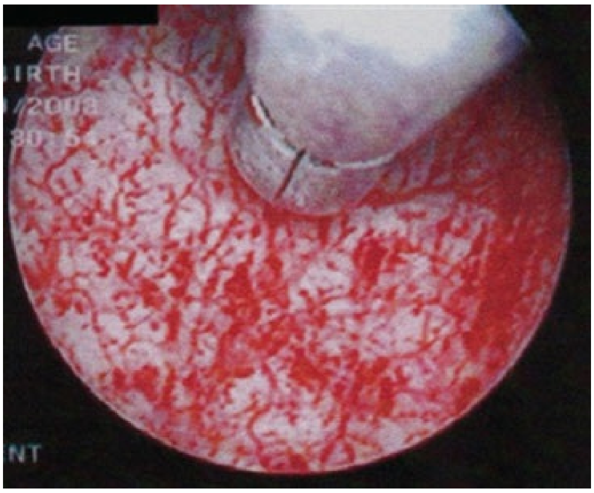


Figure 55.5 Cystoscopy showing abnormal petechial hemorrhages in investigation of bladder pain.

MANAGEMENT

The aim of treatment is to achieve symptom control by addressing the underlying pathophysiological process. This is often difficult to achieve as the etiology of the disease is not well understood. The available treatment strategies can be classified into conservative, bladder instillation therapy, medical, and surgical. The scientific evidence for most of these treatments is weak or lacking.

Treatment strategies should proceed using more conservative therapies first; surgical treatments are generally reserved for intractable disease that has not responded to other treatment modalities.

Patient education is an important initial step in disease management. Patients should be educated about the disease and informed about current knowledge of BPS/IC and available treatment modalities. They should be made aware of the fact that no single treatment is curative and that symptom control may require a trial of multiple therapeutic options (including combination therapy) before it is achieved [43]. There are several online databases, health magazines, and educational videos available that provide information about BPS/IC that patients should be encouraged to access. The Interstitial Cystitis Association (ICA) and its affiliated international organizations are also an important resource that patients should be made aware of.

Conservative

Behavioral Modification

Patients with BPS/IC typically have frequent small voids. For selected group of highly motivated patients in whom the predominant complaint is urinary frequency, behavioral modification in the form of timed voiding, controlled fluid intake, keeping a bladder diary, pelvic floor muscle training, and bladder retraining may be beneficial. Chaiken et al. [6] reported reduced daytime frequency and increased functional capacity in patients who underwent short-term behavioral therapy.

Dietary Manipulation

Avoidance of certain foods appears in some patients to improve their symptoms. Although the clinical data are lacking many, patients have reported benefit from dietary alteration. Caffeinated or alcoholic drinks, spicy foods, and citrus fruits have all been reported to aggravate symptoms. The ICA produced the IC food list, which lists foods reported by patients to trigger bladder symptoms and those that are less bothersome to the bladder. It is available to download at the ICA website, www.ichelp.org/ICFoodList.

Stress Management

Stress has been shown to exacerbate BPS/IC symptoms [45]. Stress management is an essential part of treatment where stress is contributory. Commonly used techniques include yoga, meditation, and guided imagery. Where possible, the stress-inducing factor should be removed or reduced as much as possible.

Cystoscopy and Hydrodistension under Anesthesia

This is considered to be both diagnostic and therapeutic. Cystoscopy is diagnostic as it allows identification of bladder pathology such as bladder tumors or Hunner's ulcers. If present, Hunner's ulcers can be treated. Hydrodistension enables the bladder capacity to be determined. It is also thought to be therapeutic as it has been shown to provide symptomatic relief in some patients. Its effects are, however, only short lasting and so it is not considered first-line treatment [7,29].

Oral Therapy

Amitriptyline

This is a tricyclic antidepressant commonly used for pain management. Its analgesic effect is thought to be due to its ability to inhibit serotonin and noradrenaline reuptake in the central nervous system. It also has anticholinergic effects and appears to stabilize mast cells. It can be used in doses up to 100 mg per day and has been shown to be a beneficial treatment for pain in patients with BPS/IC. A double-blind placebo-controlled trial by Ref. [52] reported greater than 30% decrease in O'Leary–Sant symptom score in the patients treated with amitriptyline compared to 13% reduction in symptoms in the placebo group. Side effects including fatigue, weight gain, and dry mouth are a common reason for patients to stop treatment.

Gabapentin

GABA agonist is usually used in the treatment of seizures. It has also been found to be useful in the treatment of neuropathic pain and can be used as an analgesic in patients with BPS/IC. The most common reported side effect is fatigue.

Antihistamines

Cimetidine, an H_2-receptor antagonist, has been found to be effective in the treatment of BPS/IC [48]. Its mechanism of action, however, remains unknown.

Pentosan Polysulfate Sodium

Pentosan polysulfate sodium (PPS) is a synthetic highly sulfated polysaccharide. Its structure is similar to heparin sulfate, one of the GAGs in the bladder. When taken orally, it appears that 2%–6% of it is excreted unchanged in the urine. Its mechanism of action is thought to be by replacing the deficient GAGs in the bladder, thus decreasing altered bladder permeability. It is available in oral formulation and given at dosage of 100 mg three times daily. In a randomized, prospective, double-blind, placebo-controlled trial conducted by [34], 32% of 148 patients treated with PPS reported significant improvement in symptoms, compared with 16% in the placebo group ($p = 0.01$). PPS remains the medication of choice for most patients. Patients should be advised that it may take up to 6–9 months for the full effect of the drug to be attained.

Intravesical Treatments

Intravesical treatments involve direct administration of the drug into the bladder. They are usually used alone as second-line treatment or in conjunction with oral therapy and other forms of conservative management. The available intravesical drug treatments include the following:

Dimethyl Sulfoxide

Dimethyl sulfoxide (DMSO) was first synthesized as a by-product of the wood industry. It was found to have anti-inflammatory and analgesic properties. It is the most widely used intravesical drug treatment for BPS/IC. Its mechanism of action is not clearly understood; however, it has been shown to be an effective treatment of BPS/IC. Objective improvement was noted in 93% of patients with cystoscopy-positive IC treated with DMSO versus 35% in the placebo group [39]. A common side effect of the drug is garlic-like odor to the breath. Treatment is usually performed on a weekly basis for 6–8 weeks after which treatment is discontinued until symptoms recur.

Heparin

It is thought that instillation with heparin, a GAG, may also afford protection to the urothelium by replacing the GAG layer. It has not been associated with coagulation abnormalities when administered intravesically and has been reported to be useful in the treatment of IC. In a study by Parsons et al., 56% of patients reported improvements in their symptoms within 3 months of treatment [36].

Bacillus Calmette–Guerin

Bacillus Calmette–Guerin (BCG) is an attenuated strain of *Mycobacterium bovis*. Its precise mechanism of action is unknown. Studies have reported it to be effective in the symptomatic management of BPS/IC. Peters et al. [40] reported improvement in symptoms in 60% of patients treated with BCG compared to 27% in the placebo group. A larger randomized trial, however, did not show a significant response in patients treated with BCG compared to those treated with DMSO [38]. The clinical benefit of this treatment remains unclear.

Botulinum Toxin A

This is a potent neurotoxin derived from the bacterium *Clostridium botulinum*. There is emerging evidence that suggests botulinum toxin is beneficial in the treatment of BPS/IC [41]. However, many of these studies are small with short-term follow-up only. The treatment regime and dose of botulinum toxin has also not been standardized. Until further evidence from larger trials become available, botulinum toxin is not recommended for use outside of carefully controlled clinical trials.

Other intravesical treatments that have been used include resiniferatoxin, capsaicin, lignocaine, and oxybutynin. Evidence of their clinical efficacy however is lacking.

Neuromodulation

Sacral nerve stimulation is often used in the management of patients with detrusor overactivity. It is a minimally invasive procedure that involves stimulation of the S3 or S4 nerve root by a mild electric current. There is emerging evidence suggesting that it may be beneficial in the treatment of BPS/IC [8,19]. It is however still considered an investigational procedure and is not currently recommended for the treatment of BPS/IC.

Surgery

Surgery is reserved for severe cases that have refractory to all other treatment options. A urological opinion should be sought. Available surgical treatments include bladder augmentation cystoplasty, cystectomy, and urinary diversion.

CONCLUSION

BPS/IC is a chronic debilitating disorder. The etiology of the disease is unknown and it remains a diagnosis of exclusion.

Patients typically complain of pain in the bladder or pelvic area associated with urinary frequency or urgency. The diagnosis is heavily dependent on the history and physical examination as there is currently no specific diagnostic test for BPS/IC. Diagnostic adjuncts such as urinary analysis, urodynamics, and cystoscopy aid the diagnosis and exclusion of other confusable diseases.

Treatment is multimodal and often multidisciplinary. It includes patient education, which is fundamental. Management should commence with conservative measures such as behavioral modification and dietary modification followed by medical management with oral or intravesical therapy, which aims to provide symptomatic relief for pain and irritable bladder symptoms. More invasive treatments such as surgery should be reserved for refractory cases as they are associated with more morbidity. There is a limited role currently in clinical practice for neuromodulation and botulinum toxin. Although the results of available studies are promising, larger trials are required on the efficacy of these therapies. Further research into the etiology of the disease is required in order to correctly define a diagnostic criterion and management plan of the disease (Figure 55.6).

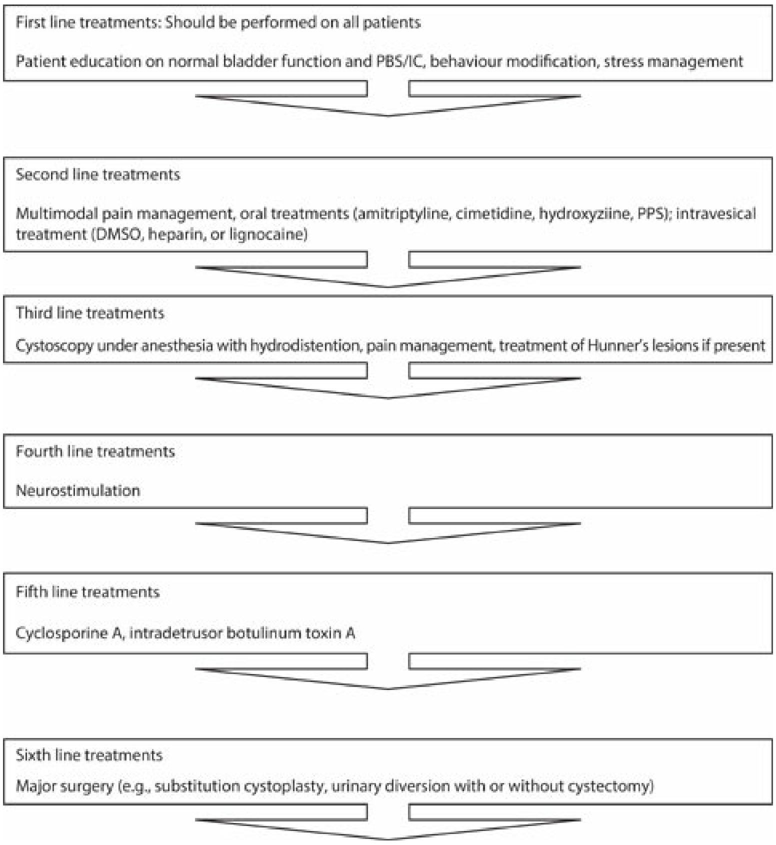

First line treatments: Should be performed on all patients
Patient education on normal bladder function and PBS/IC, behaviour modification, stress management
Second line treatments
Multimodal pain management, oral treatments (amitriptyline, cimetidine, hydroxyziine, PPS); intravesical treatment (DMSO, heparin, or lignocaine)
Third line treatments
Cystoscopy under anesthesia with hydrodistention, pain management, treatment of Hunner's lesions if present
Fourth line treatments
Neurostimulation
Fifth line treatments
Cyclosporine A, intradetrusor botulinum toxin A
Sixth line treatments
Major surgery (e.g., substitution cystoplasty, urinary diversion with or without cystectomy)

Figure 55.6 American Urological Association suggested approach for treatment of interstitial cystitis/bladder pain syndrome. (Adapted from Hanno, P.M. et al., *J. Urol*., 185, 2162, 2011.)

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56 Bacterial Cystitis in Urogynecology: An Update

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INTRODUCTION

Urinary tract infections (UTIs) are traditionally divided into infections of the upper tract (pyelonephritis) and of the lower tract (bacterial cystitis). This chapter does not discuss upper tract infections, as knowledge on this subject is normally obtained during training in obstetrics. Untreated lower UTI may ascend to the kidneys and even be associated with septicemia; however, such events are beyond the remit of this chapter, which focuses on bacterial cystitis.

Cystitis is the general term used to describe inflammation of the urinary bladder. The subjects of interstitial cystitis (IC), cyclophosphamide cystitis, or rare parasitic infestations are not covered herein (but see Chapter 55). Bacterial cystitis is an inflammatory response to bacterial infection of the lower urinary tract. The hallmark symptoms and signs include dysuria and discolored, foul-smelling urine, suprapubic tenderness, urinary frequency, and urgency ± nocturia, which may be associated with microscopic or macroscopic hematuria and pyuria.

Bacterial cystitis may be acute, chronic, or recurrent as well as being simple or complex. The natural history is dependent on the type and virulence of the urinary pathogen, resistance to antimicrobial agents, and host defenses. Diagnosis in most simple cases is based on clinical symptoms, urine dipstick testing (which is controversial), preferably with laboratory confirmation by microscopy and/or culture. Management comprises identification of the causative organism and, based on the results of urine culture and sensitivity, at the same time prescription of an appropriate antimicrobial agent for a suitable length of time. In those women with recurrent or complex infections, more detailed strategies may be needed. This chapter examines the definition, epidemiology, and pathogenesis of bacterial cystitis and reviews the management of women presenting with both simple and complex lower UTIs. Current controversies regarding low-grade bacterial cystitis in refractory detrusor overactivity (DO) are also summarized.

DEFINITIONS

Bacteriuria

The term bacteriuria indicates the presence of bacteria in urine, because traditionally urine is thought to be sterile in normal individuals. When assessing the results of urine cultures, the clinician must distinguish between true bacteriuria and contamination of the urine as it passes through the distal urethral and introitus.

The term “significant bacteriuria” was first defined in the late 1950s by Kass, a Harvard nephrologist. His goal was to determine a quantitative threshold that would accurately distinguish true bacteriuria (which he defined as “actual residence of bacteria within the urine of the urinary tract”) from bacterial contamination (“the adventitious entry of bacteria into the urine during the collection of the specimen”) [1]. In 335 asymptomatic female outpatients, he identified two populations based on catheter specimens of urine: those with low bacterial counts (0–10^5 CFU/mL) and those with high counts (>10^5 CFU/mL). Bacteria cultured from the “low-count” group frequently showed commensal organisms and a repeat urine sample taken from them rarely matched the original specimen. In contrast, counts of >10^5 were more consistent on repeat testing and known urinary pathogens were commonly isolated. The relative degrees of pyuria were not reported. He concluded that “patients with more than 10^5 bacteria per mL of urine may be regarded as having true bacteriuria” [1,2].

Kass was mainly interested in preventing pyelonephritis. He compared asymptomatic women [1,3] with those having overt upper UTI [4,5]. It is worth remembering that in the 1940s and 1950s, pyelonephritis/infected shrunken kidney was found in 15%–20% of autopsy specimens and was a major cause of death in one third of these cases [4]. Although Kass defined $>10^5$ CFU/mL as "significant" bacteriuria (i.e., likely to result in morbidity), he did acknowledge that pyelonephritis may be associated with lesser degrees of bacteriuria in some situations. Sixty years later, despite the fact that Kass' threshold was not tested systematically on women with frequency/urgency/nocturia, his criterion of 10^5 CFU/mL of urine is still widely accepted as the definition of significant bacteriuria (i.e., infection) among symptomatic women [2,6].

Reevaluation in the 1980s by Stamm et al. later found that these criteria would in fact miss approximately half of patients with clinical symptoms of bacterial cystitis [7]. Therefore, he favored a diagnostic cutoff of $\geq 10^2$ CFU/mL. Tapsall et al. also demonstrated that patients with symptoms, but without significant bacteriuria, responded just as well to antibiotics as the group with significant bacteriuria [8]. Kunin reinforced the importance of low-count bacteriuria in a study assessing 639 women with and without symptoms of cystitis [9]. Of the symptomatic patients, 46% were found to have low-count bacteriuria (10^2–10^4 CFU/mL) compared to only 10% of the asymptomatic women. This study rejected the old hypothesis that urinary dilution contributes to low-count bacteriuria and concluded that low-count bacteriuria is actually just an early phase of infection [2].

The Infectious Diseases Society of America has since revised their guidelines accordingly [10], as has the European Association of Urology [11], recommending a threshold of 10^3 CFU/mL, as this improves the sensitivity without a significant loss of specificity. However, to date, most laboratories in the United Kingdom and Australia persist with the original diagnostic cutoff of 10^5 CFU/mL (unlike the United States and Europe that now employ the more stringent cutoff). Interestingly, the 2010 ICS/IUGA report on terminology defines UTI as "the finding of microbiological evidence of significant bacteriuria and pyuria usually accompanied by symptoms such as increased bladder sensation, urgency, frequency, dysuria, urgency urinary incontinence, and/or pain in the lower urinary tract" with suggested criteria of (1) bacteriuria >100,000 (10^5) colony-forming units (CFU)/mL on voided specimen or >1,000 (10^3) CFU/mL on catheterized specimen and (2) pyuria >10 white blood cell (WBC)/mm^3 [12]. This "traditional" threshold for significant bacteriuria on voided specimens now appears controversial.

Sterile Urine: Recent Evidence

Historically, the urine in the bladder is normally considered to be completely sterile, in that uropathogens are not detected using routine cultivation techniques. Older studies comparing suprapubic puncture specimens versus midstream urine samples revealed that incidences of significant bacteriuria on suprapubic catheter stab samples from asymptomatic women were less than 1% [13]. However, very recent studies in Europe and America using sophisticated techniques demonstrate that up to 35 genera of bacteria do in fact reside in the bladder of some women [14–17]. This research uses deep 16S rRNA gene sequencing and polymerase chain reaction (PCR) to identify various species of uncultivated bacteria in the urine [15]. Such specimens taken via transurethral catheters, suprapubic catheters, and voided samples from both symptomatic and asymptomatic women found bacterial DNA in urine from all three sampling methods. The microbial genera detected by PCR amplification in the transurethral catheter specimens corresponded to those obtained from suprapubic catheters. They appeared to be the true colonies of the bladder, as they differed greatly from the mixture of urinary and genital tract bacteria DNA found in the voided samples (which suggested contamination).

The same researchers went on to evaluate whether or not the bacteria found in the preliminary study could be grown in the lab [17]. Although 92% of samples showed no growth when cultivated at 10^3 CFU/mL using routine urine culture protocol, 80% grew bacteria when an expanded quantitative urine culture (EQUC) protocol was used (i.e., different types of agars in various aerobic and anaerobic conditions). Bacteria of 35 different genera and 85 species were present at levels below the cutoff used in standard culture protocols, which correlated with the 16S rRNA gene sequencing results. Thus, DNA studies show that viable bacteria inhabit the normal adult female bladder, in contrast with previous beliefs that the normal bladder is "sterile."

Pyuria

Traditionally, infection is distinguished from colonization by evidence of tissue injury/inflammation. In practical terms, this is indicated by the finding of pyuria [18]. Pyuria is present in most women with high-count UTIs [18,19]. However, the relationship between low-count bacteriuria 10^2–10^5 CFU/mL and pyuria is less clear [2]. Levels more than 10 leukocytes/mm^3 are considered pathological. However, the prevalence of pyuria increases with the concentration of bacteriuria, so that low-count bacteriuria is not always associated with pyuria [9,20]. For example, Stamm et al. [20] reported that incorporating pyuria into the diagnostic standard for acute infection (i.e., insisting on $>10^2$ CFU/mL plus pyuria) made little difference compared to quantification of bacteria alone [7]. The large case–control study by Kunin et al. established that the prevalence of pyuria (>20 WBC/mm^3) rises with the level of bacteriuria. This again supports the notion that low-count bacteriuria is just an early phase of classical bacterial cystitis [9].

Asymptomatic Bacteriuria

Asymptomatic bacteriuria (ABU) (i.e., the absence of dysuria, foul-smelling, discolored urine, loin pain, fever) is found in 1%–9% of young women and increases with age, reaching a prevalence of 14%–75% in the elderly or institutionalized [21]. Long-term ABU is defined as a persistent colonization of >3 weeks (to several years) of duration [21]. In general, treatment of ABU is not recommended, as routine antibiotics contribute to resistance as well as causing other adverse events and ABU may even be protective of recurrent UTI [22]. However, ABU requires treatment in circumstances such as pregnancy, instrumentation of the lower urinary tract, and renal transplant patients. *Escherichia coli* is the most commonly detected bacteria in ABU [21]. ABU with *Streptococcus agalactiae* (group B streptococcus) is common in pregnancy and requires treatment as it is associated with chorioamnionitis [23] and neonatal sepsis [24]. Note that group B streptococcus bacteria is increasingly recognized as a uropathogen (see later section).

Recurrent Bacterial Cystitis

This term describes symptomatic infections, which recur after a previous UTI, usually after treatment. It may be due to bacterial persistence or due to a new infection with the same or different bacteria. Risk factors for recurrent infection are shown in Table 56.1. Bacterial persistence often leads to frequent recurrence within days or weeks. The infection is usually by the original organism from a focus inside the urinary tract and is associated with an underlying anatomical problem [25]. Bacterial persistence may also occur if empiric treatment was given without proper urine culture and checking of the bacterial antibiotic sensitivity, or if the patient did not complete the antibiotic course, or if the bacteria developed resistance after the original (correct) treatment was started. In urogynecology patients (who often have coexisting incontinence or prolapse, voiding dysfunction, recent surgery, diverticula, etc.), the economically expedient practice of performing a simple dipstick and treating empirically cannot be recommended, as these patients are, by definition, prone to recurrence.

Table 56.1 Risk Factors for Recurrent Urinary Tract Infection

Lower urinary tract obstruction and chronic retention of urine
Bladder stones or intravesical foreign bodies
Trauma
Enterovesical and vesicovaginal fistulae
Urethral diverticula
Malformations of the urinary tract
Cystocele
Vesicoureteric reflux
Infected paraurethral glands
Contraceptive diaphragm use

Reinfection occurs after a prolonged interval (months) from the original infection and is often caused by a different organism [25]. Older studies found that about 80%–90% of recurrent cystitis is due to reinfection, of which about a third arose from the same organism invading the urothelium again [26].

Clinical Classification of Cystitis

In summary, UTIs as a whole are classified according to their location, clinical symptoms, and laboratory and microbiological findings, as shown in Table 56.2 modified from the European Association of Urology (EUA) guidelines [11].

Complicated UTI

Although this chapter primarily concerns bacterial cystitis, the urogynecologist must be constantly vigilant for what are described as "complicated" UTIs. As seen in Table 56.3, many "complicated" UTIs involve upper urinary tract, e.g., renal calculi and cysts, ureteric stricture, vesicoureteric reflux, ureteric stents, nephrostomy tubes, and renal transplants. However, the urogynecologist should be mindful that lower tract anomalies, e.g., bladder cancer, urethral stricture/diverticula, and urogenital fistula, incomplete emptying, and use of indwelling catheter, commonly feature sessile, non–*E. coli* organisms such as pseudomonas, which are frequently multiresistant organisms.

Table 56.2 Definitions of Cystitis Terminology

Description	**Clinical features**
Acute cystitis	
"Classical" uncomplicated bacterial cystitis	Significant bacteriuria > 10^5 CFU/mL with pyuria (>10 white blood cells per high power field)
Low-count/"occult" bacterial cystitis	Bacteriuria 10^3–10^5 CFU/mL ± pyuria
Recurrent UTI	Bacterial cystitis that reoccurs >3 times a year
Complicated UTI	UTIs associated with a condition that increases the risk of infection or of therapy failing (see Table 56.3)
Symptomatic UTI	Significant bacteriuria with dysuria, frequency, urgency, nocturia: foul-smelling urine, ± loin pain, febrile symptoms
Asymptomatic bacteriuria	Bacteriuria >10^5 CFU/mL of urine, without pyuria or symptoms

Table 56.3 Conditions Associated with Complicated Lower Urinary Tract Infection

Structural	Urolithiasis
	Malignancy
	Ureteric stricture
	Urethral stricture
	Bladder diverticula
	Renal cysts
	Fistulae
	Urinary diversions
Functional	Neurogenic bladder
	Vesicoureteric reflux
	Voiding difficulties (incomplete bladder emptying)
Foreign bodies	Indwelling catheter
	Ureteric stent
	Nephrostomy tube
Others	Diabetes mellitus
	Pregnancy
	Renal failure
	Renal transplant
	Immunosuppression
	Multidrug resistance
	Hospital-acquired (nosocomial) infection

PREVALENCE

Lower UTI is a common clinical diagnosis in developed countries and the most prevalent bacterial infection. Very little epidemiological data are available for bacterial cystitis alone; most prevalence data refer to "UTI" as a whole. Approximately half of all women will experience UTI sometime during their life, with an estimation of 150 million cases occurring a year worldwide [27]. Other than in the elderly, UTI is more common in women than in men. They account for 1%–3% of all general practitioner consultations in the United Kingdom [28] and 0.9% of all ambulatory appointments in the United States, with a total of 10.5 million visits noted in the United States in 2007 [29,30]. Recurrent cystitis is becoming a major problem, as 20%–30% of females with an acute UTI will have a recurrence within 3–4 months [31], and recurrence occurs in 48% of women who have had more than one episode [32]. Besides being distressing for patients, UTIs cause enormous health-care expense, mainly due to the high incidence. The costs of community-acquired UTI were totalled at $2.5 billion in the year 2000 in the United States [33]. With the increasing resistance to antibiotics, the costs are likely to rise.

Recently, ABU has received greater attention, partly because chronic infection in the elderly may be asymptomatic until it leads to fever. The prevalence varies greatly, from 1%–100% across different patient populations. "Healthy" women demonstrate a prevalence between 1% and 9% [21], with doubled risk in pregnant women (2%–15%) and threefold risk in diabetics (1%–30%). Although the elderly are particularly at risk of ABU, with the prevalence rising to 2%–50% and 14%–75% in the community-dwelling and institutionalized adults, respectively, morbidity and mortality are not increased. The prevalence of ABU is greatest in those with indwelling catheters (9%–100%).

PATHOGENESIS

As discussed earlier, urine is not "sterile," contradictory to what was originally thought. However, pathogenic bacteria must gain access to the bladder, generally from neighboring sites. The fecal–perineal–urethral route of infection is well documented. *E. coli* is the main causative organism, with the rectal flora serving as the main reservoir [34], explaining why fecal incontinence is associated with a higher risk of UTI [35]. Other colonization sites include the perineum, vaginal vestibule, urethra, and paraurethral tissues.

Traditionally, uropathogens are required to ascend the urethra, against the stream of urine, to colonize the bladder [34]. The mechanism of urethral ascension is still poorly understood. It may be facilitated by sexual intercourse or catheterization. The periurethral area is heavily colonized with bacteria. Urinary incontinence generally predisposes healthy postmenopausal women to develop recurrent cystitis [36]. The use of incontinence pads is associated with a significant increase in the incidence of symptomatic cystitis in the elderly [37].

However, just because bacteria gain access to the bladder, cystitis does not necessarily result. The bacteria must attach to the urothelial cells to begin the inflammatory process (see the succeeding text for more detail). Even virulent organisms require some degree of host susceptibility [38]. Patients with symptomatic bacteriuria are more likely to be neutropenic compared to those with ABU [39]. This study showed no difference in the virulence of the strains between the asymptomatic and symptomatic group nor any difference in resistance to antibiotics; thus, the authors suggested that host factors may be more important than bacterial virulence.

HOST DEFENSES

The bladder has several mechanisms to resist infection. Most important is the hydrokinetic or "washout" effect, in which diuresis and voiding act to dilute the bacterial load and wash away infecting organisms. In a 1969 study, 40% of women with bacteriuria became free of infection spontaneously within 12 months [40], while a 1971 study demonstrated that the urine of 80% of women with simple infections became sterile on placebo alone [41]. Thus, the risk of infection will depend on the size of the bacterial load, the multiplication rate of the organism, the urinary residual, the frequency of voiding, and the volume of fluid intake.

Antimicrobial Factors

The composition of urine may inhibit bacterial growth. Extremes of urine pH, high osmolality, and high urea concentration tend to be protective [42], which is why historically urine has been used as an antiseptic. Urea is the principal antibacterial electrolyte in urine, and its effect is also modulated by concentration and pH [43]. The acquisition of iron is also an important requirement for bacterial virulence, because bacteria need iron to grow. The *E. coli* bacteria is most studied in this regard [44], as it has been shown to upregulate the genes that control iron acquisition systems [45]. Urothelial cells that are invaded by *E. coli* respond by upregulating their own production of the transferrin receptor so as to prevent bacterial acquisition of iron [46].

Epithelial Factors

The inner (luminal) surface of the urothelium is lined by uroplakin membrane proteins that lie within the plasma membrane of the superficial urothelial cells (also known as umbrella cells). These uroplakin plaques are composed of four proteins (UPIa, UPIb, UPII, and UPIIIa) [47]. They form a permeability barrier, to prevent the resorption of urine solutes across the urothelium but also to limit the availability of receptors for bacterial adherence factors [48]. The urothelium is also coated by a proteoglycan mucin layer, which further reduces permeability. This acts to oppose bacterial colonization, partly due to the high negative charge of the sulfated and carboxylated glycosaminoglycans [49]. Unfortunately, uropathogens that express certain kinds of type 1 pili (mannose binding) can block this adherence barrier by binding to the UPIa protein (as it contains a high mannose content) using an adhesin protein called FimH [50]. Soluble factors normally found in the urine, such as Tamm–Horsfall protein, also protect the bladder. This mucoprotein is shed from the renal tubular cells and is excreted in the urine. It can bind and trap *E. coli*, partly by competing for the binding sites on the type 1 pili [51]. However, if the uropathogens are able to adhere to the urothelium, then the acute pathogenic cycle of bladder infection can begin.

Immunologic Factors

The fact that recurrent cystitis affects 20%–30% of women suggests that some women do not develop long-lasting protective adaptive immunity following their initial infection [52]. The reasons for this are unknown. The T helper (CD4+) cell adaptive responses to uropathogen infection are unknown, though CD8+ T cells are reportedly recruited to uropathogenic *E. coli* (UPEC)–infected bladders [53]. Secretory immunoglobulin A (IgA) is synthesized by plasma cells within the lamina propria of the bladder wall and hence provides a degree of humoral immunity. In addition, a significant proportion of IgA originates in the urethra and this may help prevent ascending infection [54]. Secretory IgA has also been shown to prevent microbial invasion by disrupting bacterial adherence [55], and production of IgA can be deficient in women with recurrent UTI [56].

When uropathogens bind to urothelium during the process of cystitis initiation, the bacteria induce production of C-reactive protein (CRP), leading to leukocyte influx, IgA production, and cytokine release, such as IL-6 and IL-8. These cytokines promote activation of CRP and mucosal IgA.

Toll-Like Receptors

If the initial defense mechanisms are resisted and the pathogen continues to attach itself to the epithelial cells, Toll-like receptors (TLR) are activated. These TLRs play an important role in the pathogenic cascade of UTI by the host [57]. This inhibits further invasion of the microorganism, induces the production of antimicrobial peptides, and initiates apoptotic pathways, so that infected cells are exfoliated and pro-inflammatory chemokines are released, triggering neutrophil accumulation [42]. Defects in TLR pathway genes are associated with bacteriuria [57].

ROLE OF THE BACTERIAL PATHOGEN

Uropathogens have the ability to survive and multiply in the bladder as well as being able to adhere to the bladder epithelium. These unique qualities make them particularly virulent.

Adherence

The ability of bacteria to adhere to the urothelium of the lower urinary tract is an important initial step in the pathogenesis of lower UTI. The *E. coli* uropathogen has been the most widely studied, because it possesses type 1 fimbriae, which are essential for the invasion of *E. coli* into the bladder epithelial cells (Figure 56.1) [42]. *E. coli*, which do not have these type 1 fimbriae, are unable to infect the urothelium.

These fimbriae receptors bind to the surface uroplakins and other cellular proteins, thus preventing washout by the shear forces of the urine cascading across them. In animal models and one human study [58], *E. coli* are then shown to actually live inside the urothelial cells, forming intracellular bacterial communities (IBCs) unless the release of cytokines can provoke shedding of the urothelium and washout. Once the IBCs become established in the superficial umbrella cells, they can invade the lower layers of the urothelium and can become impervious to antibiotic treatment.

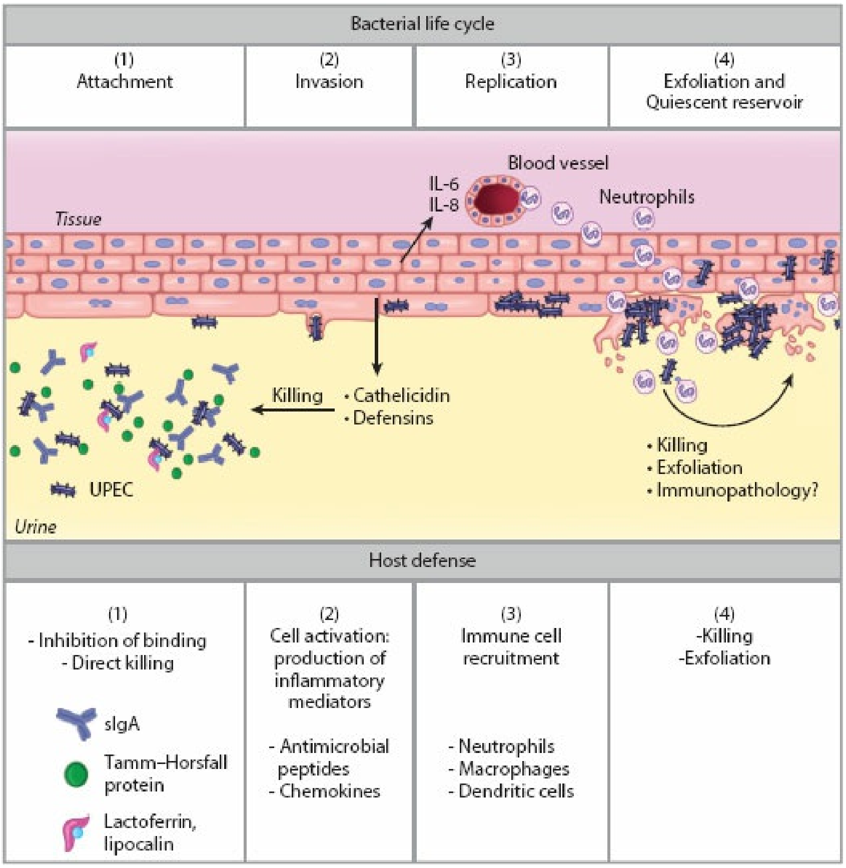


Figure 56.1 Multilayered effector mechanisms to combat urinary tract infections. Soluble factors like lactoferrin, Tamm–Horsfall protein (THP), or secretory IgA inhibit attachment of uropathogenic *Escherichia coli* to the epithelium. Despite these defense mechanisms, some bacteria are able to attach and invade the epithelium, which in turn releases antimicrobial molecules like cathelicidin or defensins. Moreover, the uroepithelium produces interleukin (IL)-6 and IL-8 to attract additional immunocompetent cells like neutrophils, which help to eliminate the pathogens. (Reprinted from Weichhart T, Haidinger M, Horl WH et al.: Current concepts of molecular defense mechanisms operative during urinary tract infection. *Eur J Clin Invest*. 2008. 38(Suppl 2). 29–38. Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.)

Uropathogens: Structure and Function

UPECs are the most common cause of UTI in the United States and abroad; they are responsible for about 80% of community-acquired cystitis and 25% of hospital-acquired infection. These are followed in the prevalence by *Staphylococcus saprophyticus* (10%–15% of community infections) and then *Klebsiella*, *Enterobacter*, *Proteus*, and *Enterococcus* species [34]. UPECs possess a number of structural factors that enhance their ability to adhere to and colonize the urothelium. Most important are adhesive fibers known as pili, or fimbriae, which live on the bacterial outer membrane [34,59]. Different types of UPEC strains are able to assemble different types of fimbriae, which recognize specific receptors on the urothelium, and enable strong adherence to the cell.

For example, FimH (on type 1 pili) binds to uroplakin 1a, which has mannose as one of its components (this is relevant to cranberry treatment, discussed later in this chapter). Type 1 pili also bind to the TLR 4. The presence of FimH-adhesive molecule is very important for triggering acute inflammation (and symptoms of pain); *E. coli* that do not have FimH tend to be nonadherent and they are often found in ABU [34,60,61].

RISK FACTORS FOR UTI

Host factors are certainly of equal importance with bacterial virulence in terms of the risk of developing cystitis. Host factors are considered in terms of congenital anomalies (such as vesicoureteric reflux, ectopic ureter, megaureter, or meningomyelocele) and acquired causes (Table 56.4). Other risk factors include a history of childhood UTI and a maternal history of UTI [34].

Age

Among children, the incidence of UTI is highest in the first year of life, with a gradual decrease to low rates at 11–15 years. Low-grade vesicoureteric reflux is an important factor. During a voiding detrusor contraction, if the vesicoureteric valves are incompetent, reflux of bladder urine up into the ureters/renal pelvis may occur. When the detrusor relaxes again, stagnant urine drains back from the upper renal tracts into the bladder, which predisposes to infection. In a review of 200 girls with recurrent lower UTI, 43% demonstrated vesicoureteric reflux, whereas in those with only one episode of infection, the corresponding rate was 36% [62].

Young girls with recurrent UTI and day wetting (likely due to DO) are known to adopt a posture of kneeling down on their heel (“the curtsy sign”) to stop urgency incontinence, which is thought to promote reflux of nonsterile urine from the lower urethra back up into the bladder [63]. This may be associated with irregular or “staccato” voiding patterns and incomplete emptying, which promotes UTI.

Table 56.4 Acquired Risk Factors for Urinary Tract Infection

Traumatic	Surgery (urinary diversion, clam cystoplasty)
	Sexual intercourse
	Sexual abuse
	Foreign bodies (catheters, stents, mesh)
	Contraceptive diaphragm
Inflammatory	Vulvourethritis
	Chronic inflammation (tuberculosis, syphilis, schistosomiasis)
	Interstitial cystitis
	Radiotherapy
	Fistula
Metabolic	Calculi
	Diabetes mellitus
Drugs	Cyclophosphamide
	Tiaprofenic acid
Anatomic	Cystocele
	Urethral diverticulum
Functional	Detrusor hypotonia
	Detrusor dyssynergia
	Constipation
Malignancy	Bladder tumors
	Other pelvic tumors (cervix, uterus, ovary)

The incidence of UTI increases in young adult women, where sexual activity is an important contributory factor, and increases again in old age. Reduced estrogen levels following the menopause are associated with vaginal flora changes. *Lactobacilli* that belong to the normal microflora of the vagina decline, which is associated with a rise in pH, allowing growth of Gram-negative bacteria increasing the risk of UTI [64]. UTIs in the elderly are common, accounting for approximately 25% of all infections [31] and 30% of those found in nursing homes [65]. The increasing prevalence of lower UTI in old age is most likely to be multifactorial in nature and is associated with a history of UTI, the presence of concomitant systemic disease, diabetes, increasing immobility, fecal and urinary dysfunction, the presence of a cystocele, instrumentation of the urinary tract, and sexual activity (although the association is less strong than in younger women) [66].

Persistent bacteriuria is not associated with significant morbidity [35] and it has a low predictive value for identifying febrile UTIs [67]. In part, this is because bacteriuria with low-virulence Gram-positive bacteria such as enterococci, coagulase-negative staphylococci, and group B streptococci are more common in this age group [21]. ABU is very common in the elderly with up to 75% of institutionalized women found to be bacteriuric [21] and treatment is not proven to be generally helpful [68]. However, UTI in the elderly can provoke fever, confusion, nausea, vomiting, dehydration, and delirium without bladder symptoms [69]. Predictive factors include severe cognitive impairment, disability in daily living, and self-reported urinary incontinence. Antibiotics must be used with particular care in the elderly because of the risk of *Clostridium difficile*.

Obesity

Studies on the association between obesity and UTI have shown contradicting results. In a large study of the factors influencing the rate of first referral for urinary infection in 17,032 women, the risk of first infection was higher in the nonobese compared to the obese [70]. A larger study of insurance claims for UTI treatment in 95,598 patients found obese women likely to be diagnosed with UTI [71]. Several studies have shown that obese patients are more at risk of developing UTIs after surgery than nonobese patients [72].

Behavioral Factors

Factors such as adequate fluid intake, voiding habits, diet, synthetic underwear, and use of perfumed soaps and bubble baths may be associated with the development of UTIs [73]. Sexual intercourse increases the risk of UTI by 90%, which increases even more with the uses of condoms [74]. Furthermore, the frequency of intercourse has also been shown to be a significant risk factor [75] and certain strains of *E. coli* may be transmitted between partners [76,77]. Theoretically, anal sex may be associated with increased risk of UTI; however, there is no literature to support this.

Instrumentation of the Urinary Tract

One of the most common forms of complicated UTI is related to the use of catheterization. The incidence of bacteriuria associated with an indwelling urinary catheter is 3%–10% per day, duration of catheterization being the most important risk factor for infection [30]. Following catheter removal, the bacteriuria will resolve spontaneously in around a third of cases [78]. While fewer than 5% of catheter-associated UTIs result in bacteremia, they are nevertheless a significant cause of morbidity, and they are also an important reservoir of antibiotic-resistant bacteria in hospitals and nursing homes. The frequency of catheter-acquired infection increases with the duration of catheterization and the failure to maintain a closed drainage system. Consequently, it is not uncommon that infections with multiple organisms occur in women with long-term indwelling catheters.

The prevalence of bacteriuria in the literature ranges from 9% to 100% [21]. *Klebsiella*, *Pseudomonas*, and *Enterobacter* are more prevalent as well as *Morganella morganii*, which is rarely found in other subgroups. UK and American evidence-based guidelines for preventing infections and treating catheter-associated UTIs have been published [79,80]. Using interventions such as topical antimicrobials, disinfectants added to the urinary drainage bag, antimicrobial coatings for catheters, or antimicrobial irrigation do not decrease the incidence of catheter-associated infections [79]. A study looked at different rates of UTI after various types of catheters (nitrofurazone-impregnated silicone catheter, standard PTFE-coated latex catheters, and silver alloy–coated hydrogel latex), but did not show any significant difference between them [81]. Bacteriuria should be expected in women with long-term catheterization, and, if asymptomatic, treatment is generally not justified as it is unlikely to give a microbiological cure and risks selecting for antibiotic-resistant microorganisms [79]. Catheters should be removed at the earliest opportunity and changed on a regular basis, as microbial colonization is inevitable over time.

As an alternative to long-term catheterization, the technique of clean intermittent self-catheterization (CISC) may be considered in women who are able to learn the technique, as it significantly reduces bacteriuria [82]. Evidence, however, would suggest that the use of prophylactic antibiotics does not improve the outcome in women performing CISC and should not be used.

Suprapubic catheterization (SPC) as an alternative method of long- or short-term bladder drainage is associated with lower infection rates. A recent study of post urogynecology surgery studied the insertion of indwelling urethral catheters for 24 and 90 hours, versus SPC for 90 hours, and found no significant difference between the three groups in the incidence of symptomatic UTI, but ABU was significantly less in the SPC group [83]. The suprapubic route has the added advantage of allowing women to void with the catheter in situ and have postvoid residuals checked without the need for repeated urethral catheterization. The rate of bacteriuria in the literature following cystoscopy ranges from 2.8% to 21% [84]. Bacteriuria can be lowered by a single dose of antibiotic prophylaxis such as gentamicin, but the risk of side effects should be considered as the majority will not develop UTI symptoms.

Voiding Dysfunction

Incomplete emptying of the bladder is an important cause of UTI [63]. It is usually secondary to detrusor failure or hypotonia but can be associated with detrusor–sphincter dyssynergia or outflow obstruction secondary to a pelvic mass, significant cystocele, surgery, or urethral stricture. As regards hypotonia, urodynamic studies have shown that, with increasing age, there is a significant increase in postvoid residual and a decrease in urinary flow rates, voided volume, and bladder capacity [85]. This would suggest that voiding function deteriorates with age and may be partly responsible for the increased incidence of UTI in the elderly. Postpartum bladder hypotonia following unrecognized overdistension is a major problem that can affect UTI risk long term.

CAUSATIVE ORGANISMS AND ANTIBIOTIC RESISTANCE

Gram-negative coliform bacilli of the family *Enterobacteriaceae* account for over 70% of cases, and *E. coli* (Figure 56.2) remains the predominant species in both primary care (approximately 70%) [86,87] and hospital practice (56%) [88]. *Proteus mirabilis*, *Enterococcus faecalis*, and *Klebsiella pneumonia* are the most prevalent hereafter (3%–8%) and are found twice as often in hospital-acquired UTIs and in patients over 65 years of the age [88]. Antibiotic-resistant noncoliform Gram-negative bacilli such as *Pseudomonas aeruginosa* and *Acinetobacter* species occur almost exclusively in hospital-acquired infections. Among Gram-positive bacteria, *S. saprophyticus* is an important cause of UTI in sexually active women. Although mainly known for its association with neonatal disease, *S. agalactiae* (group B streptococcus) is also a known uropathogen that is increasingly being reported [89], particularly in the elderly with chronic diseases [90]. The other coagulase-negative staphylococci, and *Staphylococcus aureus*, are more commonly hospital associated, apart from contaminated collections. Fastidious bacteria that can only be isolated on enriched culture media, including *Streptococcus pneumoniae* and *Haemophilus influenzae*, occasionally cause UTI in primary care.

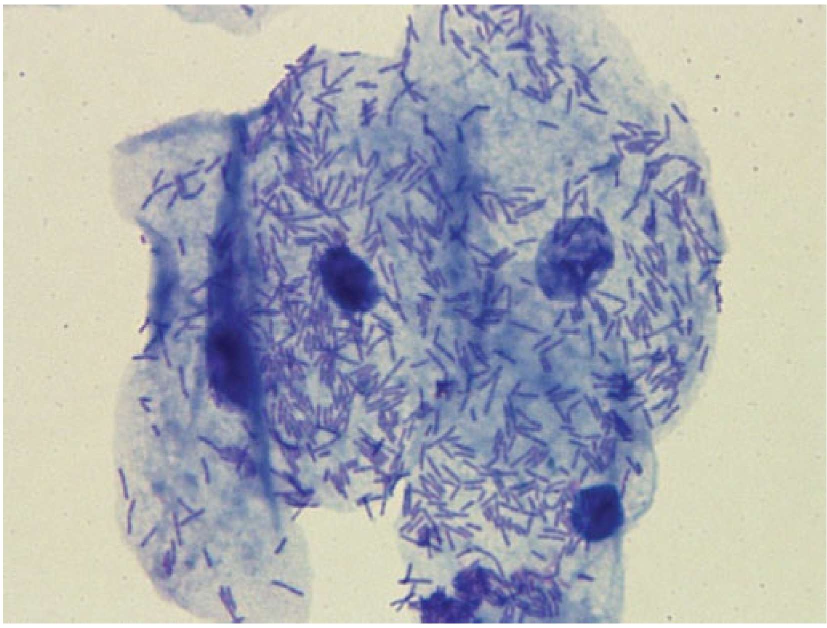


Figure 56.2 Urothelial cells associated *Escherichia coli* (Wright stain).

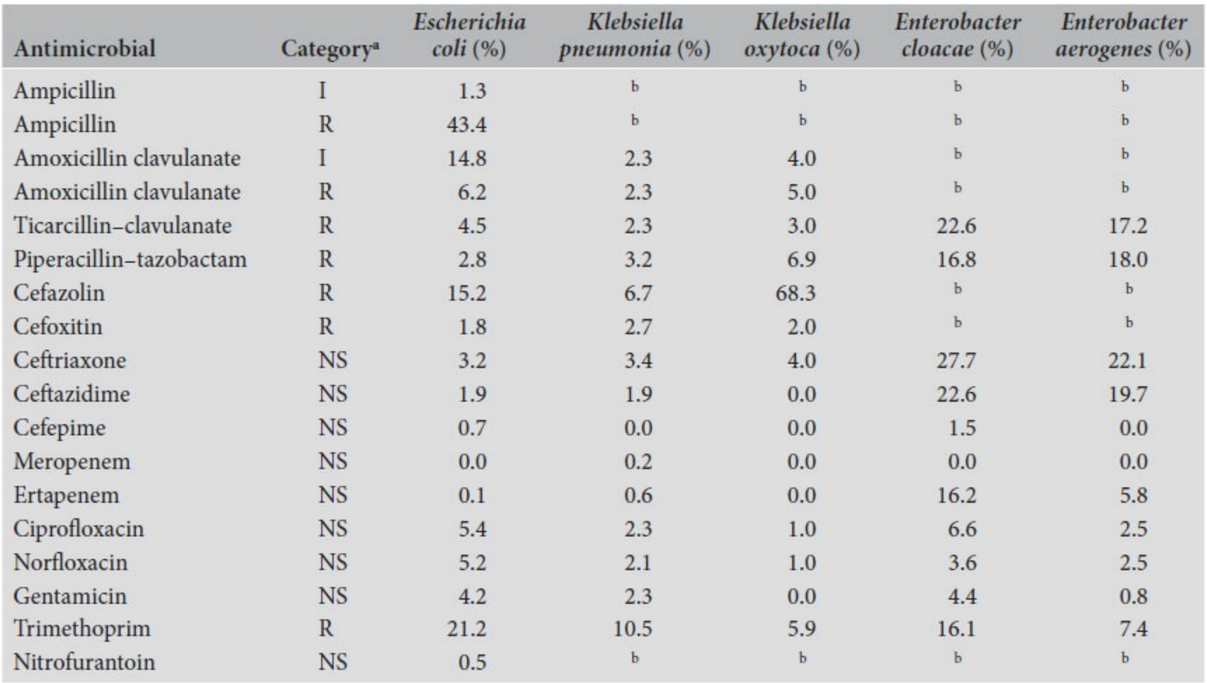
Bacteria that require special detection techniques, such as the cell wall-deficient mycoplasma (including *Ureaplasma urealyticum*) and the obligate intracellular pathogen *Chlamydia trachomatis*, are also recognized causes of cystitis. UTI can also be caused by microorganisms other than bacteria. Lower UTI due to *Candida* species is most common in patients with urinary catheters and usually reflects colonization of the catheter. Cystitis due to viruses such as polyoma and adenoviruses occasionally occurs in immunocompromised patients, especially those who have undergone renal or bone marrow transplantation.

Emerging Antibiotic Resistance

The global threat from increasing prevalence of resistance to antimicrobials among uropathogens has been reported by the World Health Organization in 2014 [91]. Rates of resistance to the commonly used oral antimicrobial agents vary between countries depending on the availability and usage of different compounds. To date, cystitis has been a relatively simple condition to treat with the available antibacterial drugs, although increasing resistance is a major concern [34,92]. The susceptibility of *E. coli* to nitrofurantoin is still high (96%–100%) [87,88]. A recent study in a general practice setting in France showed high levels of susceptibility to fosfomycin (99%), ofloxacin (97%), trimethoprim–sulfamethoxazole (87%), and amoxicillin/clavulanic acid (91%) [87]. However, increasing resistance to the traditional first-line therapy, trimethoprim–sulfamethoxazole has led to wider use of fluoroquinolones with resultant increasing bacterial resistance against norfloxacin and ciprofloxacin. An Australian study on acute pyelonephritis, which spanned 12 years, demonstrated increasing resistance of *E. coli* strains to a variety of antibiotics, with stable prevalence of resistance to ampicillin/amoxicillin between 40% and 50% [86]. Although resistance to first- and third-generation cephalosporins in *E. coli* is low, it is rising, particularly in those elderly, who have been admitted to hospital, require indwelling catheters, or are residents of nursing homes. Most community-derived urinary isolates remain susceptible to cephalosporins and co-amoxiclav, although this is not the case in hospitals where cephalosporinase-producing species such as *Enterobacter* are more common in addition to the acquired resistance to those antibiotics.

The emergence and spread of plasmid-borne extended-spectrum beta-lactamase (ESBL) genes that confer resistance to penicillins combined with clavulanate or sulbactam and third-generation cephalosporins in *Enterobacteriaceae* and other Gram-negative bacteria present a growing problem. The mobile plasmids containing these genes may also carry genes that confer resistance to other classes of antibiotics including aminoglycosides, folate antagonists, and quinolones, so their spread may be influenced by antibiotics prescribed for any condition, including UTI. The genes encoding these enzymes are readily transferred between species so that cross-infection is not recognized simply by a rising rate of antibiotic resistance within one species. Community-acquired UTIs with ESBL-producing bacteria that are resistant to all oral antibiotics are already being encountered and pose real therapeutic difficulties. Nonsusceptibilities and resistances are demonstrated in Table 56.5 [93].

Table 56.5 Nonsusceptibility and Resistance Rates for the Main Species Tested



Antimicrobial	Category[a]	*Escherichia coli* (%)	*Klebsiella pneumonia* (%)	*Klebsiella oxytoca* (%)	*Enterobacter cloacae* (%)	*Enterobacter aerogenes* (%)
Ampicillin	I	1.3	[b]	[b]	[b]	[b]
Ampicillin	R	43.4	[b]	[b]	[b]	[b]
Amoxicillin clavulanate	I	14.8	2.3	4.0	[b]	[b]
Amoxicillin clavulanate	R	6.2	2.3	5.0	[b]	[b]
Ticarcillin–clavulanate	R	4.5	2.3	3.0	22.6	17.2
Piperacillin–tazobactam	R	2.8	3.2	6.9	16.8	18.0
Cefazolin	R	15.2	6.7	68.3	[b]	[b]
Cefoxitin	R	1.8	2.7	2.0	[b]	[b]
Ceftriaxone	NS	3.2	3.4	4.0	27.7	22.1
Ceftazidime	NS	1.9	1.9	0.0	22.6	19.7
Cefepime	NS	0.7	0.0	0.0	1.5	0.0
Meropenem	NS	0.0	0.2	0.0	0.0	0.0
Ertapenem	NS	0.1	0.6	0.0	16.2	5.8
Ciprofloxacin	NS	5.4	2.3	1.0	6.6	2.5
Norfloxacin	NS	5.2	2.1	1.0	3.6	2.5
Gentamicin	NS	4.2	2.3	0.0	4.4	0.8
Trimethoprim	R	21.2	10.5	5.9	16.1	7.4
Nitrofurantoin	NS	0.5	[b]	[b]	[b]	[b]

Source: Reprinted from Turnidge JD et al., *Commun Dis Intell Rep*, 37(3), E219, Copyright 2013. With permission.

[a] R, resistant; I, intermediate; NS, nonsusceptible (intermediate + resistant).

[b] Considered largely intrinsically resistant due to natural β-lactamases.

Hospital- vs. Community-Acquired Infections

Community-acquired infections differ from those originating from within the hospital environment where *Klebsiella, Staphylococcus*, and *Pseudomonas* are more prevalent [88]. The frequency of various species causing community- and hospital-acquired UTIs cultured in the United Kingdom is demonstrated in Table 56.6 [88].

INVESTIGATIONS

Microbiologic Investigations

In primary care, the diagnosis of UTI is often made on clinical grounds, possibly supported by point-of-care dipstick urinalysis. This is not generally appropriate in a urogynecology service partly because bacterial toxins are known to enhance detrusor contractility [94,95] and inflammation can weaken urethral sphincter strength [96], thus worsening incontinence, but also because precise accurate treatment is required before placing urodynamic catheters or commencing urogynecology surgery. Furthermore, Khasriya et al. have recently highlighted the low sensitivity and specificity of dipstick urinalysis as well as microscopic examination for pyuria [97]. They compare both these tests to urine culture of both midstream and catheter specimens. The sensitivity of leukocyte esterase (LE) and microscopic pyuria was 56% and that of nitrite 10%. They emphasize the unreliability of dipstick urinalysis in diagnosing UTIs. Moreover, in patients with urinary symptoms associated with low bacterial counts, the sensitivity of combined LE and nitrite testing may be as low as 25% [73].

Microscopy and Culture

Phase contrast microscopy is mainly used to quantify leukocytes and erythrocytes and detect squamous epithelial cells (urethral) and bacteria. Gram staining can be a useful alternative; the presence of bacteria can be confirmed and indicative of the causative microorganism. Selective media used to culture urine routinely (e.g., cysteine lactose electrolyte-deficient [CLED], MacConkey, and chromogenic agars) are selected to enhance colonial morphology and distinguish mixed from pure growth of common uropathogens. Blood agar will support growth of more fastidious organisms that may not otherwise be recognized. Figure 56.3 illustrates *E. coli*, growing on horse blood and MacConkey agars. Even *Neisseria gonorrhoeae* has been isolated from urine samples when cultured on appropriate media. Liaison between the requesting clinician and the laboratory is essential to ensure optimal investigation.

Table 56.6 Relative Frequency (% of Total) of Isolation of Species Causing Various Types of UTI

Community-acquired UTI (patients < 65 years)(*n* = 397)	**Community-acquired UTI (patients > 65 years)(*n* = 392)**	**Hospital patient UTI (excluding pyelonephritis) (*n* = 394)**
Organism %	**Organism %**	**Organism %**
E. coli 77.3	*E. coli* 66.6	*E. coli* 56.3
P. mirabilis 4.3	*E. faecalis* 5.9	*E. faecalis* 8.4
E. faecalis 3.8	*K. pneumoniae* 5.9	*K. pneumoniae* 6.9
K. pneumoniae 3.5	*P. mirabilis* 4.3	*P. mirabilis* 6.3
S. saprophyticus 2.0	*P. aeruginosa* 3.1	*P. aeruginosa* 3.8
P. aeruginosa 1.8	*E. cloacae* 2.8	*E. cloacae* 2.5
S. agalactiae 1.5	*K. oxytoca* 1.8	*S. aureus* 2.5
Other species 5.8	Other species 9.7	*E. faecium* 2.0
		K. oxytoca 2.0
		Other species 9.1

Source: Reprinted from *J Infect*, 46(2), Farrell DJ et al., A UK multicentre study of the antimicrobial susceptibility of bacterial pathogens causing urinary tract infection, 94–100, Copyright (2003), with permission from Elsevier.

Further Investigations

In the majority of women with a single episode of simple acute cystitis, there is no need for further investigation. However, women with proven recurrent cystitis and those with a childhood history of UTI, persistent infection that does not respond to therapy, or persistent hematuria warrant further investigation.

Renal function should be assessed with serum creatinine, urea, and electrolytes. In specific cases, it may be helpful to exclude atypical infections (*Mycoplasma hominis*, *U. urealyticum*, and *C. trachomatis*). The usual history is of a woman suffering repeated cystitis episodes, which improve with antibiotics, but symptoms return as soon as antibiotics are stopped. Often, there have been repeated MSUs that demonstrate a sterile pyuria, but no growth on culture. One study found a positive culture for ureaplasma in 26% of the specimens tested for atypical organisms and 7.6% revealed ureaplasma and mycoplasma [98]. They were cultured in 4.3% of patients with sterile pyuria. Although the numbers are small, an improvement rate of 71% was found with 3 months of antibiotics (norfloxacin in most patients).

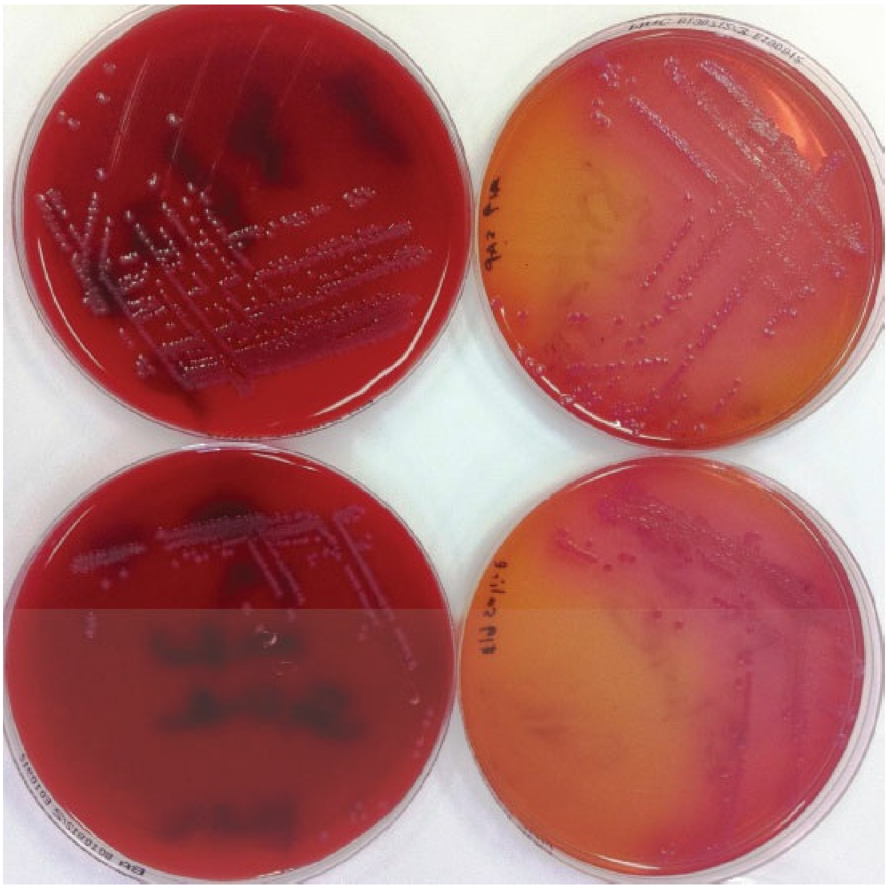


Figure 56.3 Escherichia coli growing on horse blood (left) and MacConkey (right) agars.

Ultrasound of the entire renal tract to eliminate hydronephrosis or calculi, with post–micturition scan to exclude residual >100 mL, is important. Pelvic ultrasound to rule out pelvic mass is worthwhile at the same time. The upper tracts can be imaged using CT urography, which has largely replaced intravenous pyelograms [99]. Renal imaging on dimercaptosuccinic acid scan may be needed in protracted or recurrent upper tract infection. Mercaptoacetyl triglycine and technetium-labeled diethyltriaminepentaacetic acid may also be considered in order to exclude both upper urinary tract obstruction and renal scarring.

Women with recurrent UTI not responding to simple prophylactic measures (see in the succeeding text) or those with hematuria should undergo cystoscopy (although if urine cytology is positive, this should be done by a urologist). Follicular cystitis (Figure 56.4), which may indicate IBCs, can benefit clinically from diathermy to these lesions, but this has not been systematically reviewed. Evidence of perforation of the bladder by a previous continence procedure (i.e., TVT) needs careful scrutiny with a 70-degree telescope, as this may cause recurrent UTI that is resistant to any therapy. Search for the lumen of a urethral diverticulum requires meticulous examination with a cystourethroscope (after MRI scan).

TREATMENT

Management of bacterial cystitis is aimed at treating the current infection, with eradication of clinical symptoms and microbiologically significant bacteriuria/pyuria, and preventing further recurrences, by correcting risk factors and instigating a prophylactic regime where needed.

General Measures

Patients with acute cystitis should be encouraged to increase their fluid intake in order to achieve a short voiding interval and a high flow rate, which will help to dilute and flush out the infecting organism. Symptomatic relief may be provided by alkalinization of the urine, drinking a large teaspoon of bicarbonate of soda (or commercial preparations, e.g., Ural) in a glass of water every 3–4 hours for 2–3 days. With such measures, spontaneous remission of symptoms may occur in up to 40% of women [100], although in the urogynecology patient with associated pelvic dysfunction, a urine culture should be performed and appropriate antibiotics should be given if symptoms are not greatly resolved when the culture result is known. The common practice of patients simply alkalinizing and diluting the urine is fraught with difficulty in those with coexistent cystocele or incontinence.

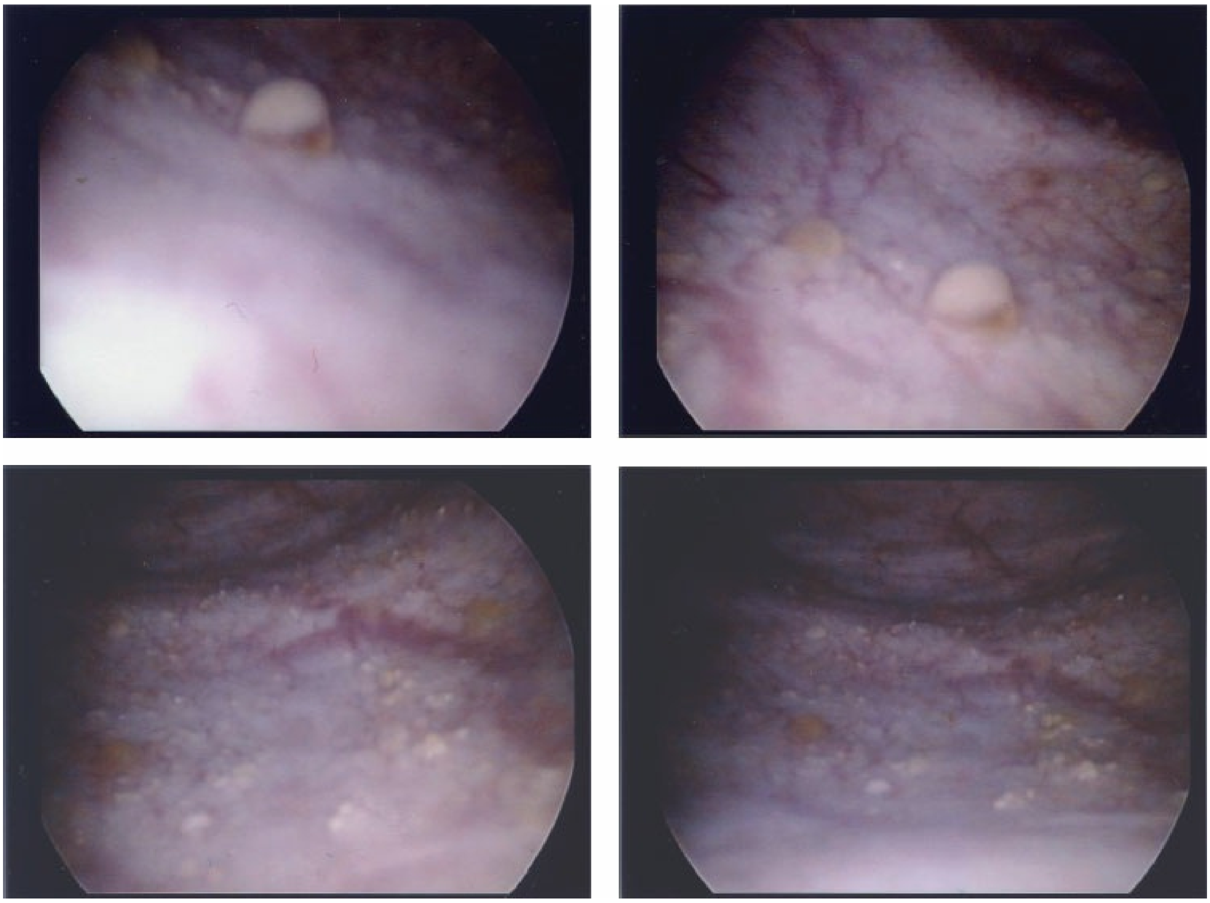


Figure 56.4 Follicular cystitis seen during cystoscopy performed for recurrent urinary tract infections.

ANTIMICROBIAL THERAPY

Ideally, drugs should be reliably absorbed after oral administration, safe, and well tolerated. Where the pathogen is known, the most precise antibiotic should be used. When treating an acute episode of cystitis encountered in the urogynecology clinic, the antibiotic with the greatest likelihood of eradicating the most common organism (*E. coli*) appears to be nitrofurantoin (100% susceptibility) [87]. Because it is highly concentrated in the urine but serum and tissue levels are subtherapeutic, it does not generally cause vaginal monilia; however, it cannot be used to treat pyelonephritis [101]. It has a complex mode of action, so that acquired resistance is uncommon [101,102]. Importantly, nitrofurantoin is one of few oral antibiotics for cystitis due to ESBL-producing organisms alongside fosfomycin and pivmecillinam with susceptibilities of 94%, 97%, and 85%, respectively [103]. Adverse effects other than nausea are rare and this can be contained by taking the drug with food, which also increases the absorption of nitrofurantoin and the duration of therapeutic levels [101]. The macrocrystalline formation, such as in macrodantin, slows absorption, which reduces nausea and vomiting.

Many of the antibiotics that were most commonly used to treat UTIs now have to be used with caution, either because resistance rates among uropathogens are high (as in the case of amoxicillin and trimethoprim) or because of the association with *C. difficile* (as in the case of cephalosporins and quinolones).

Undue emphasis is often placed on the distinction between bactericidal and bacteriostatic antibiotics. In most cases, it makes no difference to outcome. However, bactericidal antibiotics are preferred on theoretical grounds for patients with immunodeficiencies. Of the antibiotics commonly used to treat UTIs, the β-lactam antibiotics and aminoglycosides and fluoroquinolones are the most reliably bactericidal.

Individual Antibiotics

Nitrofurantoin

Nitrofurantoin is excreted in urine in high concentrations and has little action systemically. It is converted by bacterial nitrofuran reductase to active forms that attack ribosomal proteins, DNA, and other macromolecules. Resistance to this agent is uncommon and may be chromosomal or plasmid mediated. There may be antagonism with quinolones if taken in combination. This agent is generally regarded as a urinary antiseptic because of its negligible tissue penetration and low blood levels.

Although nitrofurantoin is highly effective against *E. coli*, *Klebsiella* and *Enterobacter* sp., and *Streptococcus* in acid urine, it has no effect at all against *Proteus* or *Pseudomonas* species as these organisms split urea-producing ammonia and an alkaline urine.

Nitrofurantoin is safe during pregnancy, but is contraindicated at term because of the risk of causing neonatal hemolysis. Nitrofurantoin is used in caution in the elderly, due to it being contraindicated in patients with renal insufficiency. Recent data have proven its use to be both effective and safe in those with a creatinine clearance greater than 40 mL/min [66].

Amoxicillin

Amoxicillin is a derivative of ampicillin that has a similar antibacterial spectrum but is better and more reliably absorbed. Both antibiotics contain a β-lactam ring and are effective against Gram-negative and Gram-positive organisms, targeting the cross-linkages of the bacterial cell wall, and are destroyed by bacterial beta-lactamase. These drugs are no longer recommended as first-line empiric therapy for UTIs because of the high prevalence of resistance among *Enterobacteriaceae*. Augmentin (co-amoxiclav) is a combination of amoxicillin and clavulanic acid that inhibits the β-lactamase enzymes produced by many amoxicillin-resistant bacteria. Augmentin has a spectrum of antibacterial activity suitable for treating UTIs as it is also effective against Gram-positive pathogens. Although co-amoxiclav use has been associated with *C. difficile*, the association may be less strong than with cephalosporins. Co-amoxiclav has therefore superseded second-generation cephalosporins in many hospitals, but it should still be used with caution, especially in the elderly [104].

Cephalosporins

Cephalosporins act in a similar fashion to penicillins by targeting the cross-linkages of the bacterial cell wall to prevent replication and weaken the rigid structure allowing cell death by lysis. First-generation cephalosporins are effective against most community-associated uropathogens, but they are not active against enterococci, *Enterobacter*, and *Pseudomonas*. Although serum levels of first-generation cephalosporins are poor after oral administration, they appear in high concentrations in urine, so they are useful for cystitis but not pyelonephritis. For treating UTIs, the newer and more expensive second-generation oral cephalosporins offer little or no benefits over the earlier (and cheaper) cephalosporins. The third-generation cephalosporins are resistant to the effects of simple beta-lactamases and have found widespread use in empiric therapy for acute urosepsis often in combination with an aminoglycoside.

Trimethoprim

Trimethoprim blocks the folic acid metabolic pathway in bacteria and was widely used as first-line empiric therapy for UTIs; however, resistance is increasing even in the community. Trimethoprim is best avoided in pregnancy (especially first trimester), because of the theoretical risk of teratogenicity. Co-trimoxazole (Bactrim) is a mixture of trimethoprim and sulfamethoxazole, rarely offers any benefits over trimethoprim, but has a higher risk of side effects. The U.K. Committee for Safety of Medicines recommends that co-trimoxazole should be used only where there is good bacteriologic evidence of benefit over trimethoprim.

Tetracyclines

Tetracyclines cover 50%–90% of most uropathogens, including atypical microorganisms. They are bacteriostatic and act on the bacterial ribosome to block protein synthesis. Other than doxycycline and minocycline, they are excreted mainly in the urine. However, they are little used for treating UTIs, and they are deposited in growing bones and teeth and are contraindicated in pregnancy, breastfeeding women, and children aged <12 years.

Fluoroquinolones

Fluoroquinolones block bacterial DNA replication and include ciprofloxacin, ofloxacin, and norfloxacin. Ciprofloxacin is the only orally effective antibiotic against *P. aeruginosa*. Because high drug concentrations occur in urine, they may be effective in UTIs due to Gram-positive bacteria, although they are not the recommended first-line therapy for these infections. They are contraindicated in pregnancy and recommended for use in children only where there is no alternative. Nalidixic acid is an older quinolone antibiotic that is inactive against *P. aeruginosa* and is no longer used.

Carbapenems

Carbapenems are related to β-lactam antibiotics and have found a niche as a reserve antibiotic for treating antibiotic-resistant bacteria. These are expensive very broad-spectrum β-lactam antibiotics that are for intravenous use only. Their main use in treating UTIs is in treating infections with ESBL-producing Gram-negative bacteria, including strains that are resistant to other antibiotic classes such as the fluoroquinolones and aminoglycosides. Meropenem and imipenem with cilastatin are the most commonly used carbapenems for hospital inpatients. Ertapenem is another carbapenem antibiotic. Unlike meropenem and imipenem, cilastatin has no useful antipseudomonal activity, but it has a longer half-life, permitting once daily administration so that it can be used for outpatient therapy of infections with multiresistant bacteria such as ESBL producers.

Piperacillin–Tazobactam

This is a combination of piperacillin (an antipseudomonal penicillin) and tazobactam (a β-lactamase inhibitor). It has an antibacterial spectrum that is similar to co-amoxiclav, together with activity against *P. aeruginosa*. It appears to be much less likely to select for *C. difficile* than the broad-spectrum cephalosporins and has largely superseded their use in many hospitals.

Aminoglycosides

Aminoglycosides such as gentamicin and amikacin have been used to treat serious infections, especially with Gram-negative bacteria, for several decades. Their action is at the level of ribosomes where they interfere with protein metabolism. The later introduction of broad-spectrum cephalosporins and fluoroquinolones offered an apparently safer alternative to the aminoglycosides and their use declined. However, aminoglycosides appear to be much less likely to promote *C. difficile*, and they are experiencing a renaissance as a treatment for serious infections. Once-daily administration is now generally used, being as effective and with less risk of toxicity than traditional three times daily regimens. Treatment duration should be limited and not prolonged when other antibiotics would suffice.

Duration of Antibiotic Therapy in Acute Simple UTI

Compliance with therapy may be improved by using shorter courses of antimicrobial therapy or ideally by using a single-dose regimen. However, a large number of studies have assessed the use of single-dose therapy and found it not to be as effective as a short-term (3-day) regimen [105]. There is also a risk of selecting resistance in the surviving bacteria. There is no evidence to show that protracted courses are more effective in uncomplicated lower UTIs in adult women [106].

PREVENTION OF BACTERIAL CYSTITIS

Prophylaxis

In women complaining of recurrent infections related to sexual intercourse, postcoital voiding should be encouraged. Appropriate advice regarding bladder emptying such as double voiding may also help those with voiding difficulties. Meticulous attention to perineal hygiene, including bathing the perineum with a salt-water solution at the first symptoms of infection and postcoitally in affected women, is a useful self-help regime as published by Kilmartin [107].

Antibiotic Prophylaxis

Antibiotics are effective when used as a prophylaxis for recurrent UTIs [108] in premenopausal women who do not respond to the aforementioned measures and in postmenopausal women who do not respond to topical estrogen (described in the succeeding text). A long-term low-dose prophylaxis with nitrofurantoin or trimethoprim for 6 months may be considered. Patients are less likely to stop nitrofurantoin prematurely due to side effects if the macrocrystalline formation (Macrodantin) is used rather than the microcrystalline form [102]. Nitrofurantoin should not be used for more than 12 months continuously due to the small risk of pulmonary fibrosis (usually in those with renal insufficiency) [101]. Self-diagnosis and self-treatment by the patient have been proven as efficacious as continuous therapy in both younger women [109] and the elderly [110]. Adverse effects were significantly lower, suggesting it may be a good alternative as well as reducing antibiotic use and costs. Postcoital therapy has been proven to be as effective as daily long-term medication [111]. The choice of antibiotic depends on the bacteria found on culture and their patterns of resistance, as well as the patient's history and known allergies. Side effects can be a disadvantage. However, with the ever-rising bacterial resistance to antibiotics, other methods in treating recurrent UTIs are becoming increasingly important.

Estrogen Therapy in Postmenopausal Women

Endogenous estrogen levels drop after menopause, resulting in a decrease in lactobacilli colonization of the vagina, a rise in vaginal pH, and a subsequent increase in colonization with uropathogenic bacteria. Estrogens encourage the growth of *Lactobacilli*, lowering the pH to the desired level of 4.5, which inhibits bacterial growth [112]. Additionally, it induces the expression of antimicrobial peptides and promotes tighter intercellular connection, prohibiting bacteria from reaching cells [112]. Moreover, estrogen also possibly helps decrease postvoid residual due to improved contractility of the bladder, therefore reducing another risk of cystitis. Estrogens can be administered either locally (cream, pessaries, estradiol-releasing rings) or orally. Although oral estrogens do lower the vaginal pH, they have not been effective in preventing the recurrence of UTIs [64]. Administering estrogens locally, by applying estriol cream or inserting an estrogen pessary, significantly decreases the vaginal pH as well as reducing recurrent UTIs. A randomized controlled trial by Raz et al. compared estriol cream to placebo cream with a follow-up of 8 months [113]. There was a significant reduction in UTI episodes in the group given estriol cream (0.5 versus 5.9 episodes a year, $p < 0.001$). A higher percentage of women also remained UTI-free. After estriol treatment, the colonization of *Enterobacteriaceae* halved and was replaced by *Lactobacilli*, absent prior to treatment. A trial comparing estradiol-releasing silicone ring (Estring) to no treatment demonstrated a greater percentage remaining UTI-free in those in the treatment group (45% versus 20%, $p = 0.08$). Estring was also associated with a reduction of recurrences and a prolonged interval between infections [114]. Overall, the evidence supports the use of local estrogen in postmenopausal women with recurrent UTIs and should be offered.

Methenamine Salts

Methenamine hippurate (Hiprex) is the most common form of methenamine salts used to prevent UTIs. It produces formaldehyde from hexamine, which has bacteriostatic effects. However, studies have demonstrated that a urinary pH below 5.5 is required to generate bacteriostatic levels of free formaldehyde from methenamine hippurate [115]. Therefore, certain bacteria that increase the pH of urine, such as *Proteus* and possibly *Pseudomonas*, may not be prevented. Ascorbic acid can be used in high doses (1–4 g) to help lower the urinary pH. Overall, methenamine hippurate is well tolerated and it is not associated with antibiotic resistance.

A Cochrane review published in 2012 included 13 studies of variable quality [116]. Subgroup analyses demonstrated possible benefits in patients without renal tract abnormalities and a significant reduction in symptomatic UTIs was seen when treating these patients in the short term (7 days or less). However, the authors recommend further well-designed RCTs due to the mixed quality of the included studies.

Cranberry

Cranberry (*Vaccinium macrocarpon* Ait) products such as tablets and juice have long been used to reduce cystitis. There is increased interest in research regarding cranberry efficacy, because of the emergence of antibiotic-resistant strains of bacteria.

Recent studies found two types of chemical compounds in cranberries that prevent bacterial adhesion, the monosaccharide fructose and proanthocyanidins (PACs) [117]. In vitro studies have demonstrated that fructose inhibits adhesion of (mannose-sensitive) type 1 fimbriae to uroepithelial cells, although this effect has not yet been clinically proven. PACS, especially the A-type linkages, are thought to be of significant importance in preventing P-fimbriated *E. coli* adhesion to uroepithelial cells [117,118].

Although cranberry has been shown to prevent adhesion of UPEC to urothelial cells in vitro, clinical trials have shown varying results. Stothers et al. randomized 150 women to treatment with cranberry juice, cranberry tablets, or placebo [119]. Both cranberry products significantly decreased the number of women suffering from at least 1 UTI a year (20% and 18%, respectively) compared to placebo (32%). The Cochrane review in 2012 [120] concluded that cranberries did not significantly reduce the risk of recurrent symptomatic UTIs, in contrast to their previous publication. However, the studies were of limited quality, as the type of product and quantity of active cranberry ingredient used differed greatly between the studies or were not even noted. A second large meta-analysis found that there was some evidence that cranberry reduces symptomatic UTIs, especially in women with recurrent UTIs, and recommended its use [121].

In vitro studies have shown that there is a clear dose dependency [118]. Although both 36 and 72 mg of PAC equivalents per day are effective in reducing anti-adherence properties of *E. coli*, 72 mg has greater efficacy at 24 hours. Therefore, if patients are using cranberry products to reduce recurrent UTIs, they should be advised to use products containing at least 36 mg PACs. It may be more beneficial to consume two doses of 36 mg, in the morning and evening. “Cysticlean R” has an extremely high PAC content (118 mg) and is the most commonly used in the United Kingdom. More human trials are required to confirm these effects in preventing UTIs.

D-Mannose Oral Therapy

Because the FimH pili of *E. coli* bind to urothelial cell receptors containing mannose, small clinical trials have shown benefit for patients who ingest D-mannose, a large molecular weight sugar that attracts *E. coli* to the molecule and facilitates binding to superficial urothelial cells that regularly desquamate and are swept out into the urine (see www.dmannose.co.uk). Randomized trials of this therapy are not yet available.

Probiotics

Probiotics are defined by the World Health Organization as “live microorganisms, which when administered in adequate amounts confer a health benefit to the host” [122]. Recent work on their effects to replete the colonization of lactobacilli has shown promising results. Stapleton et al. randomized 100 women with recurrent UTIs to *Lactobacillus crispatus* vaginal suppositories (Lactin-V) or placebo after conventional antibiotic treatment. In the treatment group, prolonged colonization with *L. crispatus* was demonstrated, and the incidence of recurrent UTI was reduced by almost half (15% in the Lactin-V group versus 27% in the placebo group, $p = 0.01$) [123]. Another study comparing *Lactobacilli* (*L. rhamnosus* and *L. reuteri*) to trimethoprim prophylaxis did not reach noninferiority criteria (recurrence in 79% versus 69%, respectively). However, there was a striking increase in antibiotic-resistant *E. coli* after trimethoprim from 20%–40% to 80%–95% [124].

Immunoprophylaxis

Various types of immunoprophylaxis have been studied using bacterial extracts. Oral immunostimulant OM-89 significantly decreased the incidence of UTIs (by approximately 50%) when compared to placebo. The percentage of patients that developed side effects was comparable to the nontreatment groups [115]. Vaginally applied vaccines have also been developed, but the success has been limited in human pilot studies. Further research in this area with larger randomized controlled trials is needed [115].

EMERGING ASPECTS OF BACTERIAL CYSTITIS IN UROGYNECOLOGY: THE WOMAN WITH REFRACTORY DETRUSOR OVERACTIVITY

Bacterial Cystitis and Overactive Bladder

Classically, bacterial cystitis results in inflammation of the lower urinary tract, which causes dysuria and foul-smelling, discolored urine. The notion that bacterial cystitis may also be associated with incontinence is not generally discussed in the infectious disease literature, although most continence clinicians are aware of this problem. For the last 40 years, urodynamic DO has been considered a separate and independent condition. However, doctors have traditionally excluded bacterial cystitis (by dipstick test or urine culture) before commencing urodynamic tests [125].

Older urological publications did propose a link between "uninhibited neurogenic bladder" [126] or urge incontinence [127] and recurrent urinary infection. The suggested mechanism was either ischemia in the bladder wall [126] or an increased sensory input from the inflamed mucosa [128,129]. In 2000 and 2004, two large urodynamic studies (n = 862 and 1017) did show that women with newly diagnosed DO had classical cystitis (8%–10%) compared to 1%–4% in those without DO [125,130,131].

In the last 10 years, urogynecologists have shifted away from the term "urodynamically proven DO" and moved toward the term "overactive bladder syndrome," which by definition excludes bacterial cystitis. Despite this move away from diagnostic urodynamic testing, clinicians became increasingly aware of the problem of refractory OAB [132]. The notion that at least one third of these refractory women were found to have some degree of bacterial cystitis (as evidenced by bacteriuria with or without pyuria or histological inflammation on biopsies) has been reported by four research groups in the last 4 years [2,125,133–142].

In a study in Sydney, 50 women with refractory idiopathic DO over 2 years were asked to provide an MSU whenever their OAB symptoms worsened. None of these patients had dysuria or foul-smelling urine [142]. The results showed that 39% had bacteriuria, versus 6% of the controls. As regards only "low-count bacteriuria," 17 of the refractory idiopathic DO (IDO) group versus 2% of the control group showed this finding [125].

The same authors consequently studied CSUs taken at urodynamic testing, from patients with newly diagnosed IDO versus other types of incontinence (n = 151), compared with CSU taken from 62 continent women with no OAB symptoms [143]. This revealed an odds ratio of 4.06 for any bacteriuria in the incontinent group versus continent controls, in particular patients with pure DO (odds ratio 4.4). Another study of catheter specimens of patients with refractory IDO revealed bacteriuria $>10^3$ CFU/mL in 27% of these refractory patients [125,144].

Simultaneously, another group in London was investigating the problem of refractory DO by evaluating bladder biopsies. Of the 106 women studied, histopathological analysis revealed chronic cystitis in 96 women and follicular cystitis in 3 women (93% combined) [135]. The same group went on to evaluate microbiological culture of homogenized bladder biopsies from 156 women with refractory OAB, of whom 38% had a history of recurrent bacterial cystitis. Although most patients had sterile CSU specimens on the day, a wide range of microbes were cultured, including some fastidious organisms, from bladder biopsies in 52% of patients [125,145].

At the same time, a further group in London was studying a broader group of patients with new-onset urgency/nocturia and other lower urinary tract diseases (LUTDs), without dysuria. A study comparing "classical cystitis" to "low-count bacteriuria" cystitis in 470 CSU specimens revealed cystitis rates of 15% versus 29%, respectively [97]. The authors concluded that the use of the "classical" threshold for UTI diagnosis in patients with nondysuric LUTD was of concern. They subsequently investigated women with chronic "urgency" associated with other LUTDs, compared to controls. CSU specimens revealed a wide array of organisms causing bacteriuria at the 10^2 diagnostic threshold in the LUTD group [125,138].

A study on women with urgency incontinence undergoing treatment with onabotulinum toxin A injection revealed increased symptoms in those in which bacterial DNA was detected using quantitative polymerase chain reaction (qPCR) [146]. Although this did not affect the outcome of the treatment, those positive for bacterial DNA were more likely to develop a UTI posttreatment.

Moreover, additional work has shown that bacteria may chronically reside in urothelial cells of the bladder, therefore forming IBCs resulting in low-count bacterial cystitis and possibly contributing to refractory OAB and recurrent UTI due to reinfection [58,147,148]. The development of drugs capable of penetrating the membrane of infected cells is needed, so as to eradicate these bacterial colonies [125].

In the last 5 years, there have been two studies of antibiotic therapy in patients with OAB. In 2011, researchers from University College treated 147 patients with OAB with nitrofurantoin or cephalexin (combined with antimuscarinic drugs and bladder training). For comparison, 212 patients with OAB, but without pyuria, who had received the same standard therapy previously, were studied. The prevalence of traditional cystitis on MSU was 25% versus 12%, respectively. The response to treatment (voids per 24 hours) was significantly greater in the antibiotic group versus standard treatment group ($p < 0.001$) [136]. Few microbiological details of patients' urine samples were provided. Arising from the bladder biopsy study of Digesu et al. [135], the same authors treated 39 women who had refractory idiopathic DO and biopsy evidence of chronic cystitis, with a 6-week course of rotating antibiotics (ciprofloxacin, doxycycline, cephalexin). This treatment yielded a significant reduction in voiding frequency, urgency scores, quality of life tests (all $p < 0.05$), as well as reduction in urinary nerve growth factor [141]. Again, no microbiological details regarding the persistence or cure of bacterial cystitis were given in this open prospective study [125]. Currently, a placebo-controlled phase II study is in progress in Australia (ACTRN12613000285752).

CONCLUSION

- Bacterial cystitis is common in women of all ages and is a major problem in urogynecology.
- In contrast to previous beliefs, urine is commonly not sterile.
- Rigid adherence to Kass's criteria for classical cystitis and the use of standard urine culture techniques lead to significant underdiagnosis of UTI, particularly in women with refractory OAB.
- In the last two decades, multiresistant uropathogens are becoming increasingly prevalent so that clinicians must be ever more vigilant in their choice of antimicrobial therapy.

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57 Vaginitis

J.D. Sobel

INTRODUCTION

Vulvovaginal symptoms are extremely common and are a major reason many women seek healthcare [1]. Vaginal symptoms include an abnormal discharge, which may be caused by either vaginal or cervical infection or may be due to numerous noninfectious causes. Other common symptoms include vulvovaginal pruritus, irritation, discomfort, burning, genital malodor, and variable discomfort or pain during or following intercourse. Women may perceive a change in normal vaginal discharge reflecting a qualitative or quantitative alteration. Clinicians should not trivialize and dismiss this complaint [2]. Instead, they should thoroughly evaluate the women's symptoms by clinical examination and routine laboratory tests such as pH, microscopy, and occasionally culture. Some patients have other comorbid disorders such as atopy and common dermatoses, e.g., eczema or psoriasis, which may be relevant to vulvar symptoms. While bacterial vaginosis (BV), vulvovaginal candidiasis (VVC), and trichomonas vaginitis are the most common infectious entities causing vulvovaginitis, it should be emphasized that vulvovaginal symptoms are more frequently the result of noninfectious etiology. Clinicians should cease to restrict consideration of differential diagnosis of vulvovaginal symptoms, considering only cervical or vaginal infection as the cause of symptomatology. Clinicians are required to reach a specific diagnosis and avoid empiricism. Prescribing empirical measures including the use of steroids when no diagnosis is available should be avoided. Syndromic medicine is not an acceptable standard of care in industrialized countries (Table 57.1).

CANDIDA VULVOVAGINITIS

Epidemiology

VVC is extremely common in adolescents and adults[3]. Of female university students, 50% will have at least one physician diagnosed episode by the age of 25 and as many as 75% of premenopausal women report having had at least one episode and 45% of women have two or more episodes [4]. VVC is less common in postmenopausal women unless they are taking estrogen therapy. It is estimated that 6%–8% of adult women suffer from recurrent *Candida* vaginitis (RVVC), which translates into millions of women worldwide [3,4]. RVVC is defined as four or more episodes in a given year. Epidemiological data are incomplete, however, for several reasons: (1) Diagnosis of VVC is nonreportable and therefore prevalence estimates rely mainly upon self-reported histories of diagnosis by a physician. (2) *Candida* infection is routinely diagnosed without the benefit of microscopy or culture, and as many as one-half of the women given this diagnosis may have other conditions. (3) Finally, the widespread use of over-the-counter (OTC) antifungal drugs makes epidemiological studies difficult to perform in most countries. Self-diagnosis and therefore self-therapy is prevalent.

Pathogenesis

Candida organisms probably gain access to the vagina via migration across the perianal area from the rectum. However, once colonization occurs, long-term colonization frequently persists for months and years. Following *Candida* colonization, the organisms persist in the presence of the normal protective vaginal flora without causing symptoms until additional precipitating factors alter the delicate relationship between the *Candida* microorganisms and the vaginal microbiota as well as protective host defenses. A large number of underlying risk factors contribute to both colonization as well was symptomatic disease (Figure 57.1).

Microbiology

Candida albicans is responsible for 90% or more of episodes of VVC [3]. The remainder of the attacks are caused by non-*albicans Candida* species, which included *C. parapsilosis*, *C. glabrata*, *C. tropicalis*, and a variety of rare *Candida* species, an occasional non-*Candida* yeast *Saccharomyces* species. Some investigators have reported an increased frequency of the non-*albicans Candida* species particularly *glabrata*, but this has not been confirmed [5]. The non-*albicans Candida* species appear to be less virulent both in patients as well as in animal models used to study pathogenesis. Nevertheless, these species are still capable of causing symptomatic vaginitis, although their causal role needs to be established in each given patient. Accordingly, all *Candida* species produce similar vulvovaginal symptoms, although the severity of symptoms appears to be milder with *C. parapsilosis* and *C. glabrata* as compared to *C. albicans*.

Risk Factors

Sporadic attacks of VVC frequently occur without identifiable precipitating factors. Nevertheless, a number of factors do predispose to symptomatic infection:

- One-quarter to one-third of women are prone to VVC during or after taking broad spectrum antibiotics. No antibiotics either systemic or local are immune from this complication. The mechanism whereby antibiotics induce *Candida* vaginitis has not been fully established. Previously, it was thought that antibiotics inhibit bacterial flora primarily in the gastrointestinal tract or possibly within the vagina allowing the overgrowth of potential pathogens such as *Candida*. However, confirmation of this hypothesis is not available. Administration of lactobacillus (oral or vaginal) probiotics during or after taking antibiotic therapy does not prevent post-antibiotic VVC [6].

Table 57.1 Vaginal Syndromes and Their Etiologies

Type	**Etiology**
Infectious	
Bacterial vaginosis	Mixed *Gardnerella vaginalis*, anaerobes (*Prevotella, Porphyromonas, Bacteroides, Fusobacterium, Peptostreptococcus, Mobiluncus, Megasphaera, Eggerthella, Leptotrichia*, members of the *Clostridiales* order), and genital mycoplasmas
Candida vulvovaginitis	90% *Candida albicans*, 10% *non-albicans Candida* species; rarely other fungi
Trichomoniasis	*Trichomonas vaginalis*
Rare bacterial	Group A *Streptococcus*
Noninfectious	
Atrophic vaginitis	Estrogen-deficient states (postmenopausal, postpartum, post-antiestrogen therapy)
Contact vulvovaginitis	Contact dermatitis (hypersensitivity)
Chemical irritant vaginitis	Soaps, detergents, topical antimycotics
Allergic vaginitis	Allergens
Desquamative inflammatory vaginitis (DIV)	Unknown (bacterial? immune mechanism?)
Erosive lichen planus	Immune mechanisms
Collagen vascular diseases (SLE)	Vasculitis
Pemphigus and pemphigoid syndromes	Immune mechanisms

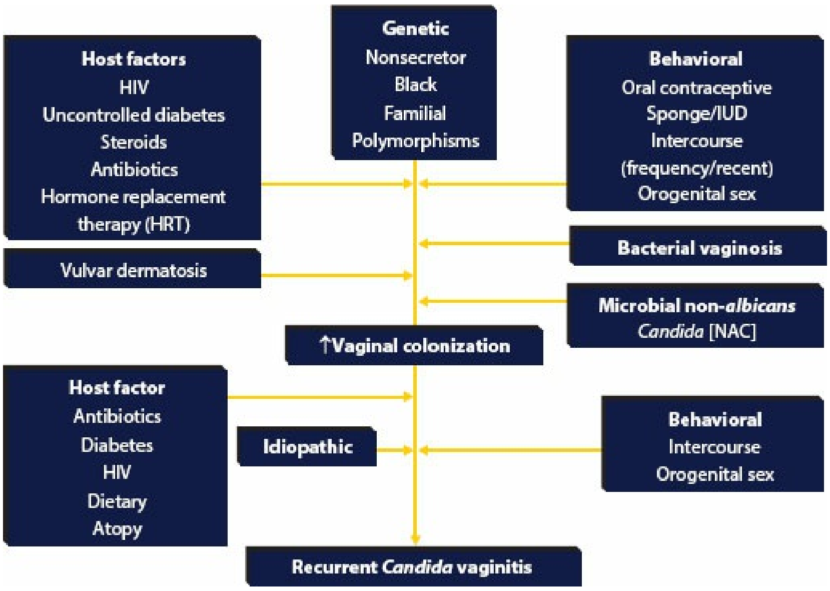

Figure 57.1 Pathogenesis of recurrent *Candida vaginitis* (RVVC).

- *Increased estrogen levels*. VVC is rare before puberty and tends to be less frequent in the postmenopausal women not taking any form of exogenous estrogen. Similarly, symptoms tend to flare in the premenstrual period on a cyclical basis. VVC appears to be more common in the setting of increased estrogen levels such as with oral contraceptives, especially when estrogen dose is high, pregnancy, and premenopausal estrogen therapy, especially with topical use of estrogen [3].
- *Diabetes mellitus*. Women with diabetes, especially those with poor glycemic control, are more prone to VVC. In particular, women with Type 2 diabetes appear to be prone to *C. glabrata* infections; nevertheless, most women with RVVC do not suffer from diabetes including prediabetes. Routine tests for diabetes are not indicated in women prone to VVC.
- *Immunosuppression. Candida* infections are more common in immunosuppressed patients especially those taking corticosteroids or with uncontrolled HIV infection [7].
- *Contraceptive devices*. Vaginal sponges, diaphragms, and IUDs have been associated with VVC. Spermicides are not thought to increase VVC.
- *Genetic susceptibility*. Although a genetic factor was suspected for many years, evidence confirming this relationship was not available until recently [8]. Earlier, suspicions were based on a family history and blood group, including blood secretor status. It is likely that more than one genetic factor is complicit in the pathogenesis of VVC. Genetic factors may be important in colonization, as well as in determining the immune response to the presence of proliferating organisms within the vagina [7,8]. Accordingly, VVC has been reported with decreased in vivo concentrations of mannose-binding lectin (MBL) and increased concentrations of IL-4 [9,10]. Two specific gene polymorphism variance in the MBL and IL-4 genes can account for this finding in some high-risk women, but their relevance remains controversial. The prevalence of a variant MBL gene is higher in women with RVVC than in controls without candidiasis [10]. Recognition of *C. albicans* by the innate hose defense system is mediated by pattern recognition from the toll-like receptor (TLR) and lectin-like receptor families. Mannans from the *Candida* cell wall are recognized by the mannose receptor, and TLR4 and TLR2 recognize phospholipomannan and collaborate with protective cytokine production [8].
- *Behavioral factors*. Although VVC is not considered a sexually transmitted disease because it occurs in celibate women and since *Candida* is considered part of the normal vaginal flora, this does not mean that the sexual transmission of *Candida* microorganisms does not occur or that VVC is not associated with sexual activity. Accordingly, one observes an increase in the frequency of VVC at the time that most women begin regular sexual activity [11]. Male partners of infected women are more likely to have penile colonization than partners of uninfected women, and usually with the same strain as indicated by strain typing [12].

- There is no high-quality evidence showing the link between VVC and hygienic habits or in using tight or synthetic clothing.
- *HIV infection*. VVC occurs with higher incidence and greater persistence but not greater severity among HIV-infected women. A significantly increased rate of symptomatic infection is confined only to HIV-infected women with very low CD4 counts and very high viral load, a population likely to manifest other AIDS manifestations. HIV testing of women, only for the indication of recurrent VVC, is not justified given that RVVC is a common condition in women without HIV infection and the majority of cases occur in HIV-uninfected women. Only women with risk factors for acquisition of HIV should be counseled and offered screening. The microbiology of recurrent VVC in HIV-infected women is the same as HIV-negative women [3].
- *Candida* colonization of the vagina in asymptomatic women may persist for prolonged periods of time until precipitating exogenous factors trigger a change in the balance between seed and soil. Triggering is most often the result of changes in the host, in which naturally occurring anti-*Candida* vaginal defensive mechanisms diminish or fail. *Candida* proliferation follows with increase in numbers of organisms and expression of virulence factors including hyphal formation and elaboration of proteases. The development of symptoms and signs of vulvovaginal inflammation, however, usually requires the involvement of the host adaptive immune response reacting to the proliferating organisms [7]. It is this latter response that is critical for the development of symptomatic VVC and may be seen as an unnecessary by-product of the host defense system reacting to the organisms.

Clinical Features

Vulvar pruritus is the dominant feature of VVC. Women may also complain of dysuria, often described as external rather than internal, irritation, soreness, and dyspareunia. There is little or no discharge and that when present is typically white and clumpy. Physical examination reveals erythema of the vulva and vaginal mucosa and vulvar edema. The discharge is typically described as clumpy and cottage cheese-like. However, it may also be thin and watery, indistinguishable from the discharge of other forms of vaginitis. Some patients, particularly those with *C. glabrata* infection, have little discharge with only erythema on vaginal examination. The vulva is invariably involved and fissures may be present. It is important to recognize that in contrast to BV, *Candida* infection involves both vulva and vagina.

Diagnosis

The vaginal pH is typically 4–4.5, which distinguishes VVC from trichomoniasis or BV. The clinical diagnosis should be confirmed by finding the organism on saline wet mount microscopy and by adding 10% KOH, which facilitates the microscopic recognition of the yeast and hyphal morphotype. Unfortunately, microscopy may be negative in 50% of patients with confirmed VVC. Empiric therapy is often considered with typical clinical findings, normal vaginal pH, and no other pathogens visible on microscopy. However, with an unconfirmed microscopy-based diagnosis, a culture should be obtained. Often empiric therapy can be delayed until the results of additional tests are available. Cultures provide confirmation of the diagnosis within 48–72 hours and also reveal the species of the organism, which facilitates the selection of the appropriate antifungal agent. Culture should always be obtained in patients with persistent or recurrent symptoms because many of these women have non-*albicans Candida* infections with reduced susceptibility to azoles. In the presence of positive microscopy and a normal pH, a routine culture is not essential, but is mandatory for microscopy-negative patients.

Low-risk commercial tests are now available as an alternative to culture. These include a DNA probe with hybridization, which is particularly useful and should provide results within several hours to confirm the initial clinical diagnosis. PCR testing is widely available through commercial laboratories and is a highly sensitive method that provides *Candida* speciation when positive. The cost efficacy of the PCR technology has not been evaluated and may take 48–72 hours for results, similar to microbial culture. Although PCR offers a more sensitive method of diagnosis, the clinical relevance of this increased sensitivity is unknown.

The mere demonstration of *Candida* presence by any of the aforementioned diagnostic methods in no way confirms the pathogenic role of *Candida* in the specific patient or clinical syndrome. This is because *Candida* is found colonizing 15%–20% asymptomatic healthy women. Accordingly, the presence of *Candida* does not imply culpability. Determination of causation of symptoms requires exclusion of other pathogens plus other noninfectious causes. There are no other infectious causes responsible for vulvovaginal symptoms at normal pH 4.0–4.5.

Differential Diagnosis

Other conditions should be considered in the differential diagnosis of symptomatic women with normal vaginal pH, and these include allergic and chemical reactions, hypersensitivity reactions, and contact dermatitis. These conditions are extremely common and frequently will cause symptoms in the presence or absence of *Candida*. If the vaginal pH exceed 4.5 or excessive polymorphonuclear leukocytes (PMNs) are present, mixed infections with BV or trichomoniasis may be present. Based on the aforementioned criteria, there should be no difficulty separating BV from *Candida* vaginitis. Self-diagnosis of VVC is frequently inaccurate. Similarly, diagnosis of *Candida* vaginitis by telephone is unreliable and is to be condemned.

Treatment

Treatment is indicated for relief of vulvovaginal symptoms. There is no indication to treat asymptomatic colonization in culture-positive women. A number of highly effective oral and intravaginal antifungals are available (Table 57.2). Nystatin is the least effective with cure rates in the 70%–75% range. The remaining antifungals have published efficacies in the 80%–88% range. Of the intravaginal imidazoles, clotrimazole, miconazole, butoconazole, and tioconazoles are available over the counter (OTC in the United States), while terconazole is available only by prescription. All these topical agents are highly effective and are prescribed as single-day to 7-day regimens. There appears to be no superiority of one regimen over another [13]. Topical regimens are well tolerated with few adverse effects, although burning may occasionally occur. Mild disease is best treated with shorter dose regimens.

Table 57.2 Therapy for Vaginal Candidiasis

Drug	**Topical agents and formulation**	**Dosage regimen**
Butoconazole[a]	2% cream	5 g × 3 days
Clotrimazole[a]	1% cream	5 g × 7–14 days
	2% cream	5 g × 3 days
	100 mg vag. tab.	1 tab. × 7 days
	100 mg vag. tab	2 tab. × 3 days
	500 mg vag. tab.	1 tab. single dose
Miconazole[a]	2% cream	5 g × 7 days
	4% cream	5 g × 3 days
	100 mg vag. supp.	1 supp. × 7 days
	200 mg vag. supp.	1 supp. × 3 days
	1200 mg vag. supp.	1 supp. single dose
Econazole	150 mg vag. tab	1 tab. × 3 days
Fenticonazole	2% cream	5 g × 7 days
Tioconazole[a]	2% cream	5 g × 7 days
	6.5% ointment	5 g single dose
Terconazole	0.4% cream	5 g × 7 days
	0.8% cream	5 g × 3 days
	80 mg vag. supp.	80 mg × 3 days
Nystatin	100,000 U vag. tab.	1 tab. × 14 days
	Oral Agents	
Ketoconazole	400 mg bid	× 5 days
Itraconazole	200 mg bid	× 1 days
	200 mg	× 3 days

Fluconazole	150 mg	Single dose

Abbreviations:vag., vaginal; tab., tablets; supp., suppository

[a] OTC in the United States

Oral agents are available in the United States for the treatment of *Candida* vaginitis and include fluconazole, which is supplied as a single 150 mg oral tablet, itraconazole, and ketoconazole. Only fluconazole is FDA approved for VVC treatment [14,15].

Selection of the appropriate antifungal agent and the duration of therapy has been facilitated by the complicated VVC and uncomplicated VVC classification. Most women (uncomplicated VVC), being healthy, host with mild to moderate, infrequent episodes of vaginitis due to *C. albicans*. Under these circumstances, patients respond to all azoles, topical or systemic, with a success rate in excess rate of 90% regardless of duration of therapy (Table 57.3).

In contrast, women with complicated VVC respond less well to short-course azole therapy. Accordingly, a compromised host women with severe vaginitis should receive more prolonged, conventional antimycotic therapy usually requiring up to 7 days of treatment [13–16]. Treatment of women infected with non-*albicans Candida* species remains problematic. *C. krusei* infection is fortunately extremely rare and resistant to fluconazole but responds rapidly to other azoles. Vaginitis due to *C. glabrata* is however refractory to all forms of azole therapy with 50% success. Somewhat improved results are achieved with vaginal boric acid and with 60%–70% eradication rates [17,18]. The best results follow vaginal therapy with 17% flucytosine cream. The latter has to be compounded, is not available commercially, and is extremely expensive. More important than selecting an antifungal agent is deciding whether to treat vulvovaginal symptoms in the presence of culture-positive *C. glabrata*. The mere finding of *C. glabrata* does not imply complicity in the pathogenesis of the clinical syndrome. More often than not, *C. glabrata* is an innocent bystander and intensive treatment regimens directed at *C. glabrata* frequently fail. Moreover, even when successful, organism elimination is not accompanied by concomitant relief or eradication of symptoms. In the experience of some investigators, less than 25% of symptomatic *C. glabrata* positive patients' symptoms can be attributed to *C. glabrata* isolated. Nevertheless, when no other explanation for symptoms is available, a trial of therapy is clearly justified, but clinicians should not trivialize the complex relationship between this yeast and vulvovaginal symptoms.

Table 57.3 Classification of Vulvovaginal Candidiasis

Uncomplicated	**Complicated**
Sporadic/infrequent VVC and	Recurrent VVC or
Mild to moderate VVC and	Severe VVC or
Likely to be *C. albicans* and	Non-*albicans* candidiasis or
Normal, nonpregnant host	Abnormal host e.g., uncontrollable diabetes debilitation, immunosuppression

Abbreviations:VVC, vulvovaginal candidiasis

Treatment of Recurrent Vulvovaginal Candidiasis

As described earlier, RVVC occurs in 5%–8% of the population in women during their reproductive period [3]. It is likely that genetic factors are operative in the overwhelming majority of such patients. Nevertheless, secondary precipitating mechanisms are frequently present and vary from patient to patient. Thus, while all patients share an underlying genetic predisposition, triggers to symptomatic episodes vary considerably. Resistance of microorganisms to azole drugs is a rare cause of RVVC.

Before embarking on any treatment protocol, the diagnosis must be confirmed by the presence of culture, which includes organism speciation. Fungal susceptibility tests are not routinely indicated unless drug breakthrough infection or refractory disease occurs with appropriate azole therapy. Every effort should be made to control trigger mechanisms including the use of antibiotics, control of diabetes, and local predisposing factors such as concomitant vulvar dermatosis. Once these factors have been excluded or treated, an induction regimen with an antimycotic followed by a long-term suppressive maintenance regimen is indicated. While this can be accomplished with topical regimens, because of the duration and frequency of therapy, oral therapy is more convenient and offers a more realistic solution.

It should be emphasized that the therapy selected is aimed at controlling symptomatic episodes rather than guaranteeing that cure will be achieved. The use of long-term suppressive maintenance regimens has been confirmed in several prospective controlled studies [19,20]. Accordingly, after an induction regimen of fluconazole 150 mg given every 72 hours for 3 doses, a weekly maintenance regimen of fluconazole 150 mg once weekly is suggested. Complete resolution of symptoms follows within a matter of weeks, and the patients remain asymptomatic for the duration of therapy, which is recommended for 6 months. During this period, the patient invariably remains culture negative and asymptomatic. Following discontinuation of therapy after 6 months, approximately 50% of the patients rapidly become recolonized and develop recurrent symptoms of VVC. However, 50% of patients will return to an attack-free life with risks similar to low-risk women. Should symptomatic recurrence rapidly follow discontinuation of therapy, repeat reinduction and maintenance therapy is recommended this time for at least 12 months. Frequently, even longer prolonged maintenance regimens are recommended and required.

BACTERIAL VAGINOSIS

Epidemiology

BV is the most common cause of vaginitis in women of childbearing age. It has been diagnosed in 17%–19% of women seeking gynecological care in family practice or student health-care settings [1]. The worldwide prevalence ranges from 11% to 48% of women of reproductive age, with variation according to population studied [21]. The prevalence increases considerably in symptomatic women attending STD clinics, reaching 24%–37%. BV has been observed in 16%–29% of pregnant women. *Gardnerella vaginalis* has been found in 10%–31% of virgin adolescent girls but is found significantly more frequently among sexually active women, reaching a prevalence of 50%–60% in some at-risk populations.

Evaluation of epidemiological factors has revealed a few clues of the cause of BV. Use of an intrauterine device and douching was found to be more common in women with BV. BV is significantly more common among black and sexually active women including lesbians.

Pathogenesis and Pathology

BV is not due to a single organism and is the result of massive overgrowth of mixed complex flora or microbiota, including peptostreptococci, *Bacteriodes* spp., *G. vaginalis*, *Mobiluncus* spp., genital mycoplasma, and a variety of recently described anaerobes [22]. There is little inflammation, and the disorder represents a disturbance of the vaginal microbial ecosystem rather than a true infection of tissues. The overgrowth of mixed flora is associated with a loss of the normal *Lactobacillus* sp.–dominated vaginal flora [21]. No single bacterial species is responsible for BV. Experimental studies in human volunteers and studies in animals indicate that inoculation of the vagina with individual species of bacteria associated with BV (e.g. *G. vaginalis*) rarely results in BV. In support of the role of sexual transmission is the higher prevalence of BV among sexually active young women than among sexually inexperienced women, and the observation that BV-associated microorganisms are more frequently isolated from the urethras of male partners of females with BV.

The cause of the overgrowth of anaerobes, *G. vaginalis*, *Mycoplasma*, and *Mobiluncus* spp., is unknown. Theories include increased substrate availability, increased pH, and loss of the restraining effects of the predominant *Lactobacillus* sp. flora. It has been reported that normal women are predominantly colonized by hydrogen peroxide–producing strains of lactobacilli, whereas women with BV have reduced population numbers of lactobacilli, and the species present lack the ability to produce hydrogen peroxide [21]. The hydrogen peroxide produced by lactobacilli may inhibit the pathogens associated with BV.

Accompanying the bacterial overgrowth in BV is the increased production of amines by anaerobes, facilitated by microbial decarboxylases. Volatile amines in the presence of increased vaginal pH produce the typical fishy odor, which is also produced when 10% potassium hydroxide is added to vaginal secretions. Trimethylamine is the dominant abnormal amine in BV. It is likely that bacterial polyamines together with the organic acids found in the vagina in BV (acetic and succinic acid) are cytotoxic, resulting in exfoliation of vaginal epithelial cells and creating the vaginal discharge. *Gardnerella vaginalis* attaches avidly to exfoliated epithelial cells, especially at the alkaline pH found in BV. The adherence of *Gardnerella* organisms results in the formation of the pathognomonic clue cells. Using broad-range DNA probes, new molecular methods have identified at least 35 new bacterial phylotypes (species), previously uncultivatable in women with BV including *Atopobium vaginae* and *Clostridial species* BVAB I, II, and III offering new insights into pathogenesis [22,23].

Prevention

Because the pathogenesis of BV is obscure, preventive measures have not been forthcoming. Although not proven to be sexually transmitted, barrier contraception may reduce occurrence and avoiding douching is recommended.

Clinical Features

As many as 50% of women with BV may be asymptomatic. An abnormal malodorous vaginal discharge, often described as fishy, that is infrequently profuse and often appears after unprotected coitus is usually described. Pruritus, dysuria, and dyspareunia are rare. Examination reveals a nonviscous, grayish-white adherent discharge.

BV has been incorrectly considered to be largely of nuisance value only. There is now considerable evidence of serious obstetric and gynecological complications of BV, including asymptomatic BV diagnosed by Gram stain. Obstetric complications include chorioamnionitis, preterm labor, prematurity, and postpartum fever [24]. Gynecological sequelae are postabortion fever, posthysterectomy fever, cuff infection, and chronic mast cell endometritis. A more recent association is reported between untreated BV and cervical inflammation and low-grade dysplasia [25]. BV is a risk factor for HIV acquisition and transmission [26]. BV is also a risk factor for acquisition of HSV-2, gonorrhea, and chlamydial infection [27].

Diagnosis

Signs and symptoms are unreliable in the diagnosis of BV. The clinical diagnosis can reliably be made in the presence of at least three of the following objective criteria:

1. Adherent, white, nonfloccular homogeneous discharge
2. Positive amine test, with release of fishy odor on addition of 10% potassium hydroxide to vaginal secretions
3. Vaginal pH > 4.5
4. Presence of clue cells on light microscopy

These Amsel features are simple and reliable, and tests for them are easy to perform. The presence of clue cells is the single most reliable predictor of BV. Clue cells are exfoliated vaginal squamous epithelial cells covered with *G. vaginalis*, giving the cells a granular or stippled appearance with characteristic loss of clear cell borders.

The offensive fishy odor may be apparent during the physical examination or may become apparent only during the amine test. Gram strain of vaginal secretions is extremely valuable in diagnosis, with a sensitivity of 93% and specificity of 70%.

Although cultures for *G. vaginalis* are positive in almost all cases of BV, *G. vaginalis* may be detected in 50%–60% of women who do not meet the diagnostic criteria for BV. Accordingly, vaginal culture has no part in the diagnosis of BV. DNA probes for G. vaginalis are both sensitive (95%) and specific (99%), but are not widely used by practitioners because of costs and lack of insurance reimbursement. Diagnostic tests are now available for rapid diagnosis measuring pH, amines, or sialidase.

Management

The most widely used oral therapy remains to be metronidazole or tinidazole [28]. Most studies using multiple divided dose metronidazole regimens of 800–1200 mg/day for 1 week achieved clinical cure rates in excess of 90% immediately, and of approximately 80% at 4 weeks. Although single-dose therapy with 2 g metronidazole achieves comparable immediate clinical response rates, higher recurrence rates have been reported. CDC-recommended regimen is metronidazole 500 mg twice daily for 7 days [28]. The beneficial effect of metronidazole results predominantly from its antianaerobic activity and because *G. vaginalis* is susceptible to the hydroxymetabolites of metronidazole. Although *Mycoplasma hominis* and *Mobiluncus curtisii* are resistant to metronidazole, the organisms are usually not detected at follow-up visits of successfully treated patients. Similarly, metronidazole and tinidazole are considered therapeutical equivalent, although tinidazole has fewer of the commonly experienced side effects.

Topical therapy with 2% clindamycin cream once daily for 7 days, clindamycin ovules for 3 days, or metronidazole gel 0.75% administered daily for 5 days have been shown to be as effective as oral metronidazole, without any of the side effects of the latter.

In the past, asymptomatic BV was not treated, especially because patients often improve spontaneously over several months. However, the growing evidence linking asymptomatic BV with numerous obstetric and gynecological upper tract complications has caused reassessment of this policy, especially with additional convenient topical therapies. Asymptomatic BV should be treated before pregnancy, in women with cervical abnormalities and before elective gynecological surgery. Routine screening for and treatment of asymptomatic BV in pregnancy remains controversial, pending the outcome of studies proving that therapy of BV reduces preterm delivery and prematurity [28,29].

Despite indirect evidence of sexual transmission, no study has documented reduced recurrent rates of BV in women whose partners have been treated with a variety of regimens, including metronidazole. Accordingly, most clinicians do not routinely treat male partners.

After therapy with oral metronidazole, approximately 30% of patients initially responding experience recurrence of symptoms within 3 months. Reasons for recurrence are unclear, including the possibility of reinfection, but recurrence more likely reflects vaginal relapse, with failure to eradicate the offending organisms and reestablish the normal protective *Lactobacillus* sp.–dominant vaginal flora. Management of BV relapse includes oral or vaginal metronidazole, or topical clindamycin, usually prescribed for 14 days. New experimental approaches including exogenous *Lactobacillus* sp. recolonization using selected bacteria-containing suppositories have been encouraging. Maintenance antimicrobial agents administered twice weekly for 4–6 months have been reasonably effective but results less than desirable [30].

TRICHOMONIASIS

Epidemiology

Studies estimate that 3–5 million American women contract trichomoniasis annually, with a worldwide distribution of approximately 180 million annual cases [31]. The prevalence of trichomoniasis correlates with the overall level of sexual activity of the specific group of women under study, being diagnosed in about 5% of women in family planning clinics, in 13%–25% of women attending gynecology clinics, in 50%–75% of prostitutes, and in 7%–35% of women in STD clinics [31]. In many industrialized countries, recent surveys indicate a decline in the incidence of trichomoniasis.

Pathogenesis and Pathology

Sexual transmission is the dominant method of introduction of *Trichomonas vaginalis* into the vagina. *T. vaginalis* was identified in the urethra of 70% of men who had had sexual contact with infected women within the previous 48 hours. There is also a high prevalence of gonorrhea in women with trichomoniasis, and both of these are significantly associated with the use of nonbarrier methods of contraception.

Recurrent trichomoniasis is common and is indicative of lack of significant protective immunity. Nevertheless, an immune response to *Trichomonas* spp. does develop, as indicated by low titers of serum antibody, but this is insufficient for diagnostic serology. Antitrichomonal IgA has been detected in vaginal secretions, but a protective role is not defined. The predominant host defense response is provided by the numerous PMNs, which respond to chemotactic substances released by trichomonads and are capable of killing *T. vaginalis* without ingesting trichomonads. *T. vaginalis* destroys epithelial cells by direct cell contact and cytotoxicity. The urethral, paraurethral, Bartholin's, and Skeene's glands are infected in the majority of patients, and organisms are occasionally isolated from bladder urine.

Prevention

Sexual transmission of trichomonads is efficiently prevented by use of barrier contraception. Spermicidal agents such as nonoxynol-9 also reduce transmission. Reinfection of women is common, hence the mandatory requirement of treatment, preferably simultaneously, of all sexual partners with metronidazole. Women can acquire the disease from other women, but men do not usually transmit infection to other men.

Clinical Features

Infection with *Trichomonas* spp. in women ranges from an asymptomatic carrier state to severe acute inflammatory disease [32]. Vaginal discharge is reported by 50%–75% of women diagnosed with trichomoniasis; however, the discharge is not always described as malodorous. Pruritus occurs in 25%–50% of patients and is often severe. Other infrequent symptoms include dyspareunia, dysuria, and, rarely, frequency of micturition. Lower abdominal pain occurs in fewer than 10% of patients and should alert the physician to the possibility of concomitant salpingitis caused by other organisms. Symptoms of acute trichomoniasis often appear during or immediately after menstruation. Although controversial, the incubation period has been estimated to range from 3 to 28 days [32].

Physical findings represent a spectrum depending on the severity of disease. Vulvar findings may be absent but are typically characterized in severe cases by diffuse vulvar erythema (10%–33%), edema, and a copious, profuse, and malodorous vaginal discharge, which is often described as being yellow-green and frothy, but is frequently grayish-white [32]. Frothiness is seen in a minority of patients and is more commonly seen in BV.

The vaginal walls are erythematous and in severe cases may be granular in appearance. Punctate hemorrhages (colpitis macularis) of the cervix may result in a strawberry-like appearance that, although apparent to the naked eye in only 1%–2% of patients, is present in 45% of cases on colposcopy.

The clinical course of trichomoniasis in pregnancy is identical to that seen in the nonpregnant state, and when untreated, it is associated with premature rupture of membranes and prematurity. Trichomoniasis is reported to facilitate HIV transmission. Trichomoniasis is a risk factor for the development of posthysterectomy cellulitis, tubal infertility, cervical neoplasma, and pelvic inflammatory disease [33].

Diagnosis

None of the clinical features of vaginitis caused by *Trichomonas* spp. are sufficiently specific to allow a diagnosis of trichomonal infection based on signs and symptoms alone. Definitive diagnosis requires the demonstration of the organism. Vaginal pH is markedly elevated, almost always above 5.0, and not infrequently 6.0. On saline microscopy, an increase in the number of PMNs is almost invariably present. The ovoid parasites are slightly larger than PMNs and are best recognized by their motility. The wet mount is positive in only 40%–80% of cases (low sensitivity). Gram stain is of little value because of its inability to differentiate PMNs from nonmotile trichomonads, and the use of Giemsa, acridine orange, and other stains has no advantage over saline preparations. Although trichomonads are often seen on Papanicolaou smears, this method has a sensitivity of only 60%–70% when compared with saline preparation microscopy, and false-positive results are not infrequently reported.

Several equivalent culture medium methods are available, and growth is usually detected within 48 hours. Culture, including “InPouch,” has now been replaced by PCR molecular detection of trichomonas DNA and should be considered in patients with vaginitis in whom an elevated pH is found together with PMN excess and absence of motile trichomonads [34].

Management

Therapy is indicated in all nonpregnant women diagnosed with trichomonas vaginitis even if asymptomatic and consists of administering the 5-nitroimidazole group of drugs—metronidazole, tinidazole, spcnidazole, and ornidazole—which are all of similar efficacy [9]. Oral therapy as opposed to topical vaginal therapy is preferred because of the frequency of infection of the urethra and periurethral glands, which provide sources for endogenous recurrence [28]. Treatment of all sexual partners is mandatory.

Treatment consists of oral metronidazole, 500 mg q12h for 7 days, which has a cure rate of 95%. Comparable results have been obtained with a single oral dose of 2 g metronidazole, achieving cure rates of 82%–88%. The latter cure rate increases to greater than 90% when sexual partners are treated simultaneously. The advantages of single-dose therapy include better patient compliance, lower total dose, shorter period of alcohol avoidance, and possibly decreased incidence of subsequent vaginitis caused by *Candida* spp. A disadvantage of single-dose therapy is the need to insist on simultaneous treatment of sexual partners.

The 5-nitroimidazoles are not in themselves trichomonacidal, but low-redox proteins reduce the nitro group, resulting in the formation of highly cytotoxic products within the organisms. Aerobic conditions interfere with this reduction process and decrease the antianaerobic activity of the 5-nitroimdazoles. Most strains of *T. vaginalis* are highly susceptible to metronidazole, with minimum inhibitory concentrations of 1 mg/L. Similar efficacy results are reported with tinidazole but the latter has a superior tolerance profile.

Patients not responding to an initial course often respond to an additional standard course of 7-day therapy. Some patients are refractory to repeated courses of therapy even when compliance is assured and sexual partners are known to have been treated. If reinfection is excluded, these rare patients may have strains of *T. vaginalis* that are resistant to metronidazole, which can be confirmed in vitro. Increased doses of metronidazole and longer duration of therapy are necessary to cure these refractory patients. The patients should be given maximal tolerated dosages of oral metronidazole of 2–4 g/day for 10–14 days. Rarely, intravenous metronidazole, in dosages as high as 2–4 g/day, may be necessary, with careful monitoring for drug toxicity. Considerable success has been observed in treating resistant infections with oral tinidazole [35]. Most investigators use high-dose tinidazole 1–4 g/day for 14 days [35]. Rare patients not responding to nitroimidazoles can be treated with topical paramomycin.

Side effects of metronidazole include an unpleasant or metallic taste. Other common side effects include nausea (10%), transient neutropenia (7.5%), and a disulfiram-like effect when alcohol is ingested. Caution should be taken when 5-nitroimidazoles are used in patients taking warfarin. Long-term and high-dose therapy increase the risk of neutropenia and peripheral neuropathy.

Treatment of symptomatic trichomoniasis in pregnancy is identical [28]. Metronidazole readily crosses the placenta and because of concern for teratogenicity, some consider it prudent to avoid its use in the first trimester of pregnancy. More recently investigators have become reassured with the use of metronidazole throughout pregnancy.

ATROPHIC VAGINITIS

Atrophic vaginitis, also called urogenital atrophy, refers to the extremely common condition that is characterized by atrophy of the vagina, vestibule, and vulva as a consequence of estrogen deficiency [1,36]. The dominant target of estrogen deficiency is the vaginal epithelium, which loses its rugosity and undergoes progressive thinning and atrophy. Simultaneously but often less conspicuous is progressive thinning of the vestibular epithelium. Atrophy of the vaginal epithelial lining is accompanied by reduced glycogen synthesis, which serves as a critical substrate for resident bacteria that break down glycogen to produce organic acid most importantly lactic acid further resulting in the loss of *Lactobacillus* species, the dominant component of vaginal microbiota. Accordingly, a consistent consequence of estrogen deficiency is elevation of vaginal pH, usually above 5.0. Low estrogen levels reduce vaginal secretions that result in vaginal dryness but not infrequently and paradoxically a vaginal discharge is perceived to exist, or may in fact present as a watery discharge. Atrophic vaginitis typically occurs in menopausal women, but it can also occur in women at any age who have a decrease in estrogenic stimulation to this area of the genitalia. In premenopausal women, hypoestrogenic settings include postpartum, lactation, and during administration of antiestrogenic drugs. Vaginal atrophy that follows the gradual decline of estrogen production is often associated with manifestations and at other sites including the bladder floor and urethra. Accordingly, urethral and bladder symptoms may be a manifestation of estrogen deficiency including dysuria. The loss of estrogen also has an effect on the bladder lining facilitating the development of bacterial cystitis in aging women. Another impact of estrogen deficiency relates to the loss of muscle tone and dilatation of the vaginal introitus, as well as contributing to the development of prolapse of bladder, uterus, and rectum.

Clinical Manifestations

The earliest effects of estrogen deficiency are progressive atrophy and diminished vaginal secretions manifesting as vaginal dryness experienced during intercourse. While early symptoms may be relieved in part by the use of vaginal lubricants, invariably, progressive estrogen deficiency will not be compensated for by the use of such lubricants. Ultimately, adequate vaginal lubrication for pain-free intercourse will require adequate estrogenic effect on the vaginal epithelium. Vaginal dryness is often experienced by women long before the onset of amenorrhea or the development of systemic vasomotor symptoms and is followed by dyspareunia. Dyspareunia is initially superficial or entry in nature, but with progression of the vaginal atrophy, the discomfort and pain will be experienced throughout and following intercourse with discomfort and irritation and even itching, lasting for several days after intercourse. With advanced atrophy, patients may complain of postcoital bleeding as a result of the susceptibility of the thinned vaginal epithelium to the effects of local friction and trauma.

Diagnosis

Vaginal atrophy and estrogen deficiency can be easily diagnosed without the use of sophisticated testing. The vaginal pH becomes elevated in excess of 4.5 and may reach levels in excess of 6. The vaginal pH is an excellent marker of estrogen deficiency. The elevated pH is a consequence of the loss of the lactic and other organic acid producing bacteria. Lactic acid–producing bacteria are replaced in part by gram-negative organisms, usually coliform, which in their own right are not pathogenic. On wet mount microscopy, the paucity of the typical rod-shaped bacterial morphotypes is apparent. Another important diagnostic feature is the appearance of parabasal epithelial cells reflecting a lack of maturation of basal and parabasal cells in the absence of adequate estrogen stimulation to achieve full maturation effect. Increase in the number of parabasal cells will confirm the diagnosis in the presence of elevated pH and altered bacterial flora. It is also unnecessary and often misleading to measure serum estradiol levels. The latter test is redundant and does not parallel vaginal findings. Neither does receipt of oral nor transcutaneous estrogen products preclude the development of vaginal atrophy.

Treatment

One of the most remarkable biological miracles is the reversible nature of vaginal atrophy. Following adequate estrogen replacement, especially by the vaginal route, a rapid transformation can be anticipated with reversal of the vaginal thinning together with reconstitution of healthy, protective bacterial flora with a dominant lactobacillus morphotype as well as the return to normal vaginal pH and accompanied by the disappearance of parabasal cells [37]. This dramatic change can be expected within 4–6 weeks of adequate estrogen replacement therapy. A number of local vaginal treatments may be used to rectify atrophic vaginitis. These include intravaginal estradiol as creams or vaginal suppositories of estradiol. Alternatively, intravaginal estriol may be used. Not infrequently, vaginal atrophy continues and progresses in the presence of systemic estrogen therapy. Accordingly, one should always insist on local intravaginal therapy. A more recent alternative is the use of the estrogen releasing vaginal rings of which several varieties are available. One can anticipate a return to vaginal health within 1–2 months although the use of lubricants during intercourse may still be required.

NONINFECTIOUS VAGINITIS AND VULVITIS

Women often present with acute or chronic vulvovaginal symptoms of noninfectious etiology. These symptoms are indistinguishable from those of infectious syndromes but are most commonly confused with those of acute *Candida* vaginitis (e.g., pruritus, irritation, burning, soreness, variable discharge). Noninfectious causes of vaginitis and vulvitis include physical irritants (e.g., minipads), chemical irritants (e.g., spermicides, Betadine, topical antimycotics, soaps and perfumes, topical 5-flurouracil), and allergens responsible for immunological acute and chronic hypersensitivity reactions, including contact dermatitis (e.g., latex condoms, antimycotic creams). There is an enormous list of topical factors that are responsible for local inflammatory reactions and symptoms, and many more have yet to be defined. Depending on the site of contact, symptoms may be vaginal or vulvar. A noninfectious mechanism may coexist with or follow an infectious process and should be considered when (1) the three common infectious causes of vulvovaginal symptoms, as well as hormone deficiency, are excluded, (2) the vaginal pH and saline content are normal, and (3) KOH microscopy and a yeast culture are negative. Unfortunately, given the anticipated 20% colonization rates in normal asymptomatic women, a positive yeast culture sometimes reflects the presence of an “innocent bystander" organism rather than the cause of a patient's vulvovaginal symptoms. The only logical way of establishing the role of *Candida* in this context is to treat the patient with an oral antifungal agent and assess the clinical response.

Once a local chemical, irritant, or allergic reaction is suspected as the cause of vaginitis and/or vulvitis, a detailed inquiry into possible causal factors is essential. Offending agents or behaviors should be eliminated whenever possible, including the avoidance of chemical irritants and allergens (e.g., soaps, detergents). The immediate management of severe vulvovaginal symptoms of noninfectious etiology should not rely on topical corticosteroids, which are rarely the solution to such symptoms; moreover, high-potency steroid creams often cause intense burning. Local relief measures include sodium bicarbonate sitz baths and oral antihistamines.

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58 Pregnancy and Childbirth and the Effect on the Pelvic Floor

Philip Toozs-Hobson, Aneta Obloza, and Sara Webb

INTRODUCTION

Over the past few decades, there has been an increasing recognition of the consequences of childbirth on the physical and psychological well-being of a woman. In 1991, MacArthur et al. [1] undertook a postal survey of 11,701 women between 13 months to 9 years after delivery and found that 47% experienced at least one or more health problems within 3 months of delivery. Symptoms persisting for a minimum of 6 weeks included backache, headache, hemorrhoids, depression, and bowel and bladder symptoms. Glazener et al. [2] undertook a similar postnatal symptom on three occasions after childbirth; 85% of women experienced one new symptom during the first 8 weeks and 76% reported one or more health problems persisting for up to 18 months. Sleep and Grant [3] reported that 15% of women experience dyspareunia up to 3 years after a normal vaginal delivery and up to 8% experience perineal pain 12 weeks after a normal vaginal delivery. Interesting perineal pain can occur even without perineal trauma and women who sustain anal sphincter damage have significantly greater pain ratings at 7 weeks after delivery compared to those with lesser degrees of perineal trauma [4]. However, although health problems seem to be common after childbirth, it appears women often do not seek medical attention [1]. This chapter will concentrate on urinary and fecal incontinence, which have a significant negative impact on quality of life and sexual function particularly if both are present [5].

Urinary and/or fecal incontinence and genital prolapse are often considered to be inevitable sequelae of a vaginal birth. One in every three women will experience some symptoms of incontinence during her lifetime and, of these, up to 65% will recall that it began either during pregnancy or after childbirth [5]. Certainly in prospective series, antenatal leakage was a strong risk factor for postnatal leakage [6]. Despite this, much of the clinical and epidemiological studies strongly indicate that women who undergo a vaginal delivery are at higher risk of subsequent incontinence than nulliparous women and those who undergo cesarean section (CS). This is most likely related to the detrimental impact of vaginal delivery on the pelvic floor [7–10]. Furthermore, it appears that the first vaginal delivery is the time when women sustain the most significant damage [8,11]. However, the effects of mode of delivery in higher-order pregnancies are less certain.

Supporting these findings are several studies showing a relationship between vaginal delivery and mechanical and neurological damage to the pelvic floor, which are related to the development of urinary or anal incontinence or both [11–13]. More recently, interest has turned to looking the more subtle changes with sensory nerve function [14] and further work in this area will undoubtedly add to our knowledge in the future. Other factors of relevance include an increased predisposition to pelvic floor trauma and, thus, incontinence and prolapse, due to an inherent weakness of collagen within the pelvic floor fascia [15,16].

This chapter focuses on the effect of pregnancy and childbirth on the pelvic floor and discusses the possible mechanisms by which pelvic floor damage may occur and its long-term sequelae.

MECHANISMS OF INJURY TO THE PELVIC FLOOR

There are several mechanisms of pelvic floor injury: direct muscle trauma, nerve injury, and connective tissue damage disrupting the urethral and anal sphincters and their support (Figure 58.1).

Direct Perineal Trauma

Direct perineal trauma from perineal laceration and episiotomy is a well-known complication of vaginal delivery. Episiotomy [17] is one of the commonest surgical interventions and was traditionally advocated to decrease perineal damage; it reduces anterior perineal laceration but has not been shown to reduce pelvic floor damage, urinary, or fecal incontinence or protect the newborn from intracranial trauma.

The long-term sequelae of perineal injuries include pain, dyspareunia, fistulae, and anal incontinence [11,17,18]. The incidence of lacerations involving the anal sphincter has been reported as 0%–6.4% when an episiotomy has not been performed, 0.2%–23.9% after a midline episiotomy, and 0%–9% after a mediolateral episiotomy [17]. There does not, however, seem to be a significant association between episiotomy and the development of urinary incontinence [19].

Severity and frequency of postpartum dyspareunia has been related to perineal trauma and obstetric instrumentation, with a quicker resumption of sexual activity in those with an intact perineum versus those women who have a spontaneous laceration or trauma [19,20]. Despite all these features, pelvic floor strength, as a separate entity to dispensability, may also be an important factor for predicting vaginal birth [21]; however, higher vaginal resting pressure (VRP) at midpregnancy was associated with a prolonged second stage of labor. There was no influence of VRP, PFM strength, or endurance on the rate of acute CS, prolonged second stage, instrumental vaginal delivery, episiotomy, and third- and fourth-degree perineal tear [22].

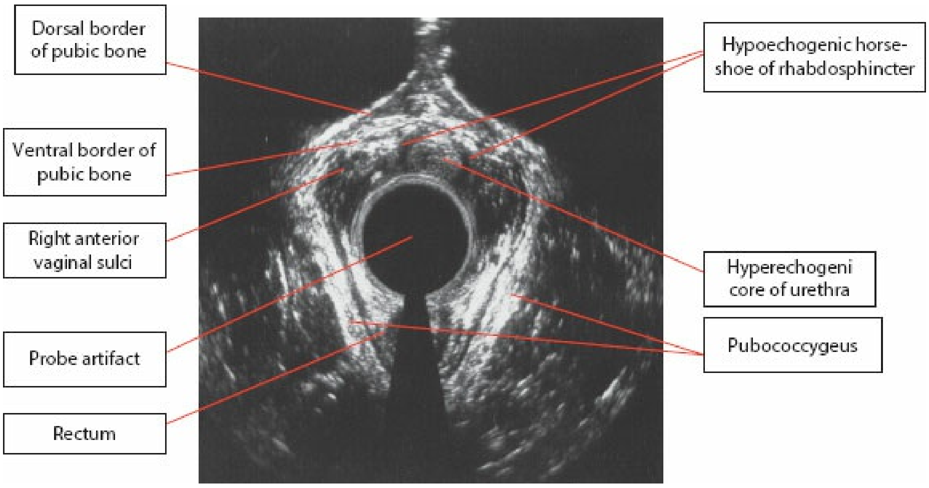
Dorsal border of pubic bone
Ventral border of pubic bone
Right anterior vaginal sulci
Probe artifact
Rectum
Hypoechogenic horse-shoe of rhabdosphincter
Hyperechogeni core of urethra
Pubococcygeus

Figure 58.1 Ultrasound of the pelvic floor. (From Chaliha C, Pregnancy and childbirth and the effect on the pelvic floor, in: Cardozo L and Staskin D, eds., *Textbook of Urogynaecology and Female Urology*, 3rd ed., Informa Healthcare, London, U.K., 2010, pp. 554–566. With permission.)

Muscle Trauma

Traditionally, much has been made of the obstetric factors [23] associated with childbirth. The physical characteristics of the soft tissue in the female pelvis, however, play an important role in successful vaginal delivery. Women with larger levator hiatus dimensions at rest and during contraction at 37 weeks gestation had a shorter duration of the active second stage. Those who had normal vaginal deliveries had significantly larger transverse diameter and levator hiatus area at rest, during contraction, and during Valsalva maneuver compared with women who had instrumental deliveries [24]. Measurement of distensibility [25] of the female pelvic floor was also shown to potentially influence mode of delivery and, in the long term, contribute to pelvic organ dysfunction [26].

An increase of all hiatal dimensions as well as bladder neck mobility was found from 21 weeks to 37 weeks gestation in nulliparous pregnant women [27]. Changes to the pelvic floor may occur from distension during descent of the fetal head and maternal expulsive efforts during the active second stage of labor. Peschers et al. [28] evaluated pelvic floor strength by means of palpation, perineometry, and perineal ultrasound and found that pelvic floor muscle strength was significantly decreased after vaginal delivery compared to CS at 3–8 days postpartum. However, at 6–10 weeks postpartum, there was no significant difference from antenatal values except for a lower intravaginal pressure in nulliparous women. Therefore, although pelvic strength is impaired shortly after vaginal birth, it recovers in most women within 2 months after the first pregnancy. This finding was also found when looking at the levator hiatus with ultrasound [29,30] where recovery seemed to occur through a reduction in the hiatus (possible recovery of flaccid denervation) and in the levator muscle's ability to contract on squeeze.

This recovery, however, is affected by avulsion injuries, which may delay or prevent recovery [31].

In the longer term, that is, 2 years, the levator ani muscle still showed a significantly larger hiatal area after vaginal delivery compared to CS [32]. Two retrospective studies [33,34] have highlighted the relationship between increased levator hiatus and prolapse, but these have not shown cause and effect. Further evidence of childbirth influencing subsequent pelvic floor dysfunction was examined in a 12-year follow-up after the childbirth using a patient-reported measure (pelvic organ prolapse symptom score [POP-SS]) in relation to objective measurement of the pelvic organ prolapsed—the pelvic organ prolapse quantification (POP-Q) system. Women who had had at least one forceps delivery had significantly higher (worse) prolapse symptom scores, POP-SS 2.91 ($p < 0.007$). The association between women's prolapse symptoms and mode of delivery (more symptoms after at least one forceps delivery) suggests that forceps delivery has an adverse effect on pelvic floor function, while delivery exclusively by CS is not protective [35].

Prospective studies, evaluating pelvic floor strength at 1 year postpartum using perineometry, found no difference between degree of perineal trauma and subsequent muscle strength [36]. However, another large study of 519 women evaluated at 3 months postpartum using symptom analysis and vaginal perineometry found that the women who had sustained an episiotomy had lower pelvic floor strength and more perineal pain and dyspareunia than those with intact perineums of first- and second-degree lacerations. There was no difference in symptoms of urinary and anal incontinence [37].

Two studies have simulated delivery using biomechanical modeling of the pelvic floor muscles during the passage of the fetal head through the birth canal [38,39] and demonstrated strain ratios varying from 1.6 to 2.73 for different parts of the levator ani muscle. They also showed that the pubococcygeus–perineal body complex undergoes a maximum of 3.26 stretches to accommodate crowning fetal head with the tissue stretch ratios proportional to both the fetal head flexion and size.

In the magnetic resonance imaging (MRI)-simulated model of vaginal birth [40], a maximum stretch ratio of 3.5 was seen in the posteromedial aspect of the puborectalis muscle. Simulated decrease in stiffness of the lateral attachments of the levator ani (iliococcygeus to tendinous arch levator ani attachments) resulted in decrease of the maximal levator stretch. Authors hypothesized that a more rigid levator in nulliparous women may be subjected to higher stretch during childbirth than multiparous. Thus, the first vaginal delivery may predominantly contribute to urinary incontinence development, which is associated with bladder neck mobility.

Subsequent research has examined the sheer forces applied to the pelvic floor. Ashton-Miller et al. [41] assessed the biomechanics of the pelvic floor muscles, demonstrating the pelvic floor sustains a pressure of 37N while standing and 19N in supine position. Straining to pass a stool increases the pressure to 92N. However, these pressures rise dramatically during an active second stage of labor to 120N during each contraction with active pushing of 113N with instrumental delivery via vacuum suction, and for forceps, it reaches 200N. A further study demonstrated that contracting pelvic floor muscles become stiffer and may be an obstacle to descending fetal head and suggested that pelvic floor muscles exercises may improve muscle control and flexibility [42]. This may result in higher risk of muscle stretch injury near the levator hiatus with a tearing direction perpendicular to the hiatal edge. Predicted hiatal stretch reached the ratio of 3.55 [43].

Women who delivered vaginally showed a persistent significant increase in hiatal dimensions on Valsalva, while women who delivered by prelabor or first stage CS showed no significant changes in hiatal dimensions on Valsalva [44]. What is interesting is that women who deliver vaginally or by elective CS have different antenatal pelvic floor characteristics [6], demonstrating that there may also be tissue factors that may predispose what type of delivery women will have. This has been investigated in animal models [45] whereby analysis of the biochemical tissue composition and biochemical properties of the ovine vagina showed that pregnancy influences remodeling tissue by increasing level of elastin, decreasing collagen, and increasing smooth muscle layer, thus allowing vaginal extensibility but at the cost of greater tissue weakness and less likelihood to return to original dimensions after a repetitive stress. In one of the few human studies, Lavin et al. [46] also demonstrated significant changes in the characteristics of the rectus sheath in pregnancy when compared with nonpregnant women. Postdelivery animal model demonstrated that the vagina undergoes various molecular remodeling that includes both synthesis and proteolytic degradation of extracellular matrix (ECM) proteins [47]. This process may have a genetic component through the homeobox genes (HOX). HOXA11 gene is responsible for the regulation of morphology and integrity of the uterosacral ligaments and expression of ECM proteins during cellular cycle. This finding may explain both the adaptive mechanism soft tissue undergoes to allow vaginal birth and also the development of pelvic organ prolapse [48].

Nerve Damage

The pudendal nerve is particularly susceptible to compression and damage at the point where it curves round the ischial spine and enters the pudendal canal enclosed in a tight fibrous sheath. Nerve damage has been shown to occur in patients with a history of chronic straining on defecation who show increased pudendal nerve terminal motor latencies [49]. Childbirth-induced denervation injuries of the pubococcygeus and external sphincter muscles may occur by a similar mechanism and have been reported after 42%–80% of vaginal deliveries [12,13]. Pudendal terminal latency testing itself is a poor discriminator of nerve function as it is a coarse test that requires a significant injury (greater than 75%) to demonstrate impairment. A better test as previously mentioned is the EMG, but this requires more invasive testing, and so is less acceptable [13].

LOWER URINARY TRACT IN PREGNANCY AND AFTER DELIVERY

Lower urinary tract symptoms are very common in pregnancy. Several large epidemiological studies have assessed the prevalence of urinary symptoms in pregnancy, mostly focusing on the symptom of stress incontinence. Most of these symptoms may be a consequence of the normal anatomic and physiological changes that occur in pregnancy; however, superimposed on these changes may be further pathological changes as a consequence of tissue damage, from either pregnancy or labor, resulting in persistent symptoms. The distinction between normal physiological changes and transient or permanent pathophysiology is often not clear and may be a continuum.

Anatomic and Physiological Changes

The urinary tract undergoes both structural and functional changes during pregnancy and after delivery. These changes may be specific in response to pregnancy and, in some women, may be compounded by pathological changes that persist after delivery.

In normal pregnancy, the kidneys increase by 1 cm in length due to an increase in vascular volume and interstitial space. Dilation of the ureters is a well-known phenomenon in pregnancy and hydroureter is noted in approximately 90% of pregnant women by the third trimester. This dilation is more marked on the right compared to the left side, probably related to the relative dextrorotation of the uterus. There is a 40%–50% increase in glomerular filtration rate and a 60%–80% increase in the effective renal plasma flow [50]. As a result, plasma creatinine, urea, and urate values are lower than the normal range for nonpregnant women.

The bladder is passively drawn upward and anteriorly as the uterus enlarges, resulting in lengthening of the urethra [51]. The urethral mucosa becomes more hyperemic and congested in pregnancy in response to the increase in circulating estrogen levels. The detrusor muscle also hypertrophies in response to estrogen. After delivery, cystoscopy of the bladder shows changes such as mucosal congestion, submucosal hemorrhage, and capillary oozing, especially around the bladder neck, trigone, and ureteric orifices. These changes have been seen in association with a decrease in bladder sensation and tone [52] and are most marked in those who underwent vaginal delivery [53].

Studies assessing bladder capacity have revealed conflicting results, with most early studies using simple cystometry only. Muellner [54] reported an increase in bladder capacity to an average of 1300 mL in the third trimester due to bladder hypotonia, with a return to normal values postpartum. However, other investigators found no change in bladder capacity in the first trimester and a reduced bladder capacity in the third trimester in association with increased detrusor irritability, rather than bladder hypotonia [55]. Dual-channel cystometry studies have found that all urodynamic variables, such as first sensation and maximum bladder capacity, are lower in pregnancy and postpartum compared to a nonpregnant population, and this may account for symptoms of frequency, nocturia, and urgency [56].

PREGNANCY AND URINARY SYMPTOMS

Frequency and Nocturia

These are among the commonest and earliest symptoms to develop in pregnancy. Normal nonpregnant women void between four and six times per day and rarely at night.

Using a definition of frequency as at least seven daytime voids and one nighttime void, Francis [55] studied the voiding habits in 400 healthy women during and after an uncomplicated pregnancy and compared them with 50 healthy nonpregnant patients of similar age. Frequency was reported by 59% in early pregnancy, 61% in midpregnancy, and 81% in late pregnancy. Parboosingh and Doig [57] defined nocturia as at least three nighttime voids and, following the questioning of 873 healthy antenatal patients, found that nearly 66% experienced nocturia by the third trimester. Cutner et al. [58] assessed lower urinary tract symptoms in 47 women undergoing termination of pregnancy at 6–15 weeks gestation and found that 40% complained of frequency and 23% of nocturia. The cause of frequency was not related to bladder capacity or the effect of posture, but due to the polydipsia and polyuria of pregnancy [57].

Both fluid intake and output rise rapidly in the first trimester, remaining constant until the third trimester, when a decrease in sodium excretion leads to a decrease in output. Despite this, frequency persists related to the pressure on the bladder by the uterus. Cutner et al. [58] found that there was a correlation between the maximum voided volumes and first sensation to void and maximum bladder capacity, which was, in turn, related to the presence of low compliance. There was no correlation between the maximum voided volumes and diurnal frequency and nocturia. Parboosingh and Doig also measured mean urine flow and solute excretion in 24 hour and overnight collections in 100 normal and nonpregnant women. An increase in sodium excretion was the major reason for increased nighttime voiding as well as the mobilization of dependent edema at night in the recumbent position.

Voiding Difficulties

Urinary hesitancy may be found in up to 27% of patients in the first two trimesters [59]. Fischer and Kittel [60] assessed flow rates in 290 women during pregnancy and found that there was a significant increase in peak flow rates in the second and third trimesters compared to controls and early pregnancy, but these higher flow rates were associated with larger voided volumes. Cutner et al. [58] assessed flow rates in pregnancy, adjusting for volume voided, and found no difference in women complaining of hesitancy or incomplete emptying, compared to pregnant women with normal voiding.

Urinary retention can occur in pregnancy associated with the enlargement of a retroverted uterus with subsequent entrapment of the fundus below the sacral promontory. Other causes include an enlarging fibroid or a pelvic mass. This retention usually resolves by 16 weeks gestation as the uterus grows out of the pelvis and can be managed in the interim with either bladder drainage or intermittent self-catheterization. Alternatively, manual reduction of the uterus can be performed or a Hodge pessary may be inserted to maintain uterine position and relieve the obstruction on the bladder neck.

Postpartum urinary retention is common, with a reported incidence of 1.7%–17.9% [61]. Risk factors include a first labor, instrumental delivery epidural analgesia, and a longer duration of labor (≥800 minutes) [62]. Studies have looked at sensation after delivery [63] and found that the bladder can take up to 8 hours to regain sensation after the last top-up of an epidural. Overdistension of the bladder may occur during this period, leading to permanent detrusor dysfunction.

Urinary Incontinence

Incontinence is a common symptom associated with pregnancy and has been reported in up to 85% of women [64]. The risk of urinary incontinence increases with advancing gestation. Francis [63] found that in the first trimester of pregnancy 16% of women complained of stress incontinence and 34% in the second half of pregnancy. Stanton et al. [65] assessed the prevalence of both stress and urge incontinence at 32 weeks gestation and found an incidence of 36% and 13%, respectively.

Viktrup and Lose [8] interviewed 305 primiparae and found that 39% had stress incontinence before, during, or after pregnancy and 7% developed de novo stress incontinence after delivery. The association with these obstetric risk factors was lost by 3 months postpartum. Only 3% had incontinence at 1 year. However, in a subsequent follow-up study of the original cohort of 278 women, they reported a prevalence of stress incontinence of 30% at 5 years. In those without symptoms after the first delivery, the incidence was 19%; however, in those who reported stress incontinence 3 months after the first delivery, there was a 92% risk of having stress incontinence 5 years later [8]. A prospective cohort study of 949 women undertaken to find risk factors for postpartum stress incontinence at 3 months found that urinary incontinence was experienced by 22.3% before pregnancy, 65.1% during the third trimester, and 31.1% after delivery [19]. New onset urinary incontinence was more common in parous compared to nulliparous women. Postpartum urinary incontinence was independently associated with incontinence prior to pregnancy and beginning during pregnancy, even among those having a CS. This study highlights the high proportion of women who suffer from urinary incontinence as 15.4% of nulliparae had prepregnancy incontinence. It confirms previous data that have found that the presence of antenatal and prepregnancy stress incontinence seems to increase the risk of future stress incontinence [66,67].

The pattern of the development of incontinence during pregnancy, with rapid postpartum recovery followed by a steady decline of continence over time, suggests a dual mechanism of nerve and tissue damage. The evidence regarding the contribution of obstetric factors to the development of stress incontinence is conflicting. The data are unclear whether it is pregnancy or the birth itself that is the major contributor to postpartum incontinence. Some investigators have found a relationship with the duration of the second stage of labor [68,69] and birth weight [1]. Conversely, other investigators have found no significant correlation between stress incontinence and fetal head circumference [70], second stage of labor [1,71], or birth weight [90–92]. However, most of these studies are relatively small population studies that differ widely in their questioning techniques and definition of stress incontinence. The largest community-based epidemiological study of incontinence (EPINCONT study) [13] assessed 15,307 women who were younger than 65 years and were grouped according to obstetric performance as “had not delivered,” “delivered only by CS,” or “only vaginal deliveries.” The authors reported that in the nulliparous group, the prevalence of any incontinence was 10.1%, 15.9% in the CS only group, and 21.0% in the vaginal delivery only group. Thus, pregnancy itself rather than the mode of delivery may also be an etiological factor in the development of urinary incontinence.

The effect of epidural analgesia is unclear. Epidural analgesia has been reported to be more protective than pudendal block against postpartum stress incontinence [90]. However, this has not been supported by other research that has found a higher incidence of stress incontinence in those who received epidural analgesia than those who did not [92]. Jackson et al. [89] found that the incidence of stress incontinence increased in women delivered with epidural analgesia, especially if the second stage of labor was longer than 120 minutes.

Changes in the Lower Urinary Tract and Pelvic Floor Related to the Development of Incontinence

The exact etiological mechanism of stress incontinence is unclear and probably multifactorial, related to nerve damage and/or physiological and structural changes of the lower urinary tract.

Functional Changes

Iosif and Ulmsten [72] compared urethral pressure profile measurements in pregnant women with stress incontinence with continent healthy women from an earlier study. They found that the absolute urethral length increased by an average of 6.7 mm and the functional urethral length by 4.8 mm. The maximum urethral closure pressure increased to 93 cmH_2O at 38 weeks and then dropped to prepregnancy values of 69 cmH_2O postpartum. These changes were not seen in women complaining of incontinence and are postulated to be a mechanism whereby continence is maintained despite an increase in intravesical pressure in pregnancy. This corresponds with other studies that have shown evidence of low urethral pressure in nonpregnant women with stress incontinence [59,73]. This increase in urethral closure pressure may be the result of an increase in urethral sphincter volume from increased blood flow. There is also an increase in the amplitude of vascular pulsations recorded from the urethral wall, especially in the first 16 weeks of pregnancy, which may be related to an increase in blood volume in pregnancy. Pregnant women with urodynamic stress incontinence showed a decrease in the amplitude of vascular pulsations in the periurethral plexus compared to continent women, suggesting that this affects urethral closure pressure [74]. Three-dimensional imaging of the urethral sphincter after vaginal delivery shows a reduction in sphincter volume, which has been implicated in the development of stress incontinence [75].

Cystometry in pregnancy has been performed by several workers. Chaliha et al. [63] found a high prevalence of urodynamic stress incontinence and detrusor overactivity. This was 8.7% and 8.1%, respectively, in the antenatal period and 5.0% and 6.8%, respectively, postpartum. The mean values for urodynamic variables in the third trimester and postpartum were lower than the values defined in a nonpregnant population and not related to obstetric or neonatal variables (Table 58.1). However, despite the high prevalence of symptoms in this study, there was poor correlation between symptoms and urodynamic findings, which agrees with data in nonpregnant women [76]. Therefore, these observed changes in bladder function were consistent with a pressure effect of a gravid uterus and not related to mode of delivery or neonatal factors.

Nerve Damage

Patients with urodynamic stress incontinence have been shown to have abnormal conduction in the perineal branch of the pudendal nerve, which innervates the periurethral striated muscle and pubococcygeus muscle [77,78]. This damage is likely to lead to a loss of striated muscle of the urethral sphincter [79]. The degree of pudendal nerve damage was greater in multiparous women and correlated with the use of forceps and a longer second stage of labor [77,78]. In 60% of these women, pudendal nerve latency had returned to normal at 2 months postpartum [12]. Using concentric needle electromyography and pudendal nerve conduction tests, Allen et al. [13] found evidence of denervation injury in 80% of women after delivery. Those women with a long (active) second stage of labor (>56.7 minutes) and a large baby (>3.41 kg) showed a greater degree of nerve damage.

Electromyography of the right and left pubococcygeus muscle has shown that childbirth induces both qualitative and quantitative changes, demonstrating sphincter weakness can be attributed to not only the loss of motor units but also the asynchronous activity in those units that remain [80].

Table 58.1 Urodynamic Values (Sitting and Standing Cystometry) and Urodynamic Diagnoses before and after Delivery

Urodynamic variable	**Antenatal values[a]**	**Postnatal values[a]**
Sit FDV (mL)	111 (70)	148 (83)
Sit SDV (mL)	188 (91)	217 (94)
Sit MXCC (mL)	301 (146)	299 (114)
Stand FDV (mL)	96 (69)	139 (90)
Stand SDV (mL)	167 (102)	209 (105)
Stand MXCC (mL)	239 (136) (*n* = 125)	271 (123) (*n* = 118)
MVP (cmH_2O)	38 (22) (*n* = 153)	32 (17) (*n* = 157)
Peak flow rate (mL/second)	28 (16.3)	23 (14)
Urodynamic stress incontinence	14 (9%)	8 (5%)
Detrusor overactivity	13 (8%)	11 (7%)

Source: Data from Chaliha C et al., *Br J Obstet Gynaecol*, 109, 1181, 2002.

Abbreviations:FDV, first desire to void; MVP, maximum voiding pressure; MXCC, maximum cystometric capacity; SDV, strong desire to void.

[a] *n* = 161.

Structural Changes

Ultrasound studies have shown changes in bladder neck position and the urethral sphincter in relation to delivery. Peschers et al. [81] evaluated bladder neck position and mobility using perineal ultrasound at 8 weeks postpartum. Bladder neck position was significantly lower and bladder neck mobility increased after vaginal delivery compared with women who had an elective CS and nulligravid controls. Meyer et al. [82] noted a significant increase in bladder neck mobility after vaginal delivery in primiparae; however, bladder neck position was only lowered after forceps delivery.

Alterations in the urethral sphincter closure mechanism have previously been described in association with stress incontinence. Toozs-Hobson et al. [29] investigated 156 primigravid women in the third trimester and at 6 weeks and 6 months postpartum using a combination of transvaginal and transperineal ultrasound to measure the levator hiatus and bladder neck mobility at rest, maximum strain, and maximum Valsalva. Urethral sphincter volume was calculated using a three-dimensional imaging probe. They found that vaginal delivery was related to an increased bladder neck mobility and larger levator hiatus, with both antenatal and postpartum mobility greater in women who delivered vaginally. The urethral sphincter was smaller postdelivery independent of mode of delivery. These results are interesting but their long-term consequences are unclear as the findings were not related to symptoms. The authors postulated that the larger sphincter volume in pregnancy was a function of the tissue and hormonal effects of pregnancy. In addition, the finding that women delivered by CS showed less pelvic floor distensibility may suggest that this may predispose them to this mode of delivery due to inherent differences in pelvic floor tissues. This supports previous observations that increased bladder neck mobility is associated with vaginal delivery.

It has been suggested that there may be a group of women at an inherent increased risk of developing incontinence due to abnormalities in collagen [83], as the collagenous component of the connective tissue contributes to structural support of the bladder neck. In pregnancy, the tensile properties of the connective tissue are reduced, with a reduction in total collagen content and increase in glycosaminoglycans [57]. Changes in collagen may result in greater mobility of the bladder neck resulting in stress incontinence. In a study of 116 primigravidae, perineal ultrasound was used to assess bladder neck mobility. Women with antenatal bladder neck mobility >5 mm on linear movement (equivalent to >10° rotation) were found to be at higher risk of developing postpartum stress incontinence. Approximately 50% of this group reported stress incontinence at 3 months postpartum [84].

ANAL SPHINCTER MORPHOLOGY DURING PREGNANCY AND AFTER DELIVERY

Sultan et al. [85] examined 20 women before and after an elective CS and found that pregnancy did not have any significant effect on anal sphincter morphology and function.

FECAL INCONTINENCE

Fecal incontinence is a distressing social handicap and vaginal delivery is a major etiological factor [12,86]. MacArthur et al. [1] investigated the prevalence of postnatal fecal symptoms in a postal questionnaire study of 906 women 10 months after delivery and reported that 36 women (4%) developed de novo fecal incontinence. Six of these women became incontinent after an emergency CS but none after an elective CS. This estimate for fecal incontinence is conservative, as it did not inquire about incontinence of flatus that is probably more common and has been reported to be as high as 29% at 9 months after delivery in one study of 349 primiparous women [87].

Fecal incontinence is especially common after anal sphincter rupture, with a reported prevalence of 16%–47% [88]. Tezschner et al. [70] assessed the long-term impact of obstetric anal sphincter rupture on the frequency of urinary and anal incontinence. At 2–4 years postpartum, 42% of the 94 women in their study had anal incontinence, 32% had urinary incontinence, and 18% had both urinary and anal incontinence. Despite the high number of women with incontinence, only a few had sought medical advice.

Changes in the Anal Canal and Pelvic Floor Related to Anal Incontinence

The etiology of postpartum anal incontinence is complex and both nerve and mechanical trauma have been implicated.

Nerve Damage

Denervation injury of the pelvic floor may occur from traction and straining during vaginal delivery, similar to the mechanism of nerve damage reported in patients with chronic constipation, which may result in anorectal incontinence [89]. In 80% of women with idiopathic anorectal incontinence, there is histological evidence of denervation of the striated pelvic floor muscle, particularly the puborectalis and external anal sphincter muscles [90]. Serial measurements of pudendal nerve terminal motor latencies in patients with idiopathic anorectal incontinence show progressive damage from recurrent stretch injury during straining at stool [91].

This mechanism of strain-induced damage may occur during vaginal delivery. Denervation injuries of the pubococcygeus and external sphincter muscles have been reported after 42%–80% of vaginal deliveries [12,13]. The presence of neuropathy has been found to be related to the length of the second stage of labor, size of the baby, and instrumental delivery [92]. Sultan et al. [93] investigated pudendal nerve function before and after delivery and found that pudendal nerve terminal motor latencies were significantly prolonged, especially on the left side, which the authors postulated could be due to the unequal traction from the fetal head on the two sides of the pelvic floor during descent down the birth canal. However, no relationship between abnormal neurophysiology and symptoms of anal incontinence was shown.

Sensory nerve function may also be affected by nerve damage. The anal canal has a greater variety of afferent nerve endings than the rectum. These allow the detection of differences in touch, temperature, and pain in the anal canal. The rectum has a configuration of nerve plexuses that serve as specialized sensory receptors for distension for perception of fullness, urgency to defecate, and pain [94,95].

It is believed that sensory information is critical to the preservation of continence, and in patients with fecal incontinence, there is a significant reduction in the ability to perceive electrical and other forms of stimulation [96]. In pregnancy, however, the role of anal sensation is unclear as deficits in anal canal sensation appear to be transient and unrelated to the development of incontinence [97].

Anal Sphincter Trauma

The incidence of anal sphincter damage varies between 0.5% and 2.5% in centers where mediolateral episiotomy is practiced and 7% in units performing midline episiotomies [18,98]. The use of anal endosonography has enabled accurate visualization of the sphincters, thus providing strong direct evidence of the much higher incidence of previously unrecognized occult anal sphincter trauma after delivery and its importance in the pathophysiology of anal incontinence [99] (Figures 58.2 through 58.4). This can be diagnosed immediately after delivery if suspected [100].

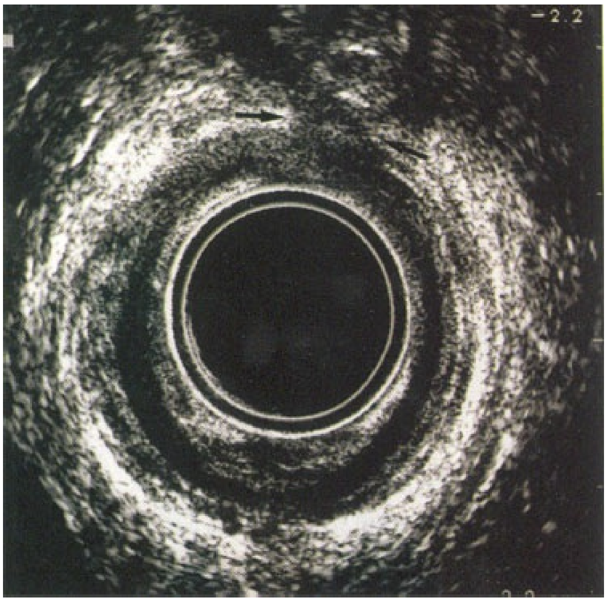

Figure 58.2 Two-dimensional image of the anal sphincter, demonstrating an external sphincter defect (arrows). The external sphincter appears hyperechoic surrounding the hypoechoic external sphincter. (From Chaliha, C., Pregnancy and childbirth and the effect on the pelvic floor, in: Cardozo, L. and Staskin, D., eds., *Textbook of Urogynaecology and Female Urology*, 3rd edn., Informa Healthcare, London, U.K., 2010, pp. 554–566. With permission.)

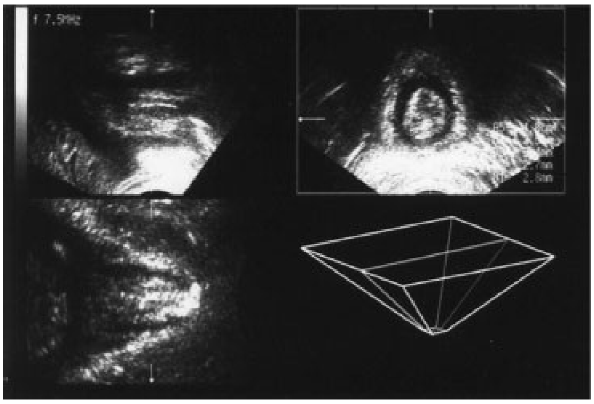

Figure 58.3 Three-dimensional image of an intact anal sphincter. (From Chaliha C, Pregnancy and childbirth and the effect on the pelvic floor, in: Cardozo L and Staskin D, eds., *Textbook of Urogynaecology and Female Urology*, 3rd ed., Informa Healthcare, London, U.K., 2010, pp. 554–566. With permission.)

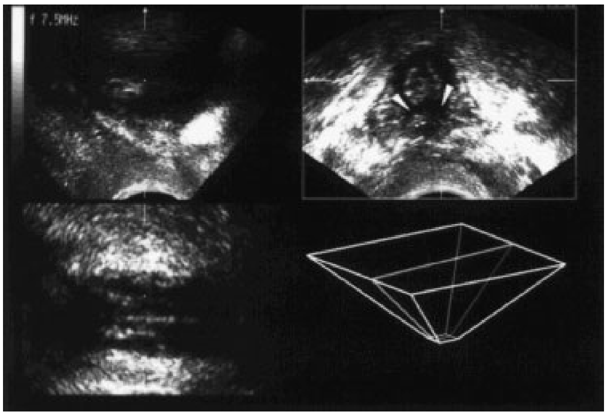

Figure 58.4 Three-dimensional image of internal and external sphincter trauma. (From Chaliha C, Pregnancy and childbirth and the effect on the pelvic floor, in: Cardozo L and Staskin D, eds., *Textbook of Urogynaecology and Female Urology*, 3rd ed., Informa Healthcare, London, U.K., 2010, pp. 554–566. With permission.)

Sultan et al. [16] investigated 202 pregnant women before and 6 months after delivery using anal endosonography, manometry, perineometry, and pudendal nerve terminal motor latencies. Thirty-two women had new abnormal postnatal findings (defects on endosonography or prolonged pudendal nerve terminal motor latencies). Ten of the 79 primiparous women (13%) and 11 of the 48 multiparous women (23%) who delivered vaginally had anal incontinence or fecal urgency when studied 6 weeks after delivery. Twenty-eight of the 79 primiparous women (35%) had a sphincter defect on endosonography at 6 weeks; the defect persisted in all 22 women studied at 6 months. Of the 48 multiparous women, 19 (40%) had a sphincter defect before delivery and 21 (44%) afterward. None of the 23 women who underwent CS had a new sphincter defect after delivery. The use of forceps was the single independent factor associated with anal sphincter damage, and there was a strong correlation with the presence of defects and the development of symptoms. This suggests that it is the first vaginal delivery that is the most important factor for damage to the anal sphincters. One criticism of this paper was the lack of blinding, and other authors have demonstrated that symptoms do not always correlate with ultrasound findings [101].

Forceps delivery results in more traumas to the anal sphincters and is associated with a higher incidence of defecatory symptoms than a ventouse delivery. Sultan et al. [11] found anal sphincter defects in 81% of women who underwent a forceps delivery compared to 24% of those who were delivered by ventouse and 36% of controls.

Subsequent studies have looked at the incidence of anal sphincter injury using endoanal ultrasound, and meta-analysis of five of these studies reveals a 26.9% incidence of anal sphincter injury in primiparous women and an 8.5% incidence of new sphincter defects in multiparous women. Overall, 29.7% of women with anal sphincter defects were symptomatic though 3.4% of women experienced postpartum fecal incontinence without a sphincter defect (Table 58.2) [96,102].

The use of episiotomy and its relationship to anal sphincter injury is unclear. Poen et al. [103] reported that the use of a mediolateral episiotomy was associated with fewer third-degree tears, and Sultan et al. [98] reported that almost half of these women who had sustained third-degree tears had undergone an episiotomy. The use of midline episiotomies, favored in the United States, has been strongly associated with a 50-fold increased risk of a third-degree tear [104]. This is reflected in the threefold increased risk of fecal incontinence following midline episiotomy versus a spontaneous perineal laceration, and so research remains divided as to the protective effect of a mediolateral episiotomy for OASIS (obstetric anal sphincter injury service). It is apparent from the published literature that even with nonmidline episiotomies, the risk of OASIS is strongly associated with the angle of incision of episiotomy [105]. Studies have demonstrated that there is little attention and much imprecision with regard to the angle of incision of mediolateral episiotomy [106]. Consequently, the inconsistent findings of research as to whether mediolateral episiotomy has a protective or influencing effect on OASIS could be due to the variation in actual position of the episiotomy incision. Until there is standardization among clinicians worldwide on the correct angle and position of a mediolateral episiotomy, whether or not it is a risk variable for OASIS will remain a matter of conjecture.

Table 58.2 Sphincter Defects and Symptoms: Meta-Analysis of Studies Reporting Obstetric Sphincter Damage

		No. of women for meta-analysis		No. of women with sphincter defect				
Reference	Total	Primip	Multip	Primip	Multip	Symptomatic defect (%)	Postpartum fecal incontinence but no new sphincter tear (%)	Follow-up rate (%)
Sultan et al. [11]	127	79	48	28	2 new (19 old)	20.4 (10 of 49)	1.3 (1 of 78)	100
Abramowitz et al. [126]	202	96	106	25	14 new	23.1 (9 of 39)	6.7 (11 of 163)	100
Varma et al. [127]	120	78	42	9	6 old and new	0	0	71.6
Fynes et al. [110]	118	59	59	20	2 new	68.2 (15 of 22)	0 (0 of 96)	100
Faltin et al. [128]	150	150	0	42	0	36.6 (15 of 41)	6.8 (7 of 103)	96
Overall	717				167 new and old, all women	32.5 (49 of 151)	4.3 (19 of 440)	

Source: Data from Oberwalder M et al., *Br J Surg*, 90, 1333, 2003.

Abbreviations:Multip, multiparae; primip, primiparae.

The degree of anal sphincter trauma may also be related to occurrence of symptoms. A questionnaire study of 208 women, 13 years after vaginal delivery, found that 25% of women after fourth-degree tears and 11.5% after third-degree tears complained of anal incontinence of gas, liquid, or solid stool [23]. In another American study [107] of 2858 primiparous women delivered vaginally, 19% were known to have sustained third- or fourth-degree tears. Although this study was limited in that it was questionnaire based and retrospective, it highlighted the high prevalence of anal sphincter tears possible, a reflection of the practice of midline episiotomy performed in the United States. The incidence of worse bowel control was 10 times higher in those with fourth-degree lacerations versus third-degree lacerations, which is not surprising as both internal and external sphincters are then compromised and as such cannot compensate so easily for the loss of function in the other. The urgency associated with internal sphincter damage may also exacerbate loss of bowel control to a greater degree. Another observation was that more than 50% reported new onset urinary incontinence indicating that similar risk factors pertaining to anal sphincter trauma may relate to damage and loss of function of the urethral continence mechanism.

There may also be an inherent predisposition to anal sphincter trauma as there are racial differences in incidence, with the incidence of trauma greater in Asian women versus white women versus with black women having a lower incidence. This suggests that there are anatomical or physiological predisposing factors [108]. Further evidence of genetic predisposition due to tissue types comes from a telephone survey of women who had undergone an instrumental delivery. This study reported that those with a history of joint hypermobility (a marker for collagen weakness) had an increased risk of postpartum anal incontinence [109].

Despite obvious injury to the anal sphincters, symptoms of anal incontinence may not occur for some time after delivery, and in women who experienced transient anal incontinence after a complete tear, 39% had a relapse of symptoms after the next vaginal delivery. The major long-term problem seen in these women was incontinence of flatus. Fynes et al. [110], in a study of women undergoing a second vaginal delivery, with a history of occult sphincter injury or transient fecal incontinence after their first delivery, found that there was a significant risk of these women having persistent fecal incontinence. Full-thickness anal sphincter disruption was the most significant risk factor in the development of fecal incontinence after a second vaginal delivery. However, other smaller studies have shown no significant change in anal incontinence or anal physiology in the short term for women with a previous obstetric anal sphincter injury following a subsequent birth [111].

CHILDBIRTH AND PROLAPSE

Genital prolapse occurs as a consequence of weakness of the fibromuscular supports of the pelvic organs. Although the etiology of genital prolapse is multifactorial, childbirth has been implicated as a major contributing factor. It is far more common in parous women, with 50% of parous women having some degree of genital prolapse, of which 10%–20% are symptomatic. In contrast, only 2% of symptomatic prolapse is found to occur in nulliparous women. The risk of prolapse is higher with increasing parity [112].

The mechanism of prolapse is unclear. Pathological and electrophysiological studies have shown that significant pelvic nerve denervation and reinnervation are associated with stress incontinence and prolapse. However, there are also collagenous changes in the pelvic floor, which are related to ageing, childbirth, and endogenous hormone changes, which may also predispose to prolapse and stress incontinence [113].

During vaginal delivery, the combination of distension and stretching of the pelvic floor by both the fetal head and increase in pressure due to maternal expulsive efforts may lead to functional and anatomic alterations in the muscles, nerves, and the connective tissue of the pelvic floor and anal canal. Trauma to the pelvic floor may also lead to repair with weaker collagen and so predispose to incontinence and prolapse. Prolapse is noted to be more common in women after a vaginal delivery compared to after a CS [114]. Using the POP-Q examination, O’Boyle et al. [115] found that the 23 nulliparous pregnant women had an increased POP-Q stage compared to 21 nonpregnant controls. An increase in POP-Q stage is also seen after vaginal delivery and this correlates well with increased mobility of the bladder base and neck [75]. These studies suggest that both pregnancy and delivery are important etiological factors for the development of pelvic organ prolapse.

The use of MRI and ultrasound has provided further insight to the ultrasound studies previously mentioned into pelvic floor dysfunction. Changes in the levator hiatus have been shown to be related to urogenital prolapse, and surgery for prolapse has been associated with a reduction in the size of the urogenital hiatus [116]. This suggests that a more distensible levator hiatus is associated with risk of pelvic organ prolapse. MRI has previously shown abnormalities in the levator ani in women with stress incontinence and prolapse. In one study [23] comparing nulliparous women and women after their first vaginal birth, 20% of primiparous women had a visible defect in the pubovisceral or iliococcygeal portion of the levator ani muscle. These defects were not seen in the nulliparae group. Those women with urinary incontinence were more likely to have a defect in the levator muscle. In another study, it was noted that increasing levator trauma was found in those with a longer second stage of labor. These defects are thought to be either due to avulsion of the muscles from their origin or as a result of denervation. However, whatever the possible mechanism, it is clear that such damage to the levator “plate” leads to a decrease in muscular supports to the pelvic organs and an increase on the load carried by the connective tissue and fascia. These injuries may themselves relate to stress incontinence or predispose to weakening of fascial and connective tissue supports resulting in stress incontinence.

Pelvic floor ultrasound has been an increasingly useful tool for revealing changes in the levator anatomy related to parity. Using translabial ultrasound, Dietz et al. reported that in a study of 68 nulliparous women during the third trimester and 2–6 months postpartum, vaginal delivery was shown to relate to an increased prevalence and size of a true rectocele (defect in the rectovaginal septum). These defects are associated with symptoms of pelvic organ prolapse and obstructed defecation (Figures 58.5 through 58.8) [117]. However, rectoceles were also seen in those after CS, so pregnancy itself may affect the integrity of the rectovaginal septum. In another study by this group, vaginal delivery was noted to be associated with avulsion of the levator ani from the pelvic side wall in one-third of women.

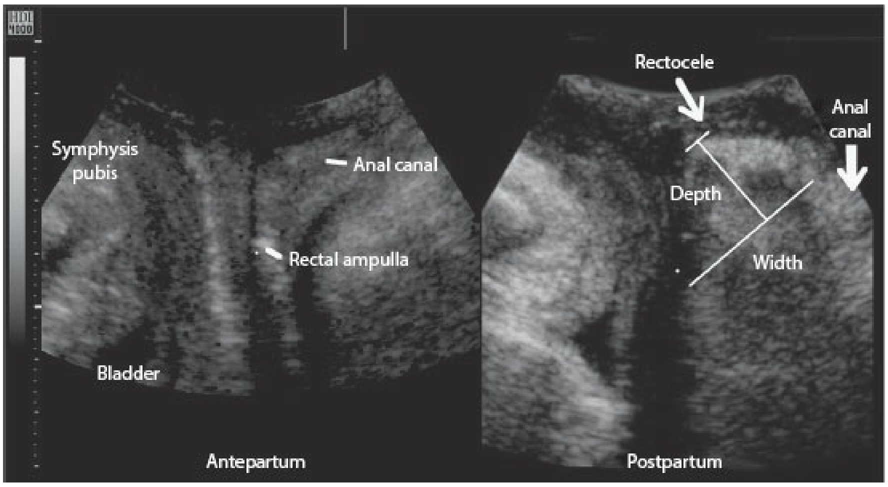

Figure 58.5 Comparison between posterior compartment imaging (midsagittal plane) in the third trimester (left) and 3 months postpartum (right) on maximal Valsalva maneuver. The anorectal junction appears normal on the left. On the right, there is a rectocele, with a depth of about 2 cm, filled with stool. (Reproduced from Dietz HP and Steensma AB, *Br J Obstet Gynecol*, 113, 264, 2006. With permission and by courtesy of H.P. Dietz.)

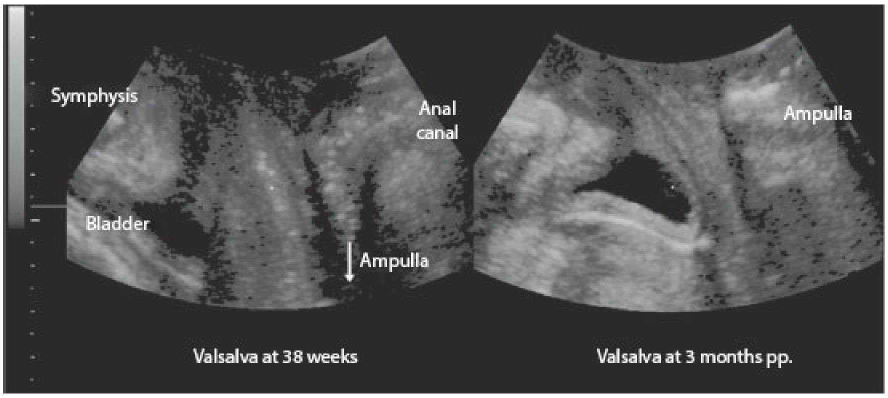

Figure 58.6 Comparison between posterior compartment imaging (midsagittal plane) in the third trimester (left) and 3 months postpartum (right), on maximal Valsalva. The anorectal junction is normal on the left. The right image shows increased bladder descent and perineal mobility, resulting in displacement of the rectal ampulla below the symphysis pubis. There is no actual rectocele, that is, no defect of the rectovaginal septum shown in Figure 58.5. (Reproduced from Dietz HP and Steensma AB, *Br J Obstet Gynecol*, 113, 264, 2006. With permission and by courtesy of H.P. Dietz.)

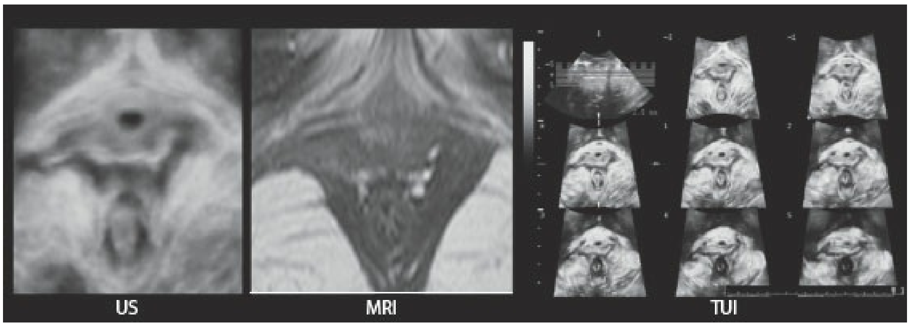

Figure 58.7 Unilateral avulsion on ultrasound, MRI, and tomographic ultrasound. (Courtesy of H.P. Dietz.)

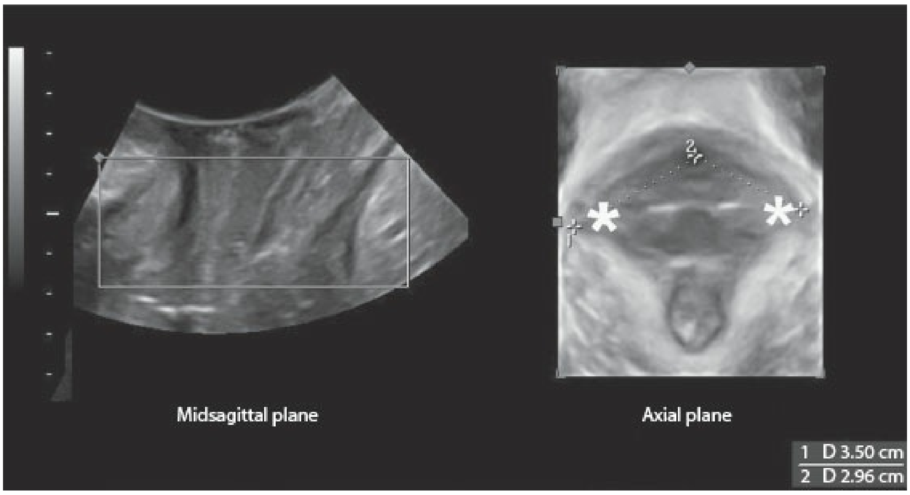

Figure 58.8 Typical bilateral avulsion injury seen in primiparous patient (forceps) as seen in the axial plane (right image). The defects are indicated by *. (Reproduced from Gamble, J.A. and Creedy, D.K., *Birth*, 27, 256, 2000. With permission and courtesy of H.P. Dietz.)

CONCLUSIONS

The development of pelvic floor disorders such as urinary and fecal incontinence and genital prolapse have been associated with pregnancy and vaginal delivery. Over the last two decades, histology, imaging, and physiological techniques have revealed mechanisms of injury to the pelvic floor, which include direct muscle trauma, disruption of connective tissue support, and denervation with the time of greatest risk of damage at the first vaginal delivery.

In recent years, there has been an ongoing debate regarding the protective effect of an elective CS in reducing the risk of pelvic floor disorders, and women are increasingly requesting CS for nonmedical reasons [130]. The debate is ongoing as the evidence supporting this is conflicting and much is derived from small studies of heterogenous cohorts with differing and inconsistent definitions of incontinence. Epidemiological studies implicate parity as associated with incontinence; however, it is less clear what specific association of mode of delivery has on incontinence. Less pelvic floor damage seems to occur after “elective” but not necessarily “emergency” CS. With regard to urinary incontinence, some data suggest that cesarean is protective; however, others suggest that it is pregnancy itself that is the major risk factor. Elective CS appears to prevent against mechanical trauma to the anal sphincter but not necessarily the urethral sphincter. However, elective CS is not wholly protective for anal incontinence [118]. In addition, it has been estimated that 167 cesarean deliveries are needed to prevent one case of fecal incontinence. Therefore, before considering these potential benefits of cesarean delivery, they must be weighed against the potential risks for the mother and child, including increased risk of postpartum hysterectomy, adhesions, ileus, placental implantation, problems in future pregnancies, and increased respiratory distress syndrome in the newborn [119,120]. An answer to this question would really only come with women randomized to either vaginal birth or elective CS, though this is, of course, impossible for clear ethical and practical reasons. However, these data are short term, and even if CS were in the short-term protective, this protective effect diminishes with time and subsequent deliveries and factors such as ageing, and the menopause may then be more relevant. A reanalysis of the EPINCONT study [121] has shown that women who have children at an older age are more likely to suffer from stress incontinence and this is supported by ultrasound studies, which show an increase in odds of levator trauma of 10% for each year of delayed childbearing [122]. These findings suggest that as women in Westernized societies delay childbearing, there will be a rise in the incidence of pelvic floor morbidity.

Given the lack of clarity with the present data, the focus should be on modifying potential risk factors that may impact on pelvic floor trauma. Women should be offered strategies to reduce pelvic floor injury and incontinence such as pelvic floor exercises, which have been shown to reduce urinary incontinence and increase pelvic floor strength [123]. Adequate training is required in recognition of perineal trauma and repair and intra- and postpartum bladder care. Consideration needs to be made of the experience and training of birth attendants as inexperienced birth attendants may increase perineal damage. Labor ward management should be reviewed with regard to choice and technique of instrumental delivery and use of episiotomy as it is known that even the angle and technique of the episiotomy can vary widely and may often be more midline than mediolateral in position. Easing the perineum with controlled delivery of the fetal head has also been shown to reduce the perineal trauma rate though this is often not used with the vogue for the “hands-off” approach employed by many birth attendants [124].

There are other modifiable factors that should also be addressed such as constipation and high body mass index, both of which were associated with an increased prevalence of urinary and anal incontinence [125]. It may be prudent to consider active programs to promote a healthy prepregnancy body mass index, not only for reducing pelvic floor morbidity but also for minimizing the risk of pregnancy complications including CS.

For those women in whom postpartum incontinence and prolapse develop, treatment strategies and follow-up should be readily available and standardized protocols developed. There are now clear guidelines indicating the relevant therapies and investigations that could be used in these situations. Long-term studies are required in assessing the outcome of interventions and treatments in women prior to and after delivery.

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59 Problems Associated with Sexual Activity

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Female sexual dysfunction (FSD) is defined as a sexual desire, sexual arousal, orgasm, and/or sexual pain disorder that causes personal distress (Table 59.1). FSD is a relatively common health issue for women with a community prevalence of 30%–50% [1]. The wide range of the reported percentages depends on the impact of different concomitant factors on sexual function, such as interpersonal and emotional relationship, well-being, and psychological factors. Studies have shown that FSD and other sexual problems have been linked to a “diminished quality of life, low physical satisfaction, low emotional satisfaction, and low general happiness” [2]. Women’s sexuality and sexual function are very complex issues, strongly modulated by psychosocial situation, and this necessitates a biopsychosocial approach for understanding the basis of dysfunction. Physiological events, such as pregnancy, childbirth, menopause, aging, and gynecological conditions like infertility, prolapse, urinary incontinence (UI), and gynecological cancers, have an impact on sexual well-being. The interaction of these conditions with sexual health needs to be better understood to deal effectively with the problems as a whole.

Sexual dysfunction is highly prevalent in women attending urogynecological services with a prevalence of 50%–64% [3–5]. Furthermore, urogynecological surgery represents an important but underestimated cause of FSD. Different problems of the pelvic floor can impact sexual activity in different ways. Interest in and publications about FSD are very recent [3].

In this chapter, we review the correlation of common urogynecological conditions on sexual activity and the impact of their treatment.

URINARY INCONTINENCE

UI is a common condition and epidemiological studies suggest that it affects up to 41% of the adult female population [6]. It is a health burden and impacts social, psychological, occupational, domestic, physical, and sexual well-being [7–10]. Women reporting lower urinary tract symptoms (LUTS) or UI complain of a deteriorating quality of life (QoL) in terms of social and psychological problems and also of sexual dysfunctions in significantly greater numbers than the general healthy population, as reported in a recent cross-sectional study [11]. Table 59.2 shows the prevalence of UI during sexual activity as shown in different population groups.

Complaints of stress urinary incontinence (SUI), overactive bladder (OAB), and LUTS have a negative impact on all domains of sexual function [7,11]. In women with pelvic floor dysfunction, the symptoms per se, along with fear of odor, embarrassment, shame, loss of self-esteem, and fear of, or actual occurrence of, incontinence, are contributory factors. The most common sexual complaints in women with UI are low desire, vaginal dryness, and dyspareunia independent of age, educational attainment, and race [12].

Even in community-dwelling women aged over 55, 5% were not sexually active due to UI, and 25% of these sexually active women reported a negative influence of urine loss on their sex life [13].

In women with SUI, the prevalence of coital incontinence ranges from 11% to 70% [14–18]. Traditional teaching has been that urodynamic stress incontinence (USI) is associated with penetration incontinence and detrusor overactivity with orgasm incontinence [16]; however, subsequent studies by Moran et al. [17] have failed to confirm this association. In their observational study, USI was associated with high rates of penetration incontinence (80%), orgasm incontinence (93%), and a combination of the two (92%). Jha et al. [18] correlated different urodynamic diagnoses to orgasm or penetration incontinence and found no association.

Among the different types of UI, OAB has a particularly high association with sexual dysfunction in various studies [19–21], which could be indicative of an underlying psychosomatic disorder [22]. However, studies assessing the overall prevalence of sexual dysfunction in women with OAB and the impact on QoL remain controversial [23], whereas menopausal and partner status have been shown to be the better predictors [24].

Until recently, the impact of treating incontinence on sexual function has been controversial. Before the introduction of minimally invasive suburethral sling procedures, Burch colposuspension was regarded as the "gold standard" for the surgical correction of SUI. There are some data regarding the impact of colposuspension on sexual health. Moran et al. [25] evaluated 55 women with SUI who reported coital incontinence before undergoing colposuspension. Preoperative coital leakage occurred in 65% with penetration, in 16% with orgasm, and in 18% with both. After surgery, 81% of the women reported no coital incontinence. Baessler et al. [14] showed similar improvements in coital incontinence following a colposuspension.

The impact of midurethral slings, specifically tension-free vaginal tape (TVT) on female sexual function (FSF), has been unclear. Different studies have shown different outcomes, with some suggesting deterioration [26–29] of sexual function and some an improvement [30–32], whereas others were equivocal [33–36]. Deterioration in function may be associated with dyspareunia [29], loss of libido, or partner-associated discomfort. There have also been anecdotal reports of anorgasmia after TVT probably related to passage of the trocar and subsequent injury to the dorsal nerve of the clitoris [37]. However, there seemed to be a consensus that TVT reduces coital incontinence rates by between three- and sixfold [29,33,38].

Table 59.1 Classification of Female Sexual Dysfunction (DSM IV TR [Text Revision])

1. Sexual desire/interest disorders
2. Sexual arousal disorders
    - Genital arousal disorder
    - Subjective arousal disorder
    - Combined arousal disorder
3. Orgasmic disorder
4. Dyspareunia and vaginismus
5. Persistent sexual arousal disorder

Source: Basson R et al., *J Sex Med*, 1(1), 24, July 2004.

The obturator approach appeared to have an overall beneficial effect [37,39] on sexual function comparable to the retropubic approach (TVT) [40]. In a comparison of the outside-in and the inside-out technique, reports are conflicting with one study suggesting the inside-out technique (TVT-O) to be better [39] and another study showing the outside-in technique (TOT) to be superior [37].

Jha et al. [41] conducted a systematic review of all continence procedures and the impact of treating urinary incontinence on sexual function. They found that coital incontinence was significantly reduced following continence surgery. However, though the pooled results suggest between two and three times greater likelihood of improvement compared to deterioration in sexual function, at least half of all women undergoing surgery for stress incontinence are likely to experience no change in sexual function. There was no difference in sexual function following the two most commonly performed procedures for SUI, i.e., the TVT and TOT/TVT-O.

In sexually active women with OAB and concurrent sexual dysfunction, sexual QoL, Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ) scores, and anxiety states were all improved with corresponding improvement in OAB scores by treatment with anticholinergics [42,43]. Treatment of OAB has also been shown to improve with both percutaneous tibial nerve stimulation [44] and sacral nerve stimulation too [45].

PELVIC ORGAN PROLAPSE

Pelvic organ prolapse (POP) is a common medical problem in parous women and particularly with advancing age. As life expectancy increases, this is acquiring greater significance, and 20% of women on gynecology waiting lists in the United Kingdom are awaiting prolapse surgery, demonstrating the enormity of this virtual pandemic. The incidence of prolapse requiring surgical correction in women who have had a hysterectomy is 3.6 per 1000 person-years of risk, the cumulative risk of prolapse being 1% at 3 years and 5% at 17 years after a hysterectomy [46].

Table 59.2 Studies Showing Prevalence of Urinary Incontinence during Sexual Intercourse

Authors	**Design and setting**	**Symptoms analyzed**	**% with UI during intercourse**
Bo et al. [152]	RCT of women with SUI; Norway	Urinary incontinence during intercourse using BFLUTS	33
Clark et al. [153]	48 women undergoing UDS; USA	Incontinence and other urinary symptoms during intercourse	56
Espuna et al. [154]	633 sexually active women	Coital incontinence	36.2
Gordon et al. [155]	100 consecutive women attending a clinic; Israel	Psychiatric assessment of sexual function	16
Hilton [16]	324 sexually active women; UK	Standardized Questionnaire	24
Jackson et al. [156]	RCT of HRT in women with SUI; UK	Urinary incontinence during intercourse using BFLUTS	10
Jha et al. [15]	Women with urodynamic stress incontinence undergoing TVT; UK	ePAQ questionnaire	68
Jha et al. [18]	Women with urinary incontinence undergoing urodynamics	ePAQ questionnaire	60
Lam et al. [157]	2631 (random) women selected: 511 had SUI; Denmark	When they have SUI	2 of general group; 12 of women with SUI
Lemack et al. [26]	56 women; USA	UI with intercourse	11
Moller et al. [158]	4000 randomly selected women from the community; Denmark	UI with intercourse	8 = sometimes 1.7 = weekly 0.4 = daily
Nygaard et al. [159]	224 random women: gynecology outpatient; USA	UI with penetration/orgasm	12.9
Weber et al. [35]	81 sexually active women undergoing surgery; USA	UI with intercourse	22
Vierhout et al. [160]	196 sexually active women attending clinic	UI with intercourse	34
Visser et al. [13]	Community dwelling women	UI with intercourse	26
Xu et al. [161]	55 women with USI undergoing TVT	UI with intercourse	21.8

A review of literature shows conflicting results on the impact of prolapse on sexual function, with some studies showing a deterioration of function and others showing no impact [12]. In their observational study, Handa et al. interviewed 1299 participants and 495 (38.1%) had evidence of pelvic floor disorders. Sexual complaints were significantly more common among women with pelvic floor disorders (53.2% vs. 40.4%, $p < 0.01$), and compared to UI, POP was not associated with any sexual complaint. A study by Weber et al. [47] examined 80 women with prolapse and compared their continence status; they also included 30 controls (women with no prolapse). The study showed no difference in global sexual function score, vaginal dryness, dyspareunia, interest in sexual activity, or satisfaction with their sexual relationship. They concluded that women with prolapse and UI do not differ from continent women without prolapse in measures of sexual function, and age is the most important predictor of sexual function. Burrows et al. [48] came to similar conclusions in their retrospective study of 352 women with prolapse. They also found that prolapse severity did not impact on sexual function. The study by Barber et al. [49] comparing the impact of prolapse and incontinence on sexual function found completely the opposite results. In their review of 343 community-dwelling women with either symptomatic prolapse or incontinence, they found that prolapse was more likely to influence sexual function than UI. This study also demonstrated that treatment of prolapse was less likely to impact on change in sexual function, whereas treatment of incontinence resulted in a mild improvement in sexual function.

Other studies have shown that prolapse causes several problems with sexual function including discomfort, UI (40%) (both orgasm and penetration), obstruction, and dryness during intercourse.

Women with prolapse were more likely to have urinary and/or fecal incontinence during sexual activity, more dyspareunia, and fewer orgasms. They were also more likely to report negative emotional reactions associated with sex and higher rates of embarrassment leading to avoidance of sex [50]. Presence of both prolapse and incontinence has a cumulative negative effect on sexual function, with libido, sexual excitement, and orgasm being significantly affected. The increasing severity of prolapse is associated with symptoms related to UI, voiding, defecation, and sexual dysfunction that do not necessarily correlate with the location of prolapse and therefore are not compartment-specific [51].

Some explanation of the differences in these findings is that assessment of the impact of POP and UI on sexual function is difficult because of the following:

1. Different tools have been used in different studies.
2. Studies cluster prolapse and incontinence under the same umbrella.
3. Study groups are small.
4. Different types of prolapse clumped together (different compartments, different grades).

As a result, the multitude of studies report on the impact of prolapse surgery on sexual function, but the results are very conflicting with some being equivocal reporting no impact of prolapse correction on sexual function and others demonstrating a deterioration of sexual function following prolapse treatment. The cause of sexual dysfunction following vaginal surgery may be classified as organic and/or psychosocial [52]. Organic causes are anatomical, physiological, vascular, neural, and hormonal. Psychosocial factors on the other hand such as life stressors, anxiety, and depression must be borne in mind. Altered perception of genital health after surgery, both by the woman and her partner, with associated apprehension and fear of damage to the internal organs, can also be contributory factors for a negative impact on sexual function.

The verdict is still open on the impact that prolapse has on sexual function, and larger epidemiological studies with careful assessment and agreement of the tolls used to assess impact are required to substantiate or refute the currently available conflicting evidence. This will also be partly achieved by the long-term follow-up of randomized controlled trials. When counseling women with a prolapse and particularly before treatment, these factors should be featured in the discussion and aid decision-making. This allows more realistic expectations from the treatments available and avoids disappointment when those goals are not met. There remain many unanswered questions, but it is important to remember that the presence of anatomical defect does not imply dysfunction. The goal of pelvic surgery should be restoration of anatomic support without deleterious effects on visceral and sexual function. Data are currently limited on QoL and sexual function following both traditional and graft-reinforced anterior vaginal prolapse surgery; further research is required to determine whether surgical technique and type of graft used impact surgical outcome and complications before introduction into routine clinical practice. Women should be counseled and managed depending on current best available evidence.

Current treatment options for vaginal wall prolapse include pelvic floor muscle training (physiotherapy), use of topical hormone replacement therapy (HRT), use of mechanical devices (ring or shelf pessaries), and surgery, with or without mesh reinforcement. The impact of these different forms of treatment for prolapse on sexual function is discussed here.

Physiotherapy

In their systematic review looking at the benefits of pelvic floor muscle training (PFMT), Hagen et al. [53] identified some benefit on sexual function in women with mild prolapse. But even more reassuringly, women who were currently performing PFMT scored significantly better on several aspects of sexual function [54,55] and PFMT is therefore to be encouraged in women.

Estrogen Therapy

There are no studies looking at the impact of estrogen therapy in women with prolapse or its impact on sexual function. However, several studies have shown an individual improvement in symptoms of atrophic vaginitis that [56] may negatively impact sexual function even in the absence of prolapse; hence, it may be considered for that indication.

Pessaries

There are a variety of pessaries available, made of rubber, plastic, or silicone-based material. The commonest pessaries are the rings and shelf, but other types being increasingly used are the inflatable, the doughnut, and the Gellhorn, all of which have slightly different uses and specifications. A recent study by Kuhn et al. [57] demonstrated that desire, lubrication, and sexual satisfaction significantly improved with pessary use, though orgasm remained unchanged (Figure 59.1).

A comparison of sexual function in women with pessaries or surgery [58] for the treatment of POP found a significant improvement in sexual function in both groups though there was increased frequency of intercourse in the surgery group (54% vs. 46%; $p = 0.028$), which was not significant when controlled for age.

Lowenstein et al. [59], on the other hand, found greater improvement following surgery than use of pessaries, and this appeared to be related to altered self-perceived body image.

Surgery

Richard TeLinde said, “Every surgeon of extensive and long experience will have to admit that he is not entirely and absolutely satisfied with the long-term results of all his operations for prolapse and allied conditions,” and this is further substantiated by the further surgery rates for recurrent prolapse being in the region of 30% [60]. White in 1908 said, “Plastic gynaecology remains the last unsolved problem of surgical gynaecology,” and this remains true even in the twenty-first century.

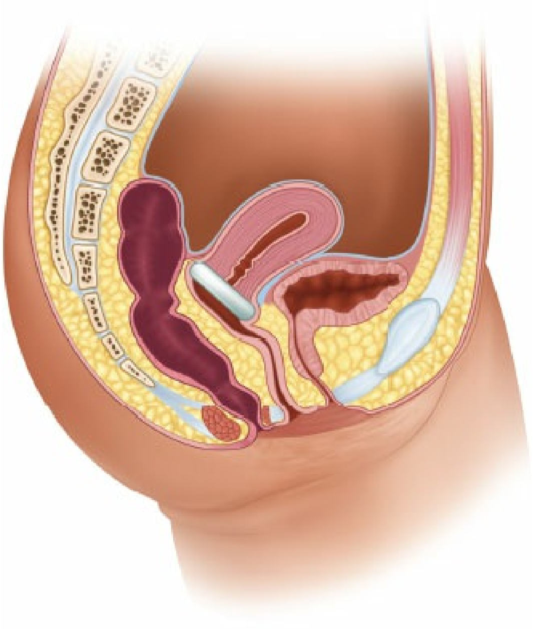

Figure 59.1 Ring pessary in situ: no interference with sexual activity.

Surgical correction of prolapse depends largely on the compartment that is affected. So for vaginal wall prolapse, it may involve an anterior colporrhaphy/anterior vaginal wall repair, posterior colporrhaphy/posterior vaginal wall repair, or a vaginal hysterectomy. For a vaginal vault prolapse, surgical correction may require sacrospinous fixation, an abdominal sacrocolpopexy, or infracoccygeal procedures that may involve the use of trocar systems (which at the time of writing included, e.g., Apogee, Post I-Stop).

Though Weber et al. [35] identified a decrease in the vaginal dimensions after surgery for prolapse, this was associated with either no alteration in sexual function or a mild improvement. This may be related to a change in vaginal dimensions during arousal and intercourse. Dua et al. had similar conclusions following anterior or posterior repair [61]. When an anterior repair was combined with a posterior repair, anterior vaginal repair does not appear to impact adversely on postoperative sexual function or cause dyspareunia. Nevertheless, there are very few data confirming this paradigm. Weber [62] compared three surgical techniques for cystocele repair; the dyspareunia rate reduced from 30%

preoperatively to 22% postoperatively.

An anterior repair (with or without a vaginal hysterectomy) for prolapse does not impact adversely on sexual function [61,63]. Both Colombo [64] and Van Geelen [65] found that anterior repair when compared to a Burch colposuspension for a cystocele did not predispose to dyspareunia. Though it was associated with significant vaginal shortening when compared to the Burch, this did not appear to impact on function unless combined with a posterior repair.

Combining a posterior vaginal wall repair with anterior colporrhaphy may however increase dyspareunia rates, and there may be a place for doing the two procedures separately where feasible. This would also indicate that a prophylactic posterior repair should be avoided at the time of an anterior repair in sexually active women. This was also shown in the study by Dua et al. [61].

Studies looking at posterior vaginal wall defect are more confusing, and whereas earlier studies suggest dyspareunia and problems with intercourse [66] with a posterior repair, this is not substantiated in more recent studies and this could be due to a recognition of the problem and a change in technique [67]. Levator ani plication is frequently implicated as the cause for dyspareunia due to postoperative midvaginal narrowing [66,68,69]. In contrast, improvement in dyspareunia has been reported with site-specific defect or midline plication procedures [70–72]. In sexually active women, therefore, levator plication should be avoided where possible and surgical techniques aimed at avoiding narrowing of vaginal introitus/mid vagina be adopted.

Vault prolapse surgery may be associated with postoperative dyspareunia and FSD. However, as this procedure often involves a concomitant repair, it is methodologically difficult to ascertain which specific procedure is causing sexual dysfunction. Maher et al. [73], in their systematic review comparing sacrocolpopexy to sacrospinous fixation, showed lower dyspareunia rates with the abdominal approach but a longer operating time, a longer time for recovery, and a greater expense. Baessler and Schuessler found that sacrocolpopexy was actually curative in women with dyspareunia and ceased in all but one of the nine patients among 33 consecutive women presenting with prolapse-related dyspareunia preoperatively [74]. Postoperative dyspareunia is reported to be between 8% and 16% after sacrospinous fixation [75–77]. When combined with a repair vaginal narrowing, excessive colpectomy occurring due to concomitant repair procedures was identified as the most common cause of postoperative dyspareunia [78], but vaginal narrowing and pudendal nerve injury have also been implicated. A sacrocolpopexy has also been shown to be superior to a vaginal mesh with lower extrusion rates and less impact on sexual function [73]. Kuhn et al. [79] demonstrated that following a sacrocolpopexy, the domains of sexual desire, arousal, lubrication, satisfaction, and pain improved significantly but orgasm remained unchanged. There was no vaginal shortening postoperatively. Therefore, in sexually active women, a sacrocolpopexy is the preferred procedure.

Iliococcygeal fixation is also performed for vault prolapse. In a matched case–control study comparing sacrospinous to iliococcygeal fixation, Maher et al. [80] found no significant difference in the percentage of women who were sexually active (58% vs. 55%), had dyspareunia (14% vs. 10%), or had buttock pain (19% vs. 14%). It is well recognized that bilateral iliococcygeal fixation may result in shortening of the vagina by 2–3 cm. In sexually active women with vault prolapse and a short vagina, bilateral iliococcygeal fixation is contraindicated, as it may cause severe postoperative dyspareunia.

Mesh

The aims of using mesh in the repair of vaginal wall prolapse are to add additional support and to reduce the risk of recurrence, particularly for women with recurrent prolapse or with congenital connective tissue disorders (such as Ehlers–Danlos or Marfan’s syndromes). A study by Abdel-Fattah et al. [81] looking at the complications of mesh reinforcement identified some very severe complications and therefore the need for caution when using synthetic materials in the absence of clear-cut indications. Further reports on problems with the use of meshes have resulted in a distinct decline in mesh usage with the commonest cause of complaints following mesh-reinforced repair according to the FDA report of 2011 [82,83] being pain or dyspareunia (590/1503, 38.6%). This has resulted in withdrawal from the market of some of the products including those by Bard and Ethicon.

Some studies have shown unacceptably high dyspareunia rates following mesh reinforcement for prolapse surgery. Milani et al. [84] demonstrated that though the use of mesh was associated with high success rates, there was a very high rate of dyspareunia of 20% when used for anterior repair and 63% when used for posterior repair. This warrants extensive counseling and caution when using meshes in women who are sexually active. These results are further borne out by other studies though some studies are equivocal and some even demonstrate an improvement following the use of mesh in vaginal repair.

Maher et al. in their systematic review [73] analyzed sexual function and dyspareunia in women undergoing surgery in the anterior compartment, posterior compartment, and apical compartment using mesh. The studies included in their systematic review were women who had mesh-reinforced colporrhaphy versus standard repair. Interestingly in contrast, the FDA report found no difference in the dyspareunia rates for native tissue anterior or posterior repair and mesh-reinforced anterior or posterior repairs.

URINARY TRACT INFECTIONS

The association of LUTS and sexual dysfunction is widely accepted. The incidence of urinary tract infections (UTIs) in women who are sexually active is about 3% per annum and about 4% of all LUT infections in this group are thought to be related to sexual activity and 60% in recurrent cases [85]. Honeymoon cystitis refers to LUTS occurring after initiation of sexual activity for the first time. Bacteria may be pushed mechanically up the urethra and into the bladder during coitus. Another hypothesis is microabrasions caused during intercourse, increasing the access of bacteria to the urinary tract. If they are not voided soon after, they multiply and may cause infection. The relative risk of UTI increased from 1.0 for unmarried women who had not been sexually active in the previous week to 9.0 for women who had had intercourse seven times during that period [86]. The term “honeymoon” was applied because, in the past, this was expected to be the time of first intercourse. The male urethra, being substantially longer, is not susceptible to the same problem. Some women are particularly sensitive to postcoital urinary tract dysfunction and this may be due to the development of a relatively high urethral pressure following intercourse. Of course, the condition of postcoital female lower urinary tract infection occurs at many times beyond the traditional “honeymoon”—from the onset of sexual activity into old age. This is further illustrated by the fact that nuns have a lower prevalence of bacteriuria than other populations of women in early adult life [87]. Following intercourse urinary bacterial count is significantly raised in 30% of women [88] and Nicolle et al. [89] reported that both symptomatic and asymptomatic bacteriuria were more frequent the day after intercourse. Several behavioral factors have been shown to enhance the risk of UTI following sexual intercourse. These include deferred voiding after intercourse [90], frequent intercourse [85], low fluid intake [91], and deferred voiding after the initial urge to micturate [92]. In addition, reduced lubrication and the use of spermicide-coated condoms and spermicides either alone or in conjunction with diaphragm have also been incriminated [93]. Contraceptive diaphragms by reducing urinary flow and spermicidal cream and the use of spermicidal-lubricated condoms can sometimes result in vaginal and urethral irritation, hence the association. These risk factors were shown to have a detrimental effect in the causation of UTI in a large prospective study by Hooton and coworkers who examined a variety of risk factors for UTI in young women [94].

The initial management of postcoital UTIs includes several simple measures that may be effective. Close attention to perineal hygiene, change of coital technique, use of a vaginal lubricant, and avoidance of the contraceptive diaphragm may all be successful first-line measures. Women should be encouraged to drink fluid before anticipated sex to facilitate postcoital voiding. Ingestion of products containing high-dose cranberry (as juice or a supplement) has long been thought to afford protection against UTIs [95]. Cranberries contain two substances (proanthocyanidins and fructose) that are thought to inhibit adhesion of infecting bacteria, particularly type 1 and type P fimbriated *Escherichia coli*, to the uroepithelium [96]. A systematic review of the literature considered the role of cranberry in the setting of recurrent UTIs and found the relative risk of developing a UTI over 6 months while taking cranberry to be reduced to 0.61 (CI 0.4-0.91) compared to 1.0 for placebo or no treatment [97]. The role of cranberry in prophylaxis against infection following intercourse, however, has yet to be established.

For women who do not respond to simple measures, regular or intermittent antibiotic prophylaxis is usually effective [98,99]. A recent systematic review of the literature found evidence that in women with recurrent UTIs associated with sexual activity, postcoital ciprofloxacin is equally as effective as a continuous daily prescription and should be considered in this setting [100]. There is evidence that local application of estrogen could be protective against infection in the context of recurrent UTIs in young women who are on oral contraceptives [101]. When simple measures fail to alleviate postcoital cystitis, further investigation including investigation for atypical organisms, such as *Mycoplasma hominis* and *Ureaplasma urealyticum*, is often worthwhile. Chlamydia causing acute urethritis should also be ruled out. Underlying abnormalities, such as voiding difficulties and vesicoureteral reflux, should always be considered and imaging of the renal tract with ultrasonography, intravenous urography, or videocystourethrography may be necessary. It is also sometimes appropriate to perform a cystourethroscopy and/or magnetic resonance imaging to exclude a urethral diverticulum or an intravesical foreign body such as a calculus.

BLADDER PAIN SYNDROME

Bladder pain syndrome (BPS), previously known as interstitial cystitis/painful bladder syndrome (IC/PBS), is a chronic, debilitating disease of unknown etiology characterized by urinary frequency, urgency, nocturia, suprapubic pressure, and pain. The true prevalence of the condition ranges from 10 to 500 cases/100,000 women depending on the strictness of the criteria used for the diagnosis [102,103]. Studies suggest that most women with IC have pelvic pain that extends to include dyspareunia and as a consequence sexually related distress; this in turn leads to a significant decline in desire and orgasm frequency [104–108]. The prevalence of sexual dysfunction in these women is higher than previously estimated and substantially affects QoL and sexuality [109]. Sacco et al. [106] showed that BPS was associated with the greatest impairment of FSF among women with LUTS. Because multiple factors contributing to sexual dysfunction (including biopsychosocial comorbidities such as stress, abuse, or chronic illness) can be present in women with IC, a variety of treatment approaches may be required. It is also important to recognize that some typical IC treatments, such as antidepressants and opioids used to manage pelvic pain, can exacerbate sexual dysfunction. Hypertonic pelvic floor dysfunction is prevalent in patients with IC [105] and contracted muscles can result in dyspareunia, vulvodynia, and vaginismus. The association between IC and syndromes such as vestibulodynia and spontaneous or provoked vulvodynia is commonly reported [110]. The magnitude of the association between vulvar and bladder symptoms is variable. This has obvious negative implications on sexual function, and sexual functioning is in fact one of the strongest predictors of poorer QOL in patients diagnosed with refractory IC/PBS [111].

Several studies have demonstrated an improvement in the dyspareunia and other levels of sexual function when PBS symptoms are alleviated either by intravesical injections of lidocaine, heparin, and sodium bicarbonate [112] or other pharmacological treatments [113] such as pentosan polysulphate and hyaluronic acid [114]. The pelvic floor muscles play an important role in female responsiveness and sexual function; thus, therapies aimed at treating the pelvic floor might be even more efficacious in improving sexual function, the woman’s self-esteem, and her relationship with her partner. Some therapies that have been reported to be helpful include pelvic floor therapy, biofeedback, neuromodulation, and botulinum toxin type A [115].

FECAL INCONTINENCE

Anal incontinence (involuntary loss of solid, liquid, or flatus) is reported to affect 8% of women in the general population [116]. Fecal incontinence (FI) (involuntary loss of solid or liquid) is known to cause sexual dysfunction, and this may be associated with anal sphincter injury related to birth trauma [117,118] or due to other causes such as neurological disorders. Fecal incontinence of solid stool and depression related to FI were correlated with poorer sexual function but do not prevent women from engaging in sexual activity thereby demonstrating that it is an important aspect of their lives [119].

Corrections of FI irrespective of the mode of repair were associated with an improvement in sexual function in most studies [118,120]. But patients who had undergone an overlapping sphincteroplasty versus an end-to-end sphincteroplasty reported pain during intercourse in 24% vs. 4% of subjects ($p = 0.04$). Sacral nerve stimulation, which is increasingly being used for the treatment of FI, has been shown to be of benefit [121,122]. However, some studies actually suggest an equivocal impact on sexual function following a repair [123]. Trowbridge [124] in his study showed that sexual function scores were not correlated with continence scores.

PREGNANCY CHILDBIRTH AND PERINEAL TRAUMA

Data on the impact of childbirth on sexual function are conflicting. There is a dearth of scientifically reliable data about the impact of childbirth on sexual function and the association with the different modes of delivery.

It is generally accepted that pregnancy itself is associated with reduced interest in sex, ranging from 57% to 75% [125–129]. Sexual interest usually improves postpartum but 23%–57% of women still report reduced sexual interest at 3 months and 21%–37% at 6 months [126,130]. Generally speaking, women are less likely to be sexually active during pregnancy, particularly in advanced pregnancy [126], with only 26% having intercourse in the third trimester. This could be due to a reduction in the ability to reach orgasm with 60% of women experiencing orgasm through the second trimester [127], declining to 50% in the third trimester [126]. Sexual function, which declined through pregnancy, was not recovered postpartum ($p = 0.017$). The main predictor for poor sexual function in early pregnancy was impaired body image, while in the postpartum period, worse urinary symptoms correlated with poor sexual function scores [131]. Interestingly, though sexual practices changed during pregnancy, they returned to early pregnancy levels in the postpartum period.

It is widely reported that postpartum dyspareunia is associated with the mode of delivery with assisted vaginal delivery being predominantly incriminated [118,132–134] with at least a twofold increase in dyspareunia when compared to spontaneous vaginal delivery. Barret et al. reported that women who delivered by cesarean section (C/S) were significantly less likely to report dyspareunia at 3 months postpartum than those with vaginal delivery [130]. However, the same authors in a subsequent study, by employing a larger cohort with longer follow-up, found that dyspareunia was equivalent in both groups [135]. This has been further substantiated in other studies that have failed to show that a C/S has a protective effect on sexual function [136,137]. With regard to vaginal delivery, however, a study by Buhling et al. [138] found the highest dyspareunia after operative vaginal delivery and least with elective C/S, which decreased uniformly in each group by 6 months. Operative vaginal deliveries had a persistent rate of dyspareunia of 14%, but there was no difference between the spontaneous vaginal delivery group with an intact perineum and C/S (3.4% dyspareunia at 6 months). Interestingly, at 3 months postpartum, all of the patients reported “enjoyment at sexual intercourse” regardless of the mode of delivery [138]. Perineal trauma with or without operative instrumental delivery was an important precursor of dyspareunia, and the greater the tear even, with spontaneous vaginal delivery, the lower the sexual desire [139,140]. Women with an intact perineum or first-degree perineal tear 6 months postpartum were more likely to experience orgasm [118] than those with a greater degree of perineal injury.

Postpartum, sexual desire and the ability to reach orgasm do improve, but the main problems encountered and impacting on sexual function are sexual arousal, excitement, and lubrication [130]. The risk of vaginal dryness and lubrication problems is increased with prolonged breastfeeding, which results in vaginal atrophy secondary to hypoestrogenism. The latter is easily corrected with topical estrogens or nonhormonal lubricants.

Owing to the inconsistencies in the definition of FSD and use of heterogeneous and invalid tools for evaluation in most of the studies, it is difficult to draw a scientifically consistent conclusion about the impact of mode of delivery on sexual health. Reports on the negative effect of vaginal childbirth on sexual health led to the concept of elective C/S to preserve sexual function. Many health-care professionals also advocate this approach with 7%–24% of obstetricians and 4.4% of midwives preferring elective C/S for themselves or their partner [141–143]. Interestingly, urogynecologists scored even higher, with 45.5% opting for primary elective C/S [143].

HYSTERECTOMY

Hysterectomy is the commonest major gynecological operation in the United Kingdom. Theoretically, it poses a risk not only to the intricate pelvic nerve plexus and damage to the autonomic nerve endings of the cervicovaginal fascia, hence impacting on orgasm or sensation during intercourse, but may also cause distortion of pelvic anatomy by shortening the vagina thereby resulting in dyspareunia. Historically, the uterus, “hystero,” was believed to be the center of female sexuality and may also have culture-dependent psychological effects leading to loss of self-esteem, female identity, and consequent FSD.

Following hysterectomy, an overall improvement [144] in the different aspects of sexual function, i.e., frequency of sexual relations, dyspareunia, orgasm, vaginal dryness, and sexual desire, was noted. The route of hysterectomy appears to play no role. A prospective study by El-Toukhy et al.

[145]compared hysterectomies performed abdominally, vaginally, or laparoscopically found that patients reported significantly lower rates of deep dyspareunia (18.8%, 19.7%, and 26.3% reduction, respectively) after surgery than before the operation, regardless of the routes and technique used. This was not substantiated in the study by Ayoubi et al. [146], who found greater postoperative delay in resuming sexual activity after abdominal hysterectomy (62.4 ± 9.3 days) than after vaginal (45.2 ± 6.7 days) hysterectomy. They also found that deterioration of sexual function occurred more frequently after abdominal hysterectomy (24%) than after vaginal (13.5%) or laparoscopic (8.5%) hysterectomy.

The belief that the cervix is necessary to achieve orgasm or that total abdominal hysterectomy (TAH) leads to local innervation damage with subsequent impairment of sexual function is not supported by current evidence. This belief was held for several years following a study by Kilkku et al. that found that women had a lower libido and orgasm following a TAH [147] when compared to a STAH. However, the same group subsequently reported an improvement in dyspareunia rates irrespective of the type of hysterectomy. Subsequent larger studies specifically comparing subtotal abdominal hysterectomy (STAH) and TAH [148] have also failed to identify a difference in sexual function. A study [149] looking at the long-term follow-up of women following a vaginal hysterectomy versus a Manchester Fothergill repair showed no difference in sexual function between the two groups, which further dispels this myth.

CONCLUSION

In spite of the common presentation of sexual dysfunction in association with pelvic floor disorders, overall assessment by clinicians remains low, and a recent survey of the members of the British Society of Urogynaecology (BSUG) demonstrated that only half of all clinicians routinely asked about FSD in the clinic and similar numbers at the postoperative follow-up visit [5]. Similar trends have been seen among the U.S. clinicians, and a recent survey of members of the American Urogynecologic Society (AUGS) has shown that 77% and 76% of AUGS members enquired of FSD, respectively, in similar situations [150]. Lack of time, uncertainty about therapeutic options, and older age of the patient were cited as potential reasons for failing to address sexual complaints as part of routine history. Clinicians dealing with women with these conditions need greater training to manage FSD in association with the underlying pathology.

Currently available evidence of pelvic floor problems and their impact on sexual function is conflicting. Greater and more robust research into different urogynecology conditions impacting on sexual function and their treatment is required. Assessment of patients with urogynecology problems not only requires a history and direct enquiry into sexual function, but also requires the development of standardized tools with well-defined end point to assess the severity of the problem. Broadly speaking, however, there is a body of evidence presented that treating pelvic floor conditions at worst does little harm and at best may significantly help. The aim now should be to increase awareness among clinicians to try and raise standards relating to this particularly as FSD may be an important part of individualized goal setting and treating what is important to patients.

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60 Menopause

Timothy C. Hillard

INTRODUCTION

The menopause is a biological event unique to humans. The average age of the menopause in western women is approximately 52 years, so with women living well into their 80s, they can now expect to live over a third of their life in the postmenopause. Consequently, over the last 50 years, there has been an increasing interest in the effects of the menopause on long-term health, its effects on quality of life, and its potential treatments. In evolutionary terms, the menopause was considered advantageous as it allowed women who were no longer fertile to look after their children's offspring and allow their children to continue breeding—the so-called grandmother effect. The increasing use of grandparents as childminders to allow the mother to return to work could be considered a modern adaptation.

DEFINITIONS

The term "menopause" means the final menstrual period (from the Greek *menos*, month; *pausos*, ending). It occurs as a result of loss of ovarian follicular activity leading to a fall in estradiol levels below the level needed for endometrial stimulation. Strictly speaking, it can only be said to have occurred after 12 consecutive months of amenorrhea. While the menopause can sometimes be a sudden event, for most women, there is a gradual change in menstrual pattern in the years preceding the menopause as ovarian activity fluctuates, which may be accompanied by troublesome symptoms; this is often called the "perimenopause." The menopause, or final menstrual period, represents a watershed in the reproductive life of a woman as represented in the staging system originally described by the American Society for Reproductive Medicine and updated at the Stages of Reproductive Aging Workshop (STRAW +10) (Figure 60.1) [1].

The term "climacteric" is often used synonymously with perimenopause but means the phase of transition from the reproductive to the nonreproductive state, the menopause being a specific event within that phase. It is recommended that the term now be abandoned in clinical practice to avoid confusion [2].

A surgical menopause occurs when functioning ovaries are removed such as at hysterectomy for malignancy or severe endometriosis. A menopause may also be iatrogenically induced by other treatments such as radio- or chemotherapy for malignancy or temporarily during treatment with gonadotropin-releasing hormone (GnRH) analogues for a variety of conditions.

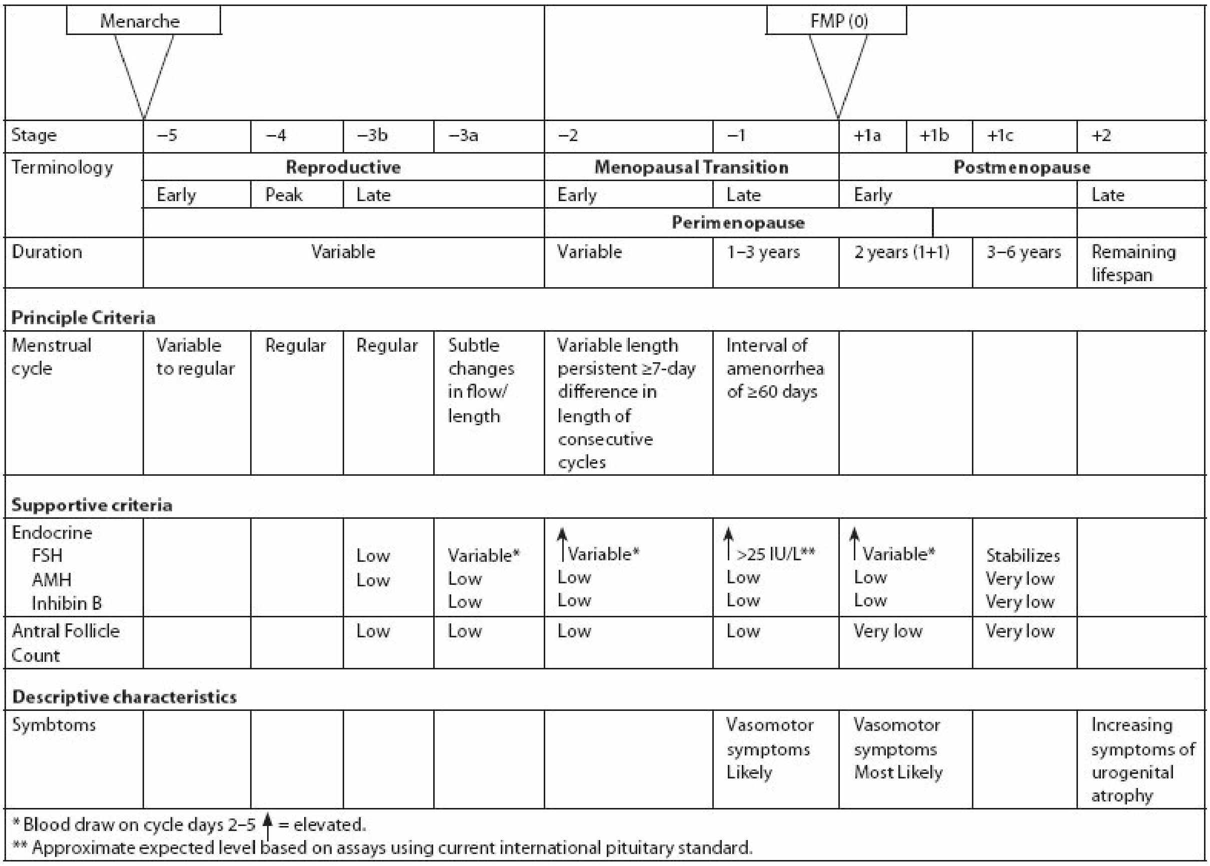
A "premature" menopause occurs if the menopause happens before the age of 45. This may occur naturally, be induced following surgery or other treatments, or be for other reasons (see Table 60.1). Women who have had a premature menopause are at an increased risk of a number of complications later in life and need special support.

ETIOLOGY

The ovaries produce three principal steroid hormones, estradiol, progesterone, and testosterone, although the latter plays no part in menstrual cycle control. Ovarian function and the normal menstrual cycle are controlled by the gonadotropins, follicle-stimulating hormone (FSH), and luteinizing hormone (LH), which are released from the anterior pituitary gland. Their release is controlled by the release of GnRH from the hypothalamus, which in turn is governed by the negative feedback from circulating levels of estradiol, progesterone, and inhibin (a peptide hormone produced by the ovary).

A detailed description of reproductive physiology can be found elsewhere [3]. In summary, each ovary contains several million germ cell units (oocytes), which achieve maximal levels in utero. There is a steady decline in these units over the prepubertal and reproductive years, but the maturation of these follicular units during this time is one of the key components of ovulation, corpus luteum formation, and ovarian steroidogenesis. It is estimated that up to 1000 follicles fail for every one that matures to ovulation (Figure 60.2). As the ovary ages, the remaining follicles, which are probably the least sensitive to gonadotropins, are increasingly less likely to mature and so ovulation declines and ovarian function gradually fails. Eventually, the level of estradiol production is no longer sufficient to stimulate endometrial proliferation and menopause ensues. Further decline in estradiol levels over subsequent years has effects on all estrogen-responsive tissues (which are widespread throughout the body—see Table 60.2). As a result, the effects of ovarian failure are often noted before the last period and the effects can go on for many years. Menopause may only be a single event, but it represents a significant change in a woman's hormonal milieu, which has implications for her future health and quality of life—hence the importance of postreproductive health for women.

The mean age of menopause in the Western world is around 51–52 years and has been so since Greek times [4]. There are significant variations around the world with some African and Asian communities reportedly having younger menopause [5]. Certain genetic and environmental factors may influence age of menopause such as growth restriction in utero, low weight gain in infancy, and poor nutrition in childhood and family history [6]. Smoking may reduce the age of menopause by up to 3 years and women with Down's syndrome are also more likely to have an early menopause.



	Menarche					FMP (0)				
Stage	−5	−4	−3b	−3a	−2	−1	+1a	+1b	+1c	+2
Terminology	**Reproductive**				**Menopausal Transition**		**Postmenopause**			
	Early	Peak	Late		Early	Late	Early			Late
					Perimenopause					
Duration	Variable				Variable	1–3 years	2 years (1+1)		3–6 years	Remaining lifespan
Principle Criteria										
Menstrual cycle	Variable to regular	Regular	Regular	Subtle changes in flow/ length	Variable length persistent ≥7-day difference in length of consecutive cycles	Interval of amenorrhea of ≥60 days				
Supportive criteria										
Endocrine FSH AMH Inhibin B			Low Low	Variable* Low Low	↑ Variable* Low Low	↑ >25 IU/L** Low Low	↑ Variable* Low Low		Stabilizes Very low Very low	
Antral Follicle Count			Low	Low	Low	Low	Very low		Very low	
Descriptive characteristics										
Symbtoms						Vasomotor symptoms Likely	Vasomotor symptoms Most Likely			Increasing symptoms of urogenital atrophy

* Blood draw on cycle days 2–5 ↑ = elevated.
** Approximate expected level based on assays using current international pituitary standard.

Figure 60.1 The stages of reproductive aging workshop +10 staging system for reproductive aging in women. (From Harlow SD et al., *Climacteric*, 15, 105, 2012. With permission.)

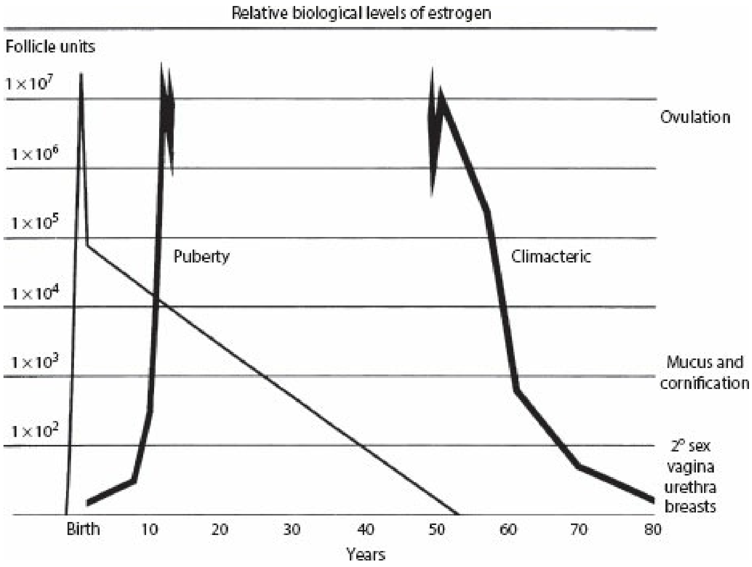


Figure 60.2 Correlation of follicle maturation, follicle availability, and estrogen production. (From Speroff L et al., *Clinical Gynecologic Endocrinology and Infertility*, Williams and Wilkins, Baltimore, MD, 1990, pp. 121–164. With permission.)

Table 60.1 Causes of Premature Ovarian Failure

Primary
Chromosome anomalies (e.g., Turner's syndrome, fragile X)
Autoimmune disease (e.g., hypothyroidism, Addison's disease, myasthenia gravis)
Enzyme deficiencies (e.g., galactosemia, 17-α-hydroxylase)
FSH receptor gene polymorphism
Secondary
Surgical menopause after bilateral oophorectomy
Chemotherapy or radiotherapy
Infections (e.g., tuberculosis, mumps, malaria, varicella, HIV)

A premature menopause (now called premature ovarian insufficiency) occurs in about 5% of women under 45, 1% of women under 40, and 0.1% under 30. It is one of the commoner causes of primary and secondary amenorrhea and should always be considered in the diagnosis. The implications of this endocrine failure can be very significant particularly at a young age. The cause of spontaneous premature ovarian failure is usually unknown, but there are a number of well-established causes that should be excluded (Table 60.1). Either there may be something wrong with the ovaries themselves (primary ovarian failure), e.g., certain chromosomal abnormalities or autoimmune disorders, or something happens to the ovary, e.g., oophorectomy, radiotherapy, or chemotherapy damage or infection.

INVESTIGATIONS

When to Investigate

Usually, the diagnosis of menopause is straightforward and does not require specific investigation. For example, a woman in her late 40s with oligomenorrhea and classical menopausal symptoms is almost certainly perimenopausal and no blood tests are needed. Equally, a woman in her mid 50s with at least 12 months amenorrhea has gone through the menopause and no specific tests are required to confirm that. However, in other clinical situations, it can be helpful to confirm the diagnosis or, perhaps more commonly, to refute the diagnosis, for example, in a woman in her mid 40s with vague symptoms who thinks she is going through the menopause. Here normal FSH/LH levels will help to reassure that this is not the cause. It is mandatory however to investigate women suspected of undergoing a premature menopause. The implications of the diagnosis have major long-term consequences in terms of both long-term treatment and also potential fertility. The younger women (under 40) require detailed assessment and specialist assessment.

What Investigations

FSH measurements are the most useful for confirming the diagnosis. A level of >30 IU/L is considered diagnostic of menopause. However, there is significant daily variation of FSH levels throughout the cycle and the results should be interpreted with caution and repeated if necessary. The tests are best done on day 3–5 of the cycle when FSH levels are usually at their lowest. To confirm that a woman with amenorrhea or who has been hysterectomized is menopausal, 2 measurements at least 2 weeks and up to 3 months apart are recommended. FSH levels are no use in predicting when menopause will occur or assessing fertility status. Equally monitoring FSH levels on treatment is of little value. There is no value in using estradiol, progesterone, testosterone, or LH levels in the diagnosis of menopause. Estradiol levels may be useful in monitoring treatment in certain situations.

Thyroid function (T4 and TSH) should be checked if there are any clinical suspicions as the symptoms of hypothyroidism can be confused with menopause or may explain poor response to estrogens. In resistant cases of intractable hot flushes, 24 hour urinary collections of catecholamines (VMA), 5-hydroxyindoleacetic acid, and methylhistamine may be done to exclude rare causes such as pheochromocytoma, carcinoid syndrome, and mastocytosis, respectively.

Further Assessment

The menopause presents an opportunity to screen for significant disease in later years and introduce appropriate preventative measures. There is a wide range of investigations that can be performed:

- Breast screening and mammography
- Endometrial assessment of unscheduled bleeding
- Cardiovascular disease risk assessment
- Skeletal assessment including bone density estimation and fracture risk assessment

While the majority of these are unlikely to be instigated by a urogynecologist, some understanding is helpful. A more detailed description can be found elsewhere [7].

EFFECTS OF THE MENOPAUSE

The menopause can have significant effects throughout the body, which vary chronologically and are summarized in Table 60.2.

Menopausal Symptoms

Vasomotor symptoms, which usually manifest as hot flushes or night sweats, are the commonest symptoms of the menopause. Their exact cause is unknown, but among the many theories, it is hypothesized that a fall in circulating estrogen levels disrupts the control of the body's thermostat, located in the hypothalamus, leading to cutaneous vasodilatation and heat loss [8]. Classically, the hot flush only affects the upper trunk and head and neck. Recent renewed interest in the cause of the hot flush has implicated a possible role for serotonin and its receptors in the central nervous system [9]. Certain triggers can be identified such as stress, spicy foods, alcohol, caffeine, and hot drinks although these are often very individual. Typically, hot flushes start to occur a year or two before the menopause, peaking in frequency and intensity in the first year after menopause and on average lasting for up to 5 years. However, they can continue for 20 or more years and some unfortunate individuals continue to flush all their lives [10].

Table 60.2 Effects of the Menopause in Different Time Frames

Short term
Vasomotor symptoms (e.g., hot flushes, night sweats)
Psychological symptoms (e.g., labile mood, anxiety, tearfulness)
Loss of concentration, poor memory

Joint aches and pains
Dry and itchy skin
Hair changes
Decreased sexual desire
Intermediate
Vaginal dryness, soreness
Dyspareunia
Sensory urgency
Recurrent urinary tract infections
Urogenital prolapse
Long term
Osteoporosis
Cardiovascular disease
Dementia

About 70% of women in the west experience some form of vasomotor symptoms, but their intensity varies enormously. For some women, they are a minor nuisance, but for others, they can be very disabling and can have a major impact on their quality of life. Flushes occurring at night can lead to night sweats, which may disrupt sleep and lead to tiredness, which in turn can affect mood, concentration, and libido.

Psychological Symptoms

Symptoms such as irritability, depressed mood, anxiety, loss of memory and concentration, overwhelming tiredness, and mood swings are common around the menopause, and there is peak prevalence of women seeking help from their GP for this type of problem at this time [11]. However, whether these problems are actually caused by falling estrogen levels or a secondary effect of other menopausal symptoms or due to other coexistent factors is not clear. Several longitudinal studies have not demonstrated any association between depressed mood and the menopause transition [12,13]. Women who report psychological symptoms at the menopause are more likely to have had previous psychological problems, poor health, and premenstrual problems and have current life stresses such as dependent relatives, relationship problems, and negative attitudes to aging and the menopause [14]. The menopause occurs at a time of life when there can be many other stressful events going on, and in many societies, the woman is often the lynchpin that keeps many families together. The additional physical and emotional changes that occur at the menopause can put this balance under pressure and some women will struggle to cope. Whatever the underlying cause, many women do need additional support during this time and some may benefit from specific treatment for their symptoms such as hormone replacement therapy (HRT).

Genitourinary Problems

During the fourth to seventh weeks of fetal development, the urogenital sinus separates from the cloaca and develops into the bladder and proximal urethra in the upper part and the distal urethra and the vestibule of the vagina in the lower part. This shared embryological origin explains why both the genital tract and the lower two-thirds of the urinary tract are rich in estrogen and progesterone receptors and why the loss of estrogen at the menopause can lead to the symptoms and signs of urogenital atrophy. Urogenital atrophy is a common observation in postmenopausal women, which increases with age, but the prevalence of symptomatic atrophy is unclear. In a population-based study of Australian women observed over 7 years, vaginal dryness was a complaint in 3% of premenopausal women, 4% of women in early menopause, but up to 47% of women 3 years or more into their menopause [15].

Vaginal atrophy results in loss of the normal architecture within the vaginal epithelium (Figure 60.3), reducing its secretions and elasticity and making it more prone to trauma, dryness, spontaneous bleeding, and infection. Clinically, this manifests as vaginal dryness, itching, dyspareunia, vaginal pain, discharge, and bleeding. The term genitourinary syndrome of menopause (GSM) is now preferred to vulvo-vaginal atrophy or urogenital atrophy as it provides a more accurate and comprehensive description of this common symptomatic postmenopausal condition [16]. An increased incidence of

STDs is now being reported in postmenopausal women [17]. In part, this may be related to the increasing numbers of postmenopausal women restarting sexual activity but also because a hypoestrogenic vaginal epithelium is more susceptible to acquiring infection [18].

A midlife peak of urinary symptoms around the menopause has also been reported by numerous epidemiological studies [19–21] (Figure 60.4). Women with depressed mood scores are more likely to report symptoms of urinary incontinence [22]. Although loss of estrogen is not the principal cause of most urinary symptoms, there is no doubt that atrophy of the distal urinary tract and in particular the urethra and trigone can lead to troublesome symptoms. Typically, these women describe urinary frequency and dysuria in the absence of proven infection, sometimes referred to as the "urethral syndrome." Thinning of the urethral mucosa and trigone results in a more sensitive and trauma-prone bladder, which in turn leads to sensory urgency and recurrent urinary tract infections, symptoms that respond well to local estrogen administration [23]. Loss of estrogen also plays a role in more widespread pelvic floor dysfunction, leading to weakening of the supporting tissues and ligaments, which may already be damaged by childbirth or other traumas, thus contributing to the increased incidence of prolapse and stress urinary incontinence seen after menopause [24]. Thinning of the urethral mucosa due to atrophy probably contributes to incomplete closure of the urethra, leading to a reduction in urethral closure pressure, which may be a factor in the development of stress incontinence [25].

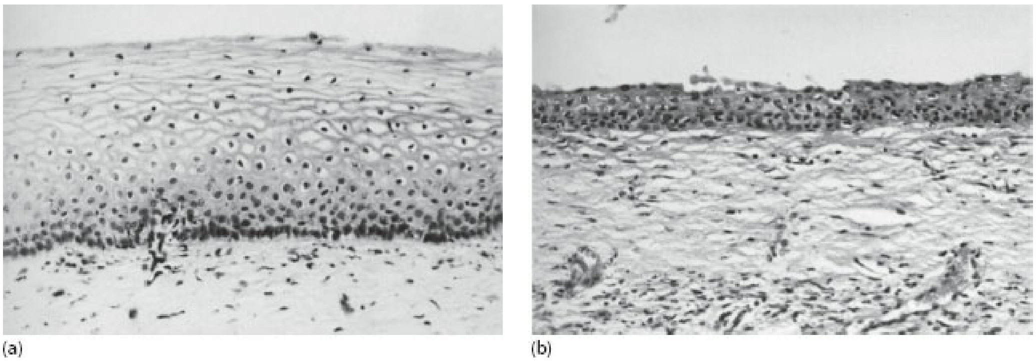


Figure 60.3 Vaginal epithelium in (a) premenopausal woman (left) and (b) postmenopausal woman (right) showing atrophic changes. (From Whitehead MI et al., *Atlas of the Menopause*, Parthenon, Athens, Greece, 1993. With permission.)

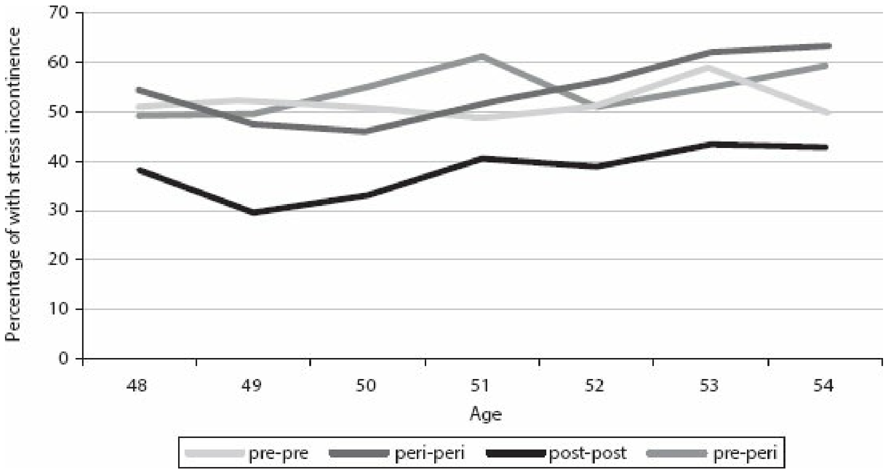


Figure 60.4 Percentage of women in selected menopausal transition categories with stress incontinence by age (n = 843). (From Mishra GD et al., *Br J Urol Int*, 106(8), 1170, 2010. With permission.)

Sexual Dysfunction

Many women complain of loss of sexual desire or libido around the menopause. The term female sexual dysfunction is now in widespread use based on a classification system introduced by the International Consensus Development Conference on Female Sexual Dysfunction [26].

The U.S. National Health and Social Life Survey [27] reported that among 18–59-year olds, sexual dysfunction was more prevalent in women (43%) than men (31%) and that the prevalence of sexual dysfunction rose from 42% to 88% during the menopausal transition. Dennerstein et al. [12] found an increased prevalence of sexual dysfunction but concluded that this was primarily secondary to vaginal atrophy and relationship difficulties. Hormonal changes and in particular loss of estrogen may have a direct effect on sexual desire and function, but the underlying reasons behind sexual dysfunction are often multifactorial. For many women, sexual desire naturally decreases with age and the menopause may coincide with other stressful major life events. In addition, menopausal symptoms and vaginal atrophy may lead to tiredness and discomfort; there may be reduced response to sexual stimuli and more difficulty reaching orgasm. Male partners may also have reduced interest and have difficulty getting or maintaining an erection. This is undoubtedly a complex area but one that does require some understanding particularly in women presenting with other genital tract problems for whom maintaining sexual function is important.

Correction of physical symptoms, often with systemic or vaginal estrogens, may be sufficient in many cases to overcome the problem, but in other women, the causes are more complex and may benefit from psychosexual input. In western society, the menopause is often viewed as a negative event and some women suffer with low self-esteem, which undoubtedly does not help, but in some cultures, the menopause can be associated with an increase in libido as the shackles of monthly bleeding and risk of pregnancy are finally cast off. The role of testosterone and other treatments are discussed later.

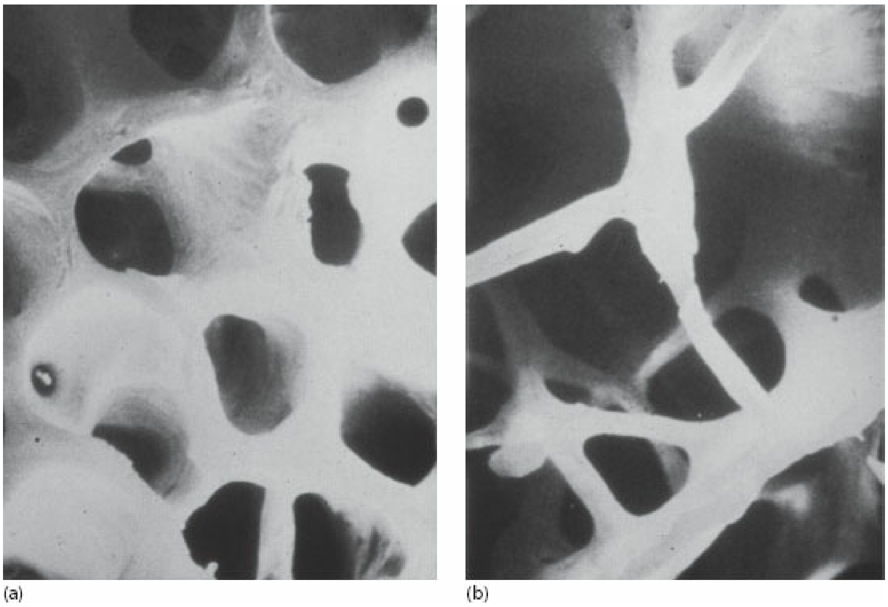


Figure 60.5 Electron micrograph of trabecular bone showing (a) normal structure (left) and (b) osteoporotic bone (right). (From Whitehead MI et al., *Atlas of the Menopause*, Parthenon, Athens, Greece, 1993. With permission.)

LONG-TERM EFFECTS

Estrogen receptors are widespread throughout the body and the fall in circulating estradiol levels leads to a number of changes in a variety of organs and systems that can have notable effects on quality of life and a potentially major impact on long-term morbidity and mortality. These conditions often develop without obvious clinical manifestation in the early postmenopause but pose a significant economic burden for the future particularly with an increasingly aging population. For women who undergo a premature menopause, the prolonged time they spend without estrogen increases the risk of these conditions developing at a younger age.

Osteoporosis

Osteoporosis is defined as “a skeletal disorder characterised by compromised bone strength predisposing to an increased risk of fracture” [28]. Bone strength is principally a reflection of bone quality and bone density (Figure 60.5). The latter is clinically most relevant as it can be readily measured and a woman’s osteoporotic risk assessed using standard WHO criteria (Table 60.3). Osteoporosis is a major health problem for the Western world that will only worsen as the population ages. The commonest sites of osteoporotic fracture are the neck of femur, wrist, and vertebrae, but any long bone is susceptible. Osteoporosis is far more prevalent in women than men, and it is estimated that as many as 50% of women will suffer an osteoporotic fracture in their lifetime [29].

Table 60.3 Definitions of Osteoporosis (World Health Organization)

Description	Definition
Normal	BMD value between −1 SD and +1 SD of young adult mean (T score −1.0 to +1.0)
Osteopenia	BMD value between −1 SD and −2.5 SD of young adult mean (T score −1.0 to −2.5)
Osteoporosis	BMD value equal or below −2.5 SD of young adult mean (T score −2.5 or below)
Established osteoporosis	BMD value equal or below −2.5 SD of young adult mean (T score −2.5 or below) plus one or more fragility fracture

Bone density peaks in the midtwenties as a result of genetic and environmental influences and starts to decline in the mid 40s with an accelerated phase of around 6–10 years after menopause. Thereafter, there is a steady decline with advancing age. The accelerated postmenopausal loss is largely due to the loss of estrogen, which has antiresorptive actions. This results in an accelerated phase of bone resorption and loss of trabecular bone. The rapid fall in bone density immediately after the menopause has triggered a wide range of strategies to prevent osteoporosis over the last 30 years [30]. Estrogen replacement has been proven to both reduce bone loss [31] and reduce the subsequent rate of hip fracture in low-risk populations [32] and is thus an effective preventative treatment in appropriate individuals (see “Benefits of HRT” section at individuals identified as high risk of subsequent fracture rather than treating large sections of the population. Current models, such as the FRAX model [33], screen postmenopausal women for risk factors including age at menopause (premature menopause being particularly high risk). Those deemed as increased risk undergo DEXA bone scanning and those with low bone density offered preventative treatment. There is much debate about when to start preventative treatment as long-term treatments have potential adverse effects and are costly. In the UK, NICE (National Institute of Clinical Excellence) guidance favors a very limited role for preventative treatment in women under 75 except those with previous fracture [34]. This is contrary to previous guidance based on a more clinical approach [35]. Prevention of osteoporosis remains a lifelong strategy even if for some or most of that time no specific treatment is used. A detailed description of all the treatments and their potential role can be found elsewhere [30,31,36].

Coronary Heart Disease (CHD)

While CHD is the single commonest cause of death in women in the United Kingdom, it is relatively uncommon before the menopause. Menopausal status is considered an independent risk factor [37], and after the menopause, the risk increases considerably and there is a large body of evidence suggesting that estrogen has a protective influence against CHD [38]. Early oophorectomy without additional estrogen is associated with a two- to fourfold increased risk of CHD compared to premenopausal women of similar age [39], and large-scale population studies over 20 years suggested that taking estrogens around the time of the menopause leads to a reduction in risk [40]. Estrogens reverse many of the adverse changes in cholesterol and other postmenopausal CHD risk factors [41] and also appear to reduce atherogenesis in animal studies [42]. However, the large Women’s Health Initiative (WHI) randomized trial did not show any convincing evidence that taking estrogen after the menopause has any CHD benefits [43]. The mean age of women in this study was 63 years, but when the data were reanalyzed for those women under the age of 60, no harmful effect was found; indeed there was a suggestion of a beneficial effect [44]. This is more consistent with the previous epidemiological data that estrogens that started around the time of menopause may have a beneficial effect on future CHD risk [45]. A recent 10-year randomized trial of women receiving HRT that started early after menopause observed a significant reduction in mortality, heart failure, and stroke compared to the untreated group

[46].

Dementia

Decline in cognitive function inevitably occurs with age, but once this interferes substantially with social or occupational functioning, it becomes dementia. The incidence of dementia, of which Alzheimer's disease is the commonest form, is increasing and doubles every 5 years after the age of 65 [47]. Alzheimer's disease is more common in women than men, and estrogen receptors are widespread in the central and peripheral nervous systems facilitating autonomic regulation and cognitive function. However, the evidence for a role of estrogen and menopause in the pathophysiology of cognitive decline and dementia is conflicting and may depend on age and timing of intervention. During the menopause in two midlife studies, 36%–62% of women reported memory changes [48,49], but natural menopause does not seem to be associated with objective loss of memory [50]. However, early surgical menopause is associated with an increased risk of dementia in later life, as well as other neurological problems [51]. A meta-analysis of postmenopausal estrogen use around the time of the menopause suggested that it may improve cognitive function and reduce the risk of Alzheimer's disease [52]. Conversely, the WHI memory study reported an increased incidence of dementia with HRT usage; however, this was in a relatively old population (over 65 years), who wouldn't normally expect to be starting estrogens [53]. If estrogens do have any beneficial effect on cognitive function and dementia, they probably need to be started around menopause, but there is insufficient evidence at the moment to suggest this is a benefit of HRT.

MANAGEMENT

The menopause is a natural event, and for many women, there is no need to "manage" it at all, although awareness of the long-term implications such as osteoporosis and cardiovascular disease should be part of good preventative medicine. However for other women, the menopause can be a difficult time and there are a variety of treatment options available. While HRT is an extremely effective option, it is only one of a number of possible approaches. For most women, menopausal symptoms are relatively short lived and will settle within a few years, but for some they will go on much longer and longer-term treatment may be needed. The menopause is a hormonal milestone and provides an opportunity to establish firm strategies for the prevention of the long-term disorders outlined earlier.

Lifestyle

Dealing with the effects of the menopause should incorporate a holistic approach. It is an ideal time to encourage lifestyle changes that can build for a healthy future and help maximize health potential. For many women, the menopause can be a time of uncertainty and may be the first time they've sought professional help for themselves for many years. Smoking is associated with an earlier menopause and an increased risk of cardiovascular disease, lung cancer, and osteoporosis. Smoking cessation leads to a steady reduction in all the increased risks and should be encouraged as part of a health promotion strategy.

Diet

Body weight increases on average 1 kg/year around menopause, although this does not seem to be a direct effect of the menopause itself [54]. In addition, there are metabolic changes and changes in body fat distribution with body fat shifting from the hips and thighs (gynecoid) to a more android distribution (abdomen) [55]. Thus, it is particularly important that women going through menopause eat sensibly and try and avoid excessive weight gain. A recommended diet should be rich in fruit and vegetables, whole grain and high-fiber foods, oily fish twice a week, saturated fat intake less than 10%, cholesterol less than 300 mg/day, alcohol intake no more than 1 unit/day, and sodium to 1 tsp/day [56]. For women with obesity problems, entering the menopause specialist dietary advice may be helpful. HRT is not per se associated with an increase in weight gain [57] although in some women it can increase fluid retention and over time may lead to a reversal of the body fat changes seen at menopause.

Exercise

Regular physical activity has positive effects on a variety of conditions and physical activity can be effectively used to reduce vasomotor symptoms [58] possibly by an effect on endorphins. Regular exercise, even of relatively low intensity, can be beneficial to cardiovascular health [59]. Exercise also has a key role to play in the maintenance of bone health; not only does regular weight-bearing exercise help to conserve bone density in the hip and spine, it also helps to maintain muscle strength, joint flexibility, and overall balance, all factors that will reduce the risk of falls and subsequent fracture [60].

Alternative and Complementary Therapies

A wide variety of nonhormonal prescription drugs, complementary and alternative medicines, are used to improve menopausal symptoms. Some of the licensed preparations such as clonidine, venlafaxine, and gabapentin have short-term randomized trials demonstrating their efficacy [61], but robust evidence for the efficacy and safety of most of the complementary and alternative products or methods is notably lacking [61]. Despite this, the use of such treatments is widespread and increasing [62]. In our own clinic, we identified that up to 40% of women were taking additional over-the-counter supplements for their menopausal symptoms and 10% were taking more than four different products concurrently [63]. These products are currently unregulated in the United Kingdom, and while the majority are likely to be harmless, a number of serious and potentially fatal interactions have been reported between herbal supplements and standard medications [64]. By contrast, the use of phytoestrogens, plant substances with similar activity to estrogen, and black cohosh appear to have some beneficial effects on menopausal symptoms [61]. A meta-analysis of 17 RCTs of soy and red clover isoflavones demonstrated a significant reduction in hot flushes particularly in those with frequent flushes [65]. The effects on other parameters such as bone loss are less clear. Cognitive behavioral therapy (CBT) can also be effective in alleviating low mood or anxiety that arise as a result of the menopause [61].

Hormone Replacement Therapy

HRT is the mainstay of medical treatment available for troublesome menopausal symptoms and simply acts by replacing the hormones that are normally produced by the human ovary at physiological levels. Estrogen is the principal hormone and can be given either alone or in combination with progestogen, which should be given to all nonhysterectomized women. A third hormone, testosterone, can also be given in conjunction with estrogen.

Estrogen

There are a variety of different types of estrogen available, which can be given at varying doses and by different routes [66]. For the vast majority of women, the type and route of administration are not important, and provided an adequate dose of estrogen is given, it is likely to be effective. However, there are some women who do not show an appropriate response and adjustment to a different type of estrogen may be helpful.

The appropriate dose depends on age and severity of symptoms, but as with any treatment, the lowest effective dose should be used. Generally, 1 mg estradiol, 0.625 mg conjugated equine estrogens (CEEs), or 50 mg transdermal estradiol is a reasonable starting dose for an average peri- or early postmenopausal women. The dose may be increased if symptoms are not controlled. Very low or ultralow doses of HRT (0.3 mg CEE or 0.5 mg of estradiol or 14 mcg transdermal estradiol) may also be effective in relieving menopausal symptoms [67,68] and slowing down the rate of bone loss [69].

Different routes of estrogen administration have different pharmacokinetic profiles. Nonoral routes, such as percutaneous and transdermal administration, avoid the first-pass effect with consequent less impact on coagulation and hemostatic mechanisms, making them more suitable for women at increased venous thromboembolism (VTE) [70]. However, oral estrogens, because of their first-pass effect, have potentially greater beneficial effects on lipids and lipoproteins and glucose and insulin metabolism [66,71], so women with hypercholesterolemia or hypertriglyceridemia may benefit more from oral estrogens. For the vast majority of patients, the route of administration is not important provided adequate estrogen levels are achieved. Nonoral routes tend to be more expensive, and for those women who need a progestogen, there can be logistical problems administering the progestogen component simultaneously.

Progestogens

Giving unopposed estrogens to nonhysterectomized women substantially increases their risk of developing endometrial cancer [72]. Progestogens added for at least 10 days per calendar month negate this risk [73]. They can be given either cyclically, mimicking the natural 28-day cycle and resulting in a regular withdrawal bleed, or continuously to prevent any bleeding, so-called “no-bleed” treatment. The latter is usually recommended for women who are clearly postmenopausal, while the former is usually prescribed for women who are perimenopausal. Long-cycle HRT can also be used where progestogen is added for 2 weeks every 3 months. While this has potential advantages in limiting withdrawal bleeds to 4/year, it carries an increased risk of breakthrough bleeding and potential endometrial abnormalities if continued long term [74].

There are several different types of progestogen used in HRT (Table 60.4). Side effects are common, particularly in the first few months, and these may vary depending on the type and dose of progestogen used. Switching from one type of progestogen to another or changing the route of administration can alleviate side effects in many cases. The advent of the levonorgestrel intrauterine system has allowed many women who could not tolerate any of the available progestogen combinations to continue HRT safely. However, all progestogens are not necessarily equal [66] particularly in their possible cardiovascular [75] and breast [76] effects.

Table 60.4 Different Progestogens Used in Hormone Replacement Therapy

Norethisterone (transdermal)
Levonorgestrel (transdermal, intrauterine)
Dydrogesterone
Medroxyprogesterone acetate
Drospirenone
Micronized progesterone (rectally)
Cyproterone acetate (not available in the United Kingdom)

Note: All are available orally. Additional routes are listed.

Testosterone

Fifty percent of testosterone production in women is from the ovaries (the other 50% is from peripheral fat stores and the adrenals). Testosterone production is not generally affected by natural menopause although a decline in sex hormone binding globulin (SHBG) may lead to a small rise in circulating free testosterone. However, women who undergo a surgery- or chemoradiation-induced menopause may become relatively testosterone deficient. Symptoms can be hard to determine specifically but classically are loss of libido, decreased sexual activity, fatigue, and reduced feelings of physical well-being [77]. There are a number of potential treatment options that are discussed later.

BENEFITS AND RISKS OF HRT

Prescribing any medication or intervention requires careful weighing up of the potential benefits and possible harm for that individual and should be done in careful informed discussion with the woman. The role of HRT has been the subject of considerable scientific and public debate in recent years, so it is important that up-to-date evidence and recommendations are used to inform any discussion [61,78–80] (Table 60.5).

Table 60.5 Benefits and Risks of Hormone Replacement Therapy Based on Grade A or B Evidence

	Benefits	**Risks**
Grade A	Vasomotor symptoms	VTE
	Urogenital symptoms	Endometrial cancer
	Osteoporosis	Gall bladder disease
	Colon cancer	
Grade B	Quality of life	Breast cancer
	Osteoarthritis	Stroke

	Cardiovascular disease	Ovarian cancer
	Sexual function	

Source: Adapted from the Endocrine Society Statement, Santen RJ et al., *J Clin Endocrinol Metab*, 95(S1), 1, 2010.

Benefits of HRT

The majority of women start HRT for the relief of their menopausal symptoms, and there is abundant evidence that estrogen is effective in treating hot flushes [81], with improvement usually noted within 4–6 weeks [61]. Comparative studies indicate that HRT is far more effective than nonhormonal preparations, such as clonidine, selective serotonin reuptake inhibitors, herbal preparations, and phytoestrogens [82,83].

The symptoms of vaginal and urogenital atrophy discussed earlier respond well to systemic or vaginal estrogens [23,61,84]. Systemic HRT offers no benefits over topical therapy for the treatment of genitourinary atrophy; indeed sensory urgency seems to respond better to topical estrogen than systemic estrogen [85]. Topical vaginal estrogens also reduce the frequency of recurrent urinary tract infections, have minimal systemic absorption, and are not associated with the risks associated with HRT (discussed in the following texts). Thus, they are the preferred treatment for genitourinary atrophy and should be continued at a low maintenance dose; otherwise, the symptoms tend to recur.

HRT is effective in the prevention of postmenopausal bone loss and osteoporotic fractures at the spine and hip [77], even in a low-risk population [32]. Thus, women taking HRT for symptom relief will derive benefit as far as their bones are concerned. What has been more debatable is whether or not HRT should be prescribed for osteoporosis prevention alone. The regulatory authorities have advised that HRT should not be used as a first-line treatment for osteoporosis prevention in postmenopausal women as the potential risks outweigh the benefits [86]. However, the long-term efficacy and safety of alternatives for osteoporosis prevention, such as the bisphosphonates, have not been established in younger (<60 years) postmenopausal women, and there are increasing concerns about the long-term safety of these preparations [87–89]. Thus, in this age group, HRT remains a suitable preventive treatment [79,90,91].

For women with premature ovarian failure under the age of 50, all professional bodies including the regulatory authorities agree that HRT is the most appropriate treatment for osteoporosis prevention [61,78–80,86,91].

Risks of HRT

Ever since the introduction of HRT, there has been controversy that the prolongation of exposure to natural hormones may have an adverse effect on the breast and other estrogen-sensitive tissues. Yet despite widespread use for over four decades and numerous studies, there remains uncertainty and controversy about exactly what the risks are and how relevant they are to the majority of healthy postmenopausal women.

Breast Cancer

A large body of epidemiological studies have suggested that less than 5 years of HRT use in the early postmenopause does not increase breast cancer risk [92]. Thereafter, there does appear to be a small increase in risk, dependent on years of exposure. The magnitude of risk appears to be similar to that associated with late natural menopause (2.3% compared with 2.8% per year, respectively). A meta-analysis of all observational data prior to 1997 estimated that current use of any HRT for more than 5 years, when started over the age of 50, increased breast cancer risk by 1.35 (95% confidence interval 1.20–1.49) [92]. In absolute numbers, this equates to 4–5 extra breast cancer cases/1000 women who use HRT from the age of 50 for 5 years. Women who start HRT early for premature menopause do not show this effect, suggesting that it may be the lifetime sex hormone exposure that is relevant. The WHI study [43], which is the largest randomized trial on HRT, reported a broadly similar risk to that seen in the epidemiological studies for combined estrogen and progestogen treatment but also found no increase in risk over 7 years with estrogen-only treatment [93]. There are conflicting reports about what happens to breast cancer risk after stopping HRT. A recent 3-year follow-up of women who were in the WHI trial claimed that the risk of breast cancer remains elevated for 3 years after treatment was stopped [94]. However, these findings are at odds with other recent publications, which imply the risk of breast cancer falls quickly after cessation of HRT [61,95,96].

In summary, otherwise healthy postmenopausal women in their late 40s and 50s wishing to take HRT should be reassured that the overall risk of developing breast cancer in the first few years as a result of their HRT is small [61] (Table 60.6). If they take estrogen alone, that risk is even lower [92,96]. Overall, other personal risk factors such as family history, BMI, and alcohol intake are likely to be more important predictive factors [98].

Endometrial Cancer

Unopposed estrogen replacement therapy increases endometrial cancer risk, which is reduced by the addition of progestogens [72,73]. When continued for more than 5 years, cyclical progestogen addition does not completely eradicate this excess risk, while continuous progestogen addition does [72]. Thus, once a woman is clearly postmenopausal, she should be switched to a continuous combined (no-bleed) regimen. Any abnormal bleeding on HRT should be investigated, although the likelihood of underlying malignancy is much lower than with postmenopausal bleeding (1% vs. 6%) [99].

Ovarian Cancer

Most of the limited data relate to estrogen alone and suggest a small increase in risk in epithelial tumors with very long-term (>10 years) treatment [100]. This increase does not seem apparent with combined therapy [101,102]. There is currently insufficient evidence to recommend any alterations in HRT-prescribing practice [79].

Venous Thromboembolism

HRT increases the risk of VTE twofold, with the highest risk occurring in the first year of use [103]. The background risk of VTE in women over 50 years not taking HRT is small (1.7/1000) [104], so the overall impact of this increase is low. However, the background risk is significantly increased in women who smoke, are obese, have an underlying thrombophilia such as factor V Leiden, or have previously suffered a VTE [103]. Transdermal HRT has less impact on hemostatic mechanisms and appears to be associated with a lower risk of VTE [70,103,105], even in women with a thrombophilia, and thus may be the treatment of choice in this group.

Coronary Heart Disease

Large-scale epidemiological studies have consistently shown that estrogens appear to have a protective effect on CHD [40], whereas some randomized trials have suggested a possible adverse effect [43]. Subsequent detailed analysis of these and other data suggest that timing of the introduction of estrogen may be critical [45,106,107]. For women starting HRT shortly after menopause, there may well be a protective effect on CHD, and this particularly appears to be the case for women undergoing premature menopause. However, in women many years past the menopause, starting HRT may have a detrimental effect, i.e., early benefit and late harm. There is no indication to use HRT for cardiovascular disease protection [79].

Stroke

Small increases in the risk of stroke with both estrogen only and combined estrogen and progestogen were reported in the WHI study [43], although there was a significant age effect, with a relatively high risk in older women and no reported increase in the 50–59 age group. In general, the data suggest a trend toward a small increase incidence of stroke with HRT although transdermal and ultralow-dose oral therapy may have a lower risk [61,78,108,109]. HRT should not generally be initiated for women over the age of 60 or those who have strong risk factors for stroke or cardiovascular disease risk without carefully weighing up the potential risks against any potential benefits.

Table 60.6 Absolute rates of Cardiovascular Disease, Stroke and Breast Cancer for Different Types of HRT Compared with Placebo (or no HRT) in Randomized Trials

	Baseline	**Estrogen**	**Estrogen + progestogen**	**Any HRT**[a]
Cardiovascular Disease	26.3	6 fewer (−10 to +1)	5 more (−3 to +18)	6 fewer (−11 to +5)

Stroke	11.3	0 (−5 to +10)	6 more (−2 to +21)	3 fewer (−7 to +8)
Breast Cancer	22.48	4 fewer (−11 to +8)	5 more (−4 to +30)	9 fewer (−16 to +7)

Source: Adapted from NICE, Menopause: Diagnosis and management, NICE guidelines [NG23], www.nice.org.uk/guidance/ng23 November 2015.

Note:Difference in incidence per 1000 menopausal women (aged 50–59) over 7.5 years (95% confidence interval). Baseline population refers to risk in the UK over 7.5 years.

[a] Studies did not specify type of HRT.

Practical Considerations for Prescribing HRT

HRT is only one option for dealing with menopausal symptoms and other options should be considered [61,82,83]. Yet despite the recent controversies, HRT remains a clinically effective and cost-effective strategy for women with menopausal symptoms [110]. For the majority of healthy symptomatic menopausal women, the potential benefits will outweigh any small risks [61,78–80]. However, like all treatments, the risks and benefits should be weighed upon individually with the patient before starting treatment.

Selecting which HRT regimen is a matter for the individual prescriber. If there are specific special circumstances, then a particular type or route of administration may be most appropriate. Follow-up should be arranged after a few months to check the treatment’s effectiveness and side effects. It is common for women to have some problems in the first few months, and if these do not settle down, a change of preparation may be advisable. Treatment should be started at the lowest appropriate dose and can be increased if there is no symptomatic improvement after a few months.

The duration of HRT use depends on the individual circumstances and indication for taking it. The “average” menopausal woman in her early 50s will probably only need it for 1–2 years, but there is no reason why she shouldn’t take it for longer if indicated. The Medicines and Healthcare Products Regulatory Agency (MHRA) recommend taking “the minimum effective dose” of HRT for the “shortest duration” without defining any specific length of time [86]. Based on other recommendations, this has generally been interpreted as about 5 years, although in reality most women don’t take it that long. However, treatment can be continued for longer in women with persistent troublesome symptoms that adversely affect their quality of life. For women with POI, the risk/benefit balance is strongly in favor of them taking HRT at least up until the age of 50 as a true physiological replacement [61,86,111].

For all women, their individual risk of VTE, stroke, and breast cancer should be appraised regularly and balanced against the benefits she is gaining from the treatment. For the majority of women, the overall increase in any risk will be very small and there are some women who opt to continue taking HRT for its benefits well into their 60s.

Stopping HRT should be done gradually reducing the dose to avoid rebound symptoms. At the same time, positive lifestyle factors should be emphasized, such as diet and regular exercise. Vaginal estrogens can be added in if troublesome genitourinary symptoms persist. As they are not absorbed systemically to any great extent, they can be continued after HRT has been stopped without significant risk [112].

Reduced sexual desire is a common complaint around the menopause, which can lead to distress and have a negative impact on psychological well-being and relationships [113]. This is a complex area and there are often multiple factors that play a part [114]. Menopausal symptoms and urogenital atrophy should be treated with systemic or local estrogens, and psychosexual counseling should be considered if appropriate. Testosterone supplementation appears to be effective in postmenopausal women when given orally or transdermally as a patch or gel in women with low sexual desire [115]. This is seen in both surgical and naturally occurring menopause [116,117] with or without concomitant estrogen treatment [118]. Subdermal testosterone implants, which have been used for many years in some countries, are no longer readily available. However, a transdermal testosterone cream, which is now available in Australia, may be a suitable alternative [119]. Tibolone, which is a synthetic steroid with estrogenic, progestogenic, and androgenic activity, has a licensed indication for women with loss of libido [120].

Contraception

Contraception should be continued until 2 years after the last period in women under 50 and 1 year in women over 50. A full review of contraceptive choices for perimenopausal women can be found elsewhere [121].

SUMMARY

The menopause is a time of significant physiological change signifying the end of the reproductive phase of life. While this can be a positive development for many women, for others, the menopause can be a difficult time with distressing symptoms that impact on their quality of life, their employment, and their relationships. The potential impact on long-term health should also be considered, and the menopause provides a good opportunity to improve lifestyle risk factors and put long-term prevention strategies in place. Women with premature ovarian failure have particular needs and will often benefit from specialist support. A wide range of potential treatments is available for helping women through the menopause and beyond. HRT is only one option but is effective and has a large body of evidence supporting its use. For the vast majority of healthy symptomatic menopausal women, the benefit/risk balance is in favor of using it for a limited period. No two women's experience of the menopause is exactly the same and any advice or treatment should therefore be tailored to the needs of the individual woman.

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61 Sports and Fitness Activities

Kari Bø

Urinary incontinence is often regarded as a problem affecting older, postmenopausal, multiparous women [1]. However, several epidemiological studies have demonstrated that the symptom of stress urinary incontinence (SUI) is also common in populations of nulliparous young females [1–10]. Prevalence data vary between 12% and 52% and may be explained by differences in definitions, study design, and populations. Typically, for prevalence studies the percentage tends to drop when the former International Continence Society (ICS) definition of symptoms being socially and hygienically problematic is used [6,11].

The most common type of urinary incontinence in women is SUI [12], defined as involuntary leakage on physical exertion, sneezing, or coughing [13]. Cross-sectional studies in the general female population reporting that physically active women have less incontinence compared to their sedentary counterparts are difficult to interpret as this association may be because women with incontinence have stopped exercising due to the condition [10,14–20]. Hence, the unanswered question is: Does physical activity cause continence, or are women able/willing to participate in physical activities because they are continent?

ASSESSMENT OF INCONTINENCE DURING PHYSICAL ACTIVITY

Usually, the diagnosis of urodynamic SUI is made during assessment in a half-sitting, lithotomy position. The validity of this evaluation can be questioned as most women only leak in a standing position. Some pad tests involve physical activities such as stair climbing and jumping [21]. Henalla et al. [22] and Hagen et al. [23] designed tests based on physical activities. The latter test involved running, jumping jacks, standing up and lying down, and abdominal curls. These were found to be nine times as provocative as the ICS test involving physical activity. The authors concluded that assessment of the degree of SUI has to be physically provocative to detect SUI. Nygaard et al. reported that 7% of women admitted to urine loss only during sports, and that 40% and 17% first noted urinary incontinence during sports while in high school or junior high school, respectively [1].

Methodological problems in study design have meant that there is a lack of studies describing bladder and urethral function during physical activity. James [24] argued that assessment of SUI should be performed in standing and working positions and during physical activity. He used ambulatory bladder pressure measurements to demonstrate peaks of bladder pressure rise during running and jumping, which occurred when the feet touched the ground. Although pressure rise was higher during coughing, some women were only leaking during exercise.

Kulseng-Hanssen and Klevmark [25] improved the methodology by placing bladder and urethral transducer catheters in a silicon cuff and sutured it to the external urethral opening to keep it stable during activity. In 16 of the patients, 115 leakage episodes were seen in 45 minutes. In 92 of these episodes, the maximum urethral pressure decrease was larger than the detrusor pressure increase. However, some patients complained of urinary leakage during strenuous exercise (running and jumping for longer periods of time), although leakage was undetected even in this test. Similar results were seen in the study of Bø et al. [26], where the test did not detect leakage in four subjects with convincing history of urinary leakage. As SUI may occur due to fatigue of the striated urethral wall and pelvic floor muscles (PFMs), some women may need even more vigorous and continuous activities to provoke the leakage they experience outside the laboratory.

Comparing change in foot arch flexibility in 47 continent and incontinent varsity athletes, Nygaard et al. [27] demonstrated a significant decreased foot flexibility in incontinent women. They suggested that the way in which impact forces are absorbed may be one etiological factor for stress incontinence and that more research is required to understand how impact forces are transmitted to the pelvic floor. The high prevalence of urine loss in gymnasts may be explained by the extremely high impact during landing and takeoff and the transmission of this pressure to the pelvic floor. However, despite this high impact, many gymnasts do not leak, and this group is therefore interesting and important to study.

PREVALENCE OF URINARY INCONTINENCE AMONG PARTICIPANTS IN SPORTS AND FITNESS ACTIVITIES

SUI implies that urine loss occurs during an increase in abdominal pressure. Therefore, one may expect that women with this condition are likely to experience urine loss during participation in most forms of physical activity. Sedentary women are less exposed to physical exertions and this may avoid urinary leakage, despite the underlying condition potentially being present.

Studies have demonstrated that SUI is common among physical education/sport students, women who exercise for fitness, and female elite athletes [28]. Bø et al. [7] demonstrated (in a study with 84% response rate) that 26% of young physical education/sport students reported having urinary leakage during different forms of physical activity. This study also showed a difference between a group exercising three times a week in addition to daytime physical activities at the university and a group of sedentary nutrition students. The respective prevalences were 31% and 10% ($p = 0.02$).

A subsequent study of first-year female students ($n = 37$) with a mean age of 20.2 years demonstrated a prevalence of 38% of SUI symptoms. Eight of 13 women (61.5%) considered the leakage a social or hygienic problem [26], giving a prevalence using the former ICS definition of 21.6% for this population of physically fit, young, exercising nulliparous women. In this latter study, ambulatory urodynamic test was used to verify urodynamic SUI. Seven women with symptoms were evaluated by urodynamics, and in six of seven, urethral sphincter incompetence was confirmed. Mean leakage measured by pad test with standardized bladder volume was 12 g (range 0–46 g).

Nygaard et al. [9] studied incontinence and exercise in a group of 326 women presenting to private gynecology offices (response rate 50%). Eighty-nine percent were exercising at least once per week, with an average of three times per week for 30–60 minutes per session. Forty-seven percent reported some degree of urinary incontinence.

Fozzatti et al. [29] found that 24.6% of nulliparous women attending gyms compared to 14.3% in a group not attending gyms or doing high-impact activities (except running) reported UI, $p = 0.006$. This supports the results from a study on group fitness instructors, showing a prevalence of 26%, with the same prevalence in those teaching yoga and Pilates [30].

There is a lack of information about incontinence in female elite athletes. In a systematic review, Bø [28] found a variation in prevalence between sports from 0% in golfers [1] up to 80% in high-impact sports [31]. Nygaard et al. [1] surveyed all 156 women participating in varsity athletics at a large state university. The response rate was 92%. Mean age was 19.9 ± 3.3 years and they were all nulliparous. The women were asked whether they had ever experienced urinary leakage during participation in sports, during coughing, during sneezing, during heavy lifting, when walking to the bathroom, during sleeping, and upon hearing the sound of running water. They rated frequency of leakage in a five-point scale. Twenty-eight percent reported urine loss while participating in their sports. There was a tendency in two-thirds of these women to be incontinent frequently rather than rarely. The proportion in different sports was as follows: gymnastics, 67%; basketball, 66%; tennis, 50%; field hockey, 42%; track, 29%; swimming, 10%; volleyball, 9%; softball, 6%; and golf, 0%. Sixteen percent were incontinent during practice sessions and 14% during competition [1]. Forty-two percent reported urine loss during at least one of the activities of daily life and 18% more often than rarely. Twenty-one percent reported urine loss only during daily life and not during sports, and 7% noted incontinence only during sports. Bø and Sundgot-Borgen [32] compared prevalence of symptoms of urinary incontinence in Norwegian elite athletes and age-matched controls and found a prevalence of 41% and 39% of SUI and 16% and 19% of urge incontinence in athletes and controls, respectively.

In order to find out whether high-impact activity contributes to later urinary incontinence, Nygaard [33] compared former female Olympians who had competed in swimming (low impact) and gymnastics or track and field (high impact). One hundred and four women participated (response rate 51%). When doing their sport as Olympians, high-impact athletes have higher prevalence (36%) compared to low-impact athletes (4.5%). However, when studied more than 20 years after cessation of the sport, there was no significant difference in prevalence of incontinence between the groups. It was concluded that participation in regular, strenuous, high-impact activity when younger did not predispose to significant urinary leakage later in life. Bø and Sundgot-Borgen [34] studied former female elite athletes 15 years later and found that they were not more likely to experience urinary incontinence later in life than controls. Former athletes from high-impact sports (running and jumping) were not more likely to report urinary incontinence. Having experienced urinary incontinence during sports was, however, strongly associated with later incontinence.

CONSEQUENCES OF SUI DURING PHYSICAL ACTIVITY

Urinary incontinence may lead to withdrawal from social activities and reduction of well-being [35]. Norton et al. [36] reported that urinary leakage frequently interfered with daily life in more than 50% of their study group. Additionally, Fall et al. [37] reported that 42% of the women with incontinence had problems during sports and physical activities.

Bø et al. [38] showed that two-thirds of sedentary women with urodynamic SUI reported urinary leakage to be the cause of inactivity. Twenty-seven out of 52 women had tried to participate in specific sports and fitness activities but had withdrawn from one or more activities because of leakage. Nineteen of the 27 women had withdrawn from aerobic and dance activities, despite these being among the most popular fitness activities for women. They all reported that the major leakage occurred during high-impact activities during the aerobics session, especially when performing “jumping jacks” (jumping with legs in subsequent abduction and adduction), which is one of the most commonly used high-impact exercises in aerobic dance and general fitness programs.

This corresponds with the results of Nygaard et al. [9], where women most frequently reported leakage with running and high-impact aerobics. Thirty percent of the exercisers noted incontinence during at least one type of exercise. Twenty percent of these women stopped doing the activity solely because of incontinence, 18% changed the way they performed an exercise, and 55% wore a pad during exercise. Frequency, time spent per session, and duration of a particular exercise had no significant impact on the prevalence [9].

Brown and Miller [10] concluded that urinary incontinence was an important barrier to women’s participation in physical activities. Regular physical activity is an important factor for women’s health at all ages. Moderate physical activity can be one important factor in prevention of coronary heart disease, high blood pressure, osteoporosis, musculoskeletal diseases, obesity, breast and colon cancer, anxiety, and depression [39]. If one consequence of incontinence is withdrawal from physical activity, the impact on women’s health is potentially huge.

CAN PHYSICAL ACTIVITY CAUSE URINARY INCONTINENCE?

Several risk factors have been suggested for the development of female urinary incontinence; hereditary weak connective tissue, weak or nonfunctional PFMs, hormonal factors, dyssynergia between detrusor and urethral smooth and striated muscle activity, pregnancy, vaginal delivery, heavy physical exertion, inactivity, obesity, cigarette smoking, menopause, and old age are suggested risk factors [12,40]. To date, there is little evidence supporting a strong causal effect for many of these factors. The reality is that urinary incontinence has a multifactorial etiology in women including failure of one or more factors to compensate for another weak factor. The speed and strength of the PFM contraction may be one such important factor [41,42].

PELVIC FLOOR AND FEMALE ATHLETES

Optimal PFM function implies a localization of the pelvic floor in an adequate anatomical position, with sufficient cross-sectional area to give structural support for the vagina, bladder, and the urethra in order to prevent descent during increase in the abdominal pressure [43]. The muscles have to be in a neurological state of “readiness for action” allowing an appropriate quick and strong response or be a part of a feed-forward loop, contracting automatically simultaneously or before the intra-abdominal pressure increase.

Typically, there are two hypotheses about female athletes and PFM strength, and the hypotheses are going in opposite directions [28]. The first hypothesis is that general physical activity may lead to reflexive strengthening of the pelvic floor, thus making the PFMs in female athletes stronger. To date, no research has verified this hypothesis. The fact that so many female athletes report SUI [28] actually contradicts this view.

The second hypothesis is that heavy exercise, e.g., marathon running with repetitive bouncing toward the pelvic floor or weight lifting, may overload the pelvic floor and weaken the muscles over time. Nichols and Randall [44] proposed that women exposed to chronic straining may have an increased prevalence of genital prolapse because of connective tissue damage due to persistent intra-abdominal pressure increase. Nichols and Milley [45] suggested that the cardinal and uterosacral ligaments, PFMs, and the connective tissue of the perineum may be damaged chronically because of repeatedly increased abdominal pressure due to, e.g., manual work and chronic cough. According to this theory, strenuous exercise raising the abdominal pressure may contribute to development of SUI in women with a predisposition to incontinence.

Davis and Goodman [46] studied 512 of 2651 female soldiers who entered the airborne infantry and found that nine developed urinary incontinence during the training period. Urodynamic investigation demonstrated “detrusor instability” in three and urodynamic SUI in six of the women. All six with SUI demonstrated a definite cystourethrocele, a hypermobile vesical neck with loss of the posterior urethrovesical angle, and visible urine loss with Valsalva after the training period. Four of the women reported feeling a tearing pain in their lower quadrant on impact during a parachute jump, and one subject related a similar event during heavy lifting and doing sit-ups. From the data available today, it is not possible to conclude whether moderate- to high-impact activities can cause connective tissue or PFM damage. It is likely that there is a self-selection of continent women who undertake high-impact sports and fitness activities.

Another contributing factor for SUI in female elite athletes may be hypothalamic amenorrhea due to either intensive exercise, eating disorders, or a combination of both with resultant low estrogen levels [1]. However, the association between low estrogen levels and prevalence of SUI is not clear [47]. Most women in the studies of Bø et al. and Nygaard et al. reporting and demonstrating SUI had regular menstrual cycles [1,26]. However, in the study by Bø and Sundgot-Borgen [32], a higher prevalence of SUI was found in those with eating disorders. Eating disorders may be associated with low estrogen levels.

Nygaard et al. [1] proposed that, e.g., gymnasts may have selected their sport because of hypermobility and that changes in collagen concentration may be one factor in the higher prevalence of incontinence in gymnasts. However, although some studies have shown reduction in collagen tissue in women with incontinence compared to continent women [48], the link between collagen, hypermobility, and SUI is not clear. There are no studies comparing the collagen structure in gymnasts and athletes with or without SUI with that of matched controls.

There are few studies measuring PFM strength in exercisers compared to sedentary controls. Bø et al. [26] did not find any significant difference between incontinent female sport students and a comparable continent group. However, the sample was small, and other studies have demonstrated significantly stronger PFMs in continent than incontinent women [41,49,50]. Borin et al. [51] compared PFM strength in 10 handball, 10 volleyball, and 10 basketball players and a nonexercising control group and found weaker muscles in the volleyball and basketball players compared with controls. They also found that lower strength correlates with increased symptoms of urinary incontinence. There is an urgent need for further studies on this topic.

PROTECTION DURING EXERCISE TO PREVENT LEAKAGE

Because of the health benefits of regular moderate exercise, it is important to emphasize that women should be encouraged to continue exercising despite their urinary leakage. However, they can be advised about choosing low-impact activities, e.g., walking, Nordic walking, dancing, low-impact aerobics, step training, bicycling, swimming, and cross-country skiing.

If an incontinent woman wants to participate in high-impact aerobics, she may use low-impact alternatives, meaning walking while the others are running, doing “step touch” while others are doing jumping jacks, etc. In addition, if she leaks or feels downward pressure during sit-ups, she should be advised to make an attempt to contract the PFMs before doing abdominal curls/sit-ups. It is important to notice that several studies have found that coughing and Valsalva (as in defecation) increases intra-abdominal pressure to a significantly higher degree than different daily movements and exercises [52,53]. Many exercises including abdominal exercise did not increase the intra-abdominal pressure more than rising up from a chair [53]. Hence, the fear that common exercises may hurt the pelvic floor may be exaggerated.

During exercise, the woman should be encouraged to use specially designed protection. Fortunately, some of the best protecting pads are now manufactured in small sizes, making active women more comfortable when wearing them while exercising. In addition, women may use urethral or vaginal devices to prevent leakage during physical activity [54,55]. In a study of Glavind [56], six women with stress incontinence demonstrated total dryness when using a vaginal device during 30 minutes of aerobic exercise.

TREATMENT

No studies have been found evaluating any treatment methods for urinary incontinence in a defined subgroup of female athletes or exercisers. Generally, the least invasive treatment should be tried first [57], with pelvic floor muscle training (PFMT) being the method recommended as first-line treatment [57]. Female elite athletes are mostly young and nulliparous, and surgery is therefore not recommended.

Several randomized controlled trials have demonstrated a positive effect of PFMT on SUI in the general population [57]. Bø et al. [38] demonstrated that after specific strength training of the PFMs, 17 of 23 women had improved during jumping and running and 15 during lifting. In addition, significant improvement was obtained while dancing, while hiking, during general group exercise, and in an overall score on ability to participate in different activities [38]. Measured with a pad test with standardized bladder volume comprising running, jumping jacks, and sit-ups, there was a significant reduction in urine loss from a mean of 27 g (95% CI, 8.8–45.1; range 0–168) to 7.1 g (95% CI, 0.8–13.4; range 0–58.3), $p < 0.01$ [58].

Two small case series on elite athletes and sport students have been published [59,60]. Rivalta et al. [59] reported total relief of reported symptoms and no leakage on pad testing after 3 months of a combination of electrical stimulation, PFMT with biofeedback, and vaginal cones. Da Roza et al. [60] reported that seven nulliparous sport students significantly improved PFM strength and reduced International Consultation on Incontinence Questionnaire (ICIQ) score and frequency and amount of leakage after 8 weeks of training. Elite athletes and women engaging in fitness activities are used to conducting regular training and are motivated for exercise. One would therefore expect that the effect of supervised PFMT would be equally effective or even more effective in these specific groups of women.

Supervised PFMT has proved to be effective in the general female population; it is a functional and physiological noninvasive treatment with no known side effects that can be very cost-effective compared to other treatment modalities. In addition, the woman herself is given the opportunity to take control over her health. She learns body awareness, and if successful, the training may enhance self-esteem and coping strategies. There is, however, a need for randomized controlled trials to discuss whether PFMT can reduce urinary leakage in subgroups of exercising women.

CONCLUSIONS

SUI is prevalent in exercising women at all levels. This may well be because the activity “unmasks” a predisposition to leak as currently it is not possible to be certain whether strenuous physical activity may cause SUI or pelvic organ prolapse. Current understanding certainly suggests that more vigorous exercise is associated with higher rates of leakage and that women with problems restrict their physical activities. More research is needed to understand how impact from different exercises may affect pelvic organs, connective tissue, and PFMs. The effect of PFMT on elite athletes and women participating in vigorous fitness activities has not yet been evaluated in randomized controlled trials. However, based on the present knowledge on effect of PFMT, it has been suggested as the first choice of treatment.

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62

Anal Incontinence

Tony Mak and Simon Radley

INTRODUCTION

Anal incontinence is the involuntary loss of solid or liquid stool per rectum. It is personally and socially incapacitating and only a half of sufferers will volunteer their symptoms spontaneously if not asked directly [1]. Although it affects men and women of all ages, incontinence is eight times more common in women than in men at the age of 45, implicating obstetric factors in the etiology. A study from Birmingham found that 4% of women develop fecal incontinence following childbirth [2]. The focus of this chapter is on obstetric injuries, which are the underlying cause of anal incontinence in most women, but other causes must be considered (Table 62.1). The principles of management are broadly similar whatever the etiology. Vaginal delivery is the most important etiological factor in postobstetric anal incontinence.

Two principal mechanisms are responsible for the development of fecal incontinence following vaginal delivery:

- Direct injury to the sphincter muscle itself
- Damage to the nerves supplying the pelvic floor or anal sphincter

Less frequently, new symptomatic anal incontinence may occur in women following cesarean delivery.

PATHOGENESIS

Sphincter Injury

Direct damage to the sphincter muscles is responsible for anal incontinence in most of the women who present early after childbirth. Sphincter injuries are more common in primiparous women; new sphincter injuries are less common with subsequent deliveries [3]. Up to 35% of primiparas have been reported to have sphincter injury; however, some remain asymptomatic [4]. Other risk factors or associations for sphincter injury include large babies, forceps delivery, a prolonged second stage of labor, and occipitoposterior presentation [5]. Some authors have raised doubts on posterolateral episiotomy and claims that it does not necessarily protect against sphincter injury [6].

It has become clear that following vaginal delivery anal sphincter injuries may be unrecognized or misclassified as a less severe injury. When perineal examination is undertaken by a trained clinician immediately following delivery, the incidence of detected sphincter injury may be significantly increased [7]. Some sphincter defects may be truly occult, occurring with minimal or no perineal injury, where the mechanism is likely to be tissue shearing during delivery. However, there is a notable variation in the incidence of recognized third-degree tears between centers publishing their data [8], and the observation that women with second-degree tears are the group most likely to develop anal incontinence postpartum [9] further suggests that a proportion of anal sphincter injury remains undetected following delivery. Even when sphincter damage is recognized and repaired at the time of delivery, up to 85% of women still have identifiable sphincter defects and around 50% of women have some symptoms of anal incontinence [5].

The development of incontinence later in life is more likely to be multifactorial in origin, resulting from a combination of one or more factors including sphincter damage, progressive neuropathy, muscle atrophy, hormonal changes [10], and alteration in bowel function [11].

Neurological Damage

Prolonged pudendal nerve motor terminal latencies (PNMTL) are a marker of nerve injury and have been demonstrated in a third of primigravidae following vaginal delivery [12]. These usually revert back to normal, but up to a third remain prolonged at 6 months. The presence of a prolonged PNMTL is not necessarily associated with incontinence. After emergency cesarean section late in labor, pudendal nerve latencies may be increased, implicating damage to the nerves supplying the pelvic floor or sphincter [13]. In some women, electromyographic studies revealed increased fiber density in the external sphincter consistent with damage to sphincter innervation. Pudendal nerve damage and increased fiber density were seen more frequently in multiparae, suggesting that nerve damage may be cumulative with subsequent deliveries. The development of neurogenic incontinence is likely to be a progressive process, rather than an acute event at the time of delivery, and therefore may be exacerbated by subsequent deliveries or prolonged straining.

PATIENT ASSESSMENT

The maintenance of continence is a complex process involving an interrelationship between intestinal function, rectal sensitivity and compliance, and anal sphincter function. This in turn depends upon the integrity of sensory and motor neural pathways and the sphincter musculature itself. The anal sphincter complex comprises two muscles—an inner circular smooth muscle maintaining constant tone to prevent incontinence during sleep and largely responsible for resting anal canal tone (the internal sphincter) [14] and an outer striated muscle under voluntary control that can be contracted to defer defecation when appropriate (the external sphincter) [15].

Table 62.1 Etiology of Fecal Incontinence

Traumatic
Obstetric
Accident/injury
Surgical
Colorectal disease
Rectal prolapsed
Inflammatory bowel disease
Hemorrhoids
Neoplasia
Fistulae
Congenital
Anal atresia
Neurological
Cerebral
Spinal
Peripheral
Miscellaneous
Impaction
Behavioral
Immobility

History

Careful questioning can give a clue to the etiology of incontinence. A change in bowel habit to increased frequency and looseness may precipitate anal incontinence and could be suggestive of underlying colorectal disease. Urgency of defecation with reduced warning time (sometimes to only a few minutes) indicates loss of voluntary muscle control and suggests damage to the striated external anal sphincter or its nerve supply. Similarly, incontinence associated with vigorous activity or coughing suggests a deficiency of external sphincter function. Incontinence occurring between episodes of defecation with no call to stool, or the involuntary passage of flatus, indicates a poor anal canal resting tone and suggests damage or degeneration of the internal sphincter muscle. Inability to discriminate solid stool from flatus suggests damage to anorectal sensory pathways. Seepage or perineal soiling may be seen in situations where there is distortion of the anal canal by scarring or in the presence of a fistula. A careful medical history should be taken with specific attention to colonic function, previous anorectal surgery, and any potential causes of anal incontinence. An obstetric history should include details of birth weight, mode of delivery, length of labor, instrumental delivery, and details of any perineal trauma. Scoring systems, such as the St. Marks score [16] (Table 62.2), Wexner score (also known as Cleveland Clinic Florida Incontinence scoring system) [17], and Birmingham Bowel and Urinary Symptoms questionnaire (BBUSQ-22) [18], may be used to quantify anal incontinence and for audit or research [16]. Disease-specific quality of life scores (Fecal Incontinence Quality of Life Score [FIQL] [19]) can be used to assess various psychometric domains: lifestyle, coping/behavior, depression, and embarrassment. The FIQL has also been translated into different languages, which have been used worldwide [20–22]. These scores can be used to assess treatment outcomes in both research and service settings.

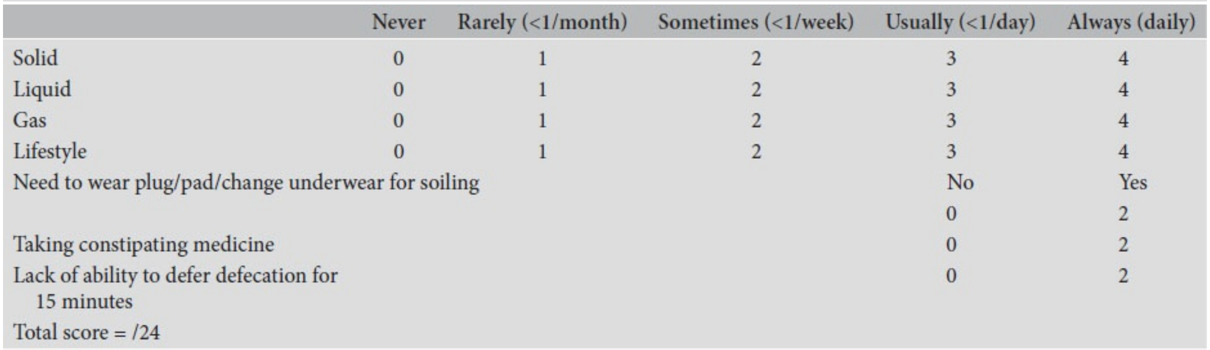
Examination

Physical examination should include inspection of the perineum, noting scarring from previous surgery or obstetric trauma. Voluntary contraction of the external sphincter can be seen and defects in the sphincter may be observed. Gaping of the anus at rest or on gentle perineal traction suggests a low resting tone and impaired internal anal sphincter function. Descent of the perineum at rest with accentuation on straining suggests pelvic floor weakness, pudendal neuropathy, or both. Straining may also reveal an unsuspected rectal prolapse. Perineal sensation can be tested by light touch and pinprick. Digital examination will allow crude assessment of resting anal tone and voluntary squeeze pressure, and any sphincter defects may be palpable.

Investigation

Special investigations can provide useful information in the management of women with incontinence (Table 62.3). Presentation with new anal incontinence, particularly in middle age, may be precipitated by a change in frequency or consistency of stool. Routine examination of the colon by barium enema or colonoscopy should be carried out to detect the presence of colonic pathology such as neoplasia or colitis. Clinical assessment of the pelvic floor and anal sphincters should be combined with anorectal physiological studies. Manometry allows measurement of functional anal canal length and of the resting and squeeze pressures. These provide objective evidence of internal and external anal sphincter function, respectively [23]. Anal canal sensation can be tested using a stimulating electrode and may be transiently impaired by vaginal delivery. Rectal sensation and compliance are usually measured by balloon distension. It is important that the rectum is compliant for preservation of continence. Inflammatory bowel disease, radiation proctitis, rectal prolapse, and diabetes can affect the rectal capacity and compliance. Measurement of PNMTL assesses pudendal nerve function by stimulating the pudendal nerve on each side and measuring the evoked response in the external anal sphincter [24]. Normal latencies do not necessarily exclude pudendal nerve damage since it may require 75% of the nerve to be disrupted to prolong the latency.

Table 62.2 St Mark's Incontinence Scoring System



	Never	Rarely (<1/month)	Sometimes (<1/week)	Usually (<1/day)	Always (daily)
Solid	0	1	2	3	4
Liquid	0	1	2	3	4
Gas	0	1	2	3	4
Lifestyle	0	1	2	3	4
Need to wear plug/pad/change underwear for soiling				No	Yes
				0	2
Taking constipating medicine				0	2
Lack of ability to defer defecation for 15 minutes				0	2
Total score = /24					

Source: Vaizey CJ et al., *Gut*, 44, 77, 1999.

Table 62.3 Investigations for Anal Incontinence

Investigation	Information

Imaging/structural	
Colonoscopy/barium enema/sigmoidoscopy	Underlying colorectal pathology precipitating or contributing to incontinence
Endoanal ultrasound (EAUS)	Integrity of internal and external anal sphincter
	Thickness of internal anal sphincter
	Fistulae
Magnetic resonance imaging (MRI)	Integrity of internal and external anal sphincter
Functional	
Manometry	Resting anal canal pressure
	Voluntary squeeze pressure
	Involuntary squeeze pressure
	Functional anal canal length
Rectal sensation and compliance	Rectal hypo/hypersensitivity
	Normal or reduced compliance
Pudendal nerve motor terminal latency (PNMTL)	Damage to pudendal nerves

Endoanal ultrasonography (EAUS) has revolutionized the understanding of anal canal anatomy (Figures 62.1 and 62.2). Both the internal and external anal sphincters can be visualized and EAUS is the investigation of choice for detection of defects in these sphincters [25]. The detection of sphincter defects enables clinicians to select women to undergo surgical sphincter repair, and the accuracy of EAUS for detecting sphincter disruption has been validated by correlation with operative findings [26]. Abnormal thinning of the internal sphincter can be measured accurately using EAUS; this may be indicative of idiopathic degeneration, whereas thickening of the muscle may be associated with prolapse syndromes.

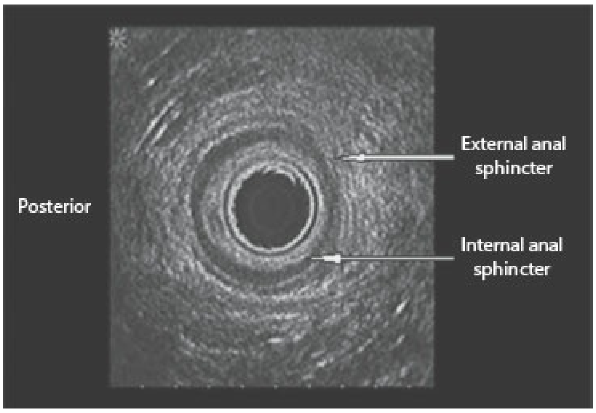


Figure 62.1 Normal endoanal ultrasound immediately postpartum.

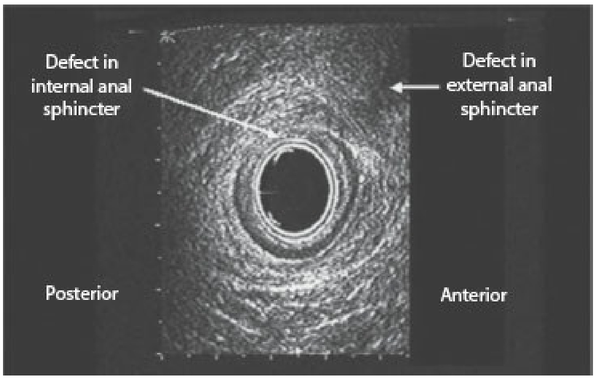

Defect in internal anal sphincter
Defect in external anal sphincter
Posterior
Anterior

Figure 62.2 Defects in internal and external anal sphincters.

Magnetic resonance imaging (MRI) using an endoanal coil provides excellent multiplanar views of the sphincter complex and can demonstrate defects in both the internal and external anal sphincters. It is probably most useful in identifying abnormalities in the external anal sphincter, the outer border of which may be difficult to visualize using EAUS. Expertise in MRI of the sphincters is not widely available and most clinicians continue to rely on EAUS. Where both imaging facilities are available, one or both may be used for diagnosis since they are complementary. Interest in functional MRI in the wider context is increasing; however, the lack of standardization of nomenclature has limited current understanding.

MANAGEMENT

Early Recognition of Obstetric Injuries

Evidence of sphincter injury should be sought by careful bimanual examination in all women who have a perineal tear or who have had an instrumental delivery. This should be carried out by someone trained in the recognition of sphincter injury. In the United Kingdom, there are a number of courses specifically for training obstetricians in the identification and management of obstetric sphincter injuries. An adjunct to bimanual examination is the use of EAUS in the delivery suite immediately postpartum. This is acceptable to women and can be used to diagnose sphincter injury and to assess the integrity of any repair [27]. Once recognized, repair of a sphincter injury should be carried out by someone adequately trained to do so, in an operating theater under regional or general anesthetic. Training in repair of sphincter injury should be part of the obstetric training program as the adequacy of sphincter repair is related to the experience of the operator [28]. At postnatal follow-up visits, women should be asked directly about anal incontinence as they are about other postpartum symptoms. Increased general awareness of the risk of postobstetric sphincter injury among midwifery and obstetric staff will also aid in the early diagnosis and treatment of anal incontinence. Early follow-up in a multidisciplinary clinic of women who have sustained obstetric trauma further increases the recognition of residual sphincter injury and enables effective early intervention where necessary [29].

Conservative Therapy

For most women, symptoms are relatively minor and should be managed conservatively, interventional procedures being reserved for those women with severe symptoms or in whom conservative measures fail.

Lifestyle

Attention to diet or the addition of a bulking agent such as ispaghula husk can improve symptoms in some individuals. Encouraging a daily routine for defecation may also help. The use of barrier creams such as zinc oxide ointment to prevent excoriation of perianal skin as a result of stool leakage is encouraged. High-fiber and a low-fat diet may help to prevent loose stools, which is a recognized risk factor of fecal Incontinence (FI) [30]. In a cross-sectional study of over 64,000 elderly women, high BMI, lack of physical activity, and cigarette smoking were identified as modifiable risk factors [31].

Drugs

Antidiarrheal agents such as codeine phosphate, loperamide, or diphenoxylate plus atropine reduce colonic motility and thus increase fluid absorption, producing more manageable formed stools. However, their side effects may include nausea, constipation, and abdominal cramping. The use of enemas or rectal washouts may help some women. The enema induces a bowel action and keeps the rectum empty between bowel movements.

Amitriptyline at low dose may be of benefit for some women with anal incontinence. Study has demonstrated its value, particularly for those with fecal urgency and increased rectal sensitivity by increasing transit time and decreasing the amplitude and frequency of rectal motor complexes, respectively [32].

There have been some reports of duloxetine hydrochloride helping women with fecal incontinence. Whether in the future this represents a viable treatment option remains to be seen.

In a Cochrane review on drug treatment for fecal incontinence in adults, the authors concluded that most of the drugs currently used are for the treatment of diarrhea rather than fecal incontinence, which may be due to the heterogenous nature of the FI population within the review [33].

Biofeedback

Biofeedback therapy can be helpful for some women with anal incontinence who are refractory to lifestyle and drug therapy. It is a behavioral technique using physical retraining of the anal sphincter and pelvic floor muscles with or without the aid of equipment, which provide auditory or visual feedback to alter physiological events [34]. The technique uses electromyography, where a sensing device monitoring external sphincter contraction is connected to a transducer producing an audio or visual response for the woman. The audiovisual record of sphincter activity assists the woman in recognizing strength and length of contraction. Using a balloon to distend the rectum, women are encouraged to improve sphincter contraction in response to decreasing rectal distension, so that over a period of time their response becomes automatic. These techniques are most useful for women who are well motivated, have some rectal sensation, and are able to contract the external sphincter voluntarily. Interestingly, results of investigative workup for fecal incontinence such as anorectal manometry, defecating proctogram, EAUS, MRI, and PNMTL do not predict the responders to biofeedback [35].

In a series of 100 patients treated with biofeedback, 43 regarded themselves as cured and 24 symptomatically improved [36], 27 of the 46 patients in this series with structural sphincter damage also reported cure or improvement.

Biofeedback is initially labor intensive, requiring a dedicated therapist, but can be carried out at home after training. It has the advantage of being painless, safe, and complementary to other interventions. Biofeedback training has been shown to improve functional outcome for women with persistent symptoms following sphincter repair [37]. However, some studies have suggested that it is the therapist rather than the technique that is important to the outcome [38].

Anal Plug

Containment may be improved by the use of a disposable anal plug or tampon to enhance continence. The device expands after insertion and is removed to allow evacuation. Use of the anal tampon has been shown to improve continence scores and quality of life but only about half of patients found it comfortable to use on a regular basis [39]. It has a role for those with severe symptoms who are awaiting (or are unsuitable for) surgery.

SURGERY

For some women, conservative therapies will fail and surgical options need to be considered. Two categories of patients may be identified:

Group 1: Women with evidence of a sphincter defect
Group 2: Women whose sphincters are intact but weakened, secondary to denervation or muscle atrophy

In the first group, direct repair of the sphincter defect should be considered; in the second group, decision-making is more difficult, the surgical options are more varied, and the outcome is less predictable.

Sphincter Repair

Sphincter repair is the operation of choice where there is a single defect of the external anal sphincter, either alone or in combination with a defect of the internal anal sphincter. Two different surgical techniques have been used: direct apposition and overlapping repair. In the context where the cause of sphincter defect is due to previous obstetric trauma, then almost all are located anteriorly and a third of them will develop symptoms of FI over time [40].

Sphincter repair by mobilization of the sphincter muscle, scar excision, and direct apposition resulted in a failure rate of around 40% [41], these poor results being attributed to the cutting out of sutures or retraction of the muscle ends. As a result, Parks and McPartlin subsequently modified this technique by identifying and repairing the torn internal anal sphincter separately and employing an overlapping repair of the muscle [42]. Authors using the former technique along with an end-to-end repair have reported a significant reduction in incontinence (up to 8%) [43]. Indeed, the results of two randomized controlled trials have shown both techniques to be similar [44,45].

Most studies seemed to be in favor of immediate rather than delayed repair for third- or fourth-degree tears following delivery. Although both immediate [46] and delayed repairs [47] have demonstrated good results, immediate repair would be more socially acceptable for the patient and delayed repairs should probably only be considered where expertise is lacking at the time of injury.

The need for a defunctioning stoma following sphincter repair has been studied and is only necessary where there is significant perineal sepsis. A temporary stoma confers no benefit in terms of functional outcome and is associated with higher morbidity and longer hospital stay related to the stoma closure [48]. Medical bowel confinement confers no benefit in terms of septic complications or functional outcome [49]. Prophylactic broad spectrum antibiotics are used to prevent infection, which may be linked to breakdown of the repair.

Review of published series shows that excellent or good results, with continence to solid and liquid stool, can be achieved in between 47% and 79% of patients undergoing sphincter repair [50–52]. The outcome data for overlapping sphincter repair should, however, be interpreted with caution for a number of reasons. Many of the reported series are small, with patients recruited over several years, often involving several different operating surgeons and follow-up tends to be short. The groups of patients reported are often heterogeneous in terms of age, sex, and indication for repair. The frequent absence of standardized scoring systems or physiological measurements to evaluate continence pre- and postoperatively does not allow series to be readily compared.

Outcome where there has also been damage to the internal sphincter is less certain. The importance of repairing the internal anal sphincter (when damaged) as well as the external sphincter has been highlighted during immediate repair of third-degree tears [53]. Such attention should probably also be applied to repairing a deficient internal anal sphincter during secondary repair. It is accepted, however, that internal sphincter defects may be more difficult to identify surgically and repair adequately, and soiling—together with incontinence to flatus—will remain a problem for some women.

Factors Predicting Outcome from Anal Sphincter Repair

A number of factors have been identified as predictive of outcome following anal sphincter repair.

Age and Body Habitus

Some authors have reported an adverse influence of increasing age on outcome [54]. Although older age is not a contraindication to surgery [51,52], it should certainly be considered in preoperative counseling when discussing outcome. Obesity has also been recognized to worsen outcome following repair of anterior anal defects [54].

Pudendal Neuropathy

Prolonged PNMTL (unilateral or bilateral) have been shown by some to be predictive of a poorer outcome after sphincter repair [55]. Although this finding may be useful in counseling women preoperatively, it should not necessarily be used to deny a woman operative correction of an obvious sphincter defect.

External Sphincter Atrophy

The detection by MRI scanning of atrophy of the external anal sphincter, which is characterized by thinning and fatty replacement, has been shown to adversely affect outcome following sphincter repair [56].

Failure of Sphincter Repair

Up to 10% of repairs may break down, resulting in persistent defects and poor functional results. Where such defects are identified, repeated sphincter repair may be successful [57]. Since the operation may be technically more difficult and tissue quality poor, the outcome following repeated sphincter repair is less certain. Where failure has resulted from significant perineal sepsis, a temporary defunctioning colostomy may be required and should be considered.

Long-Term Outcomes after Sphincter Repair

In a 5-year follow-up study of incontinent women who had an overlapping repair for obstetric trauma, only 4 out of 38 were totally continent of solid and liquid stool and none was fully continent of stool and flatus [58]. The overall success of the overlap method deteriorated with time. Whether the deterioration was due to progressive denervation of mobilized muscle or failure to repair internal sphincter defects adequately is uncertain. We however believe that sphincter repair remains the standard first approach for isolated defects, particularly in women presenting soon after obstetric injury [53]. These women should be made aware that initial good results may not be permanent and that deterioration in continence may occur in the future.

Postanal Repair and Total Pelvic Floor Repair

The operation of postanal repair (PAR) aims to restore an adequate anorectal angle, which is of theoretical importance in maintaining continence. The long-term results from PAR are poor, with only a third of women maintaining continence at 5-year follow-up. Total pelvic floor repair (TPFR) combines PAR with anterior sphincter plication and anterior levatoroplasty. Long-term follow-up indicates that TPFR rarely renders women fully continent, but around half have substantially improved continence and lifestyle [59].

The poor long-term success rates reflect progressive neuropathy or atrophy of the muscles and have led to a move away from PAR and TPFR as surgical options. These operations are, however, associated with low morbidity and thus may still have a role for women with significant symptoms who are unsuitable for more complex reconstructive procedures or who refuse a stoma.

Alternative Surgical Techniques

For women with symptomatic anal incontinence but an intact sphincter confirmed by imaging, other surgical options can be considered.

Sacral Nerve Modulation

A novel approach to women with incontinence and weak but intact internal and external sphincters is to modulate the neurological control of the anorectum. Sacral nerve modulation (SNM) (Figure 62.3.) was initially used in patients with detrusor instability and urinary retention in the 1980s [60]. The observation of a simultaneous improvement in bowel symptoms in some of these patients led to its use by Matzel et al. in patients with anal incontinence in 1995 [61].

SNM involves chronic low-frequency electrostimulation of one of the sacral spinal nerves (S2, S3, or S4). The mechanism of action of SNM is uncertain: studies have demonstrated that SNM not only modifies somatic and autonomic nervous functions [62], but also central nervous system activity [63]. However, the effect of SNM on the anal sphincter is inconsistent as some authors reported an increased anal resting tone and maximum anal squeeze pressure while others reported the contrary [64–66]. Clinical studies on SNM have demonstrated improvement in continence in patients with external sphincter defects, suggesting the sphincter mechanism is not solely responsible for maintaining continence [67]. The effects of SNM on rectal sensitivity and compliance are also unclear and conflicting [64,68,69]. Possible reasons include small sample size and the heterogeneous etiology of anal incontinence within sample groups. Anorectal physiological studies do not appear to be a useful predictor of outcome for SNM.

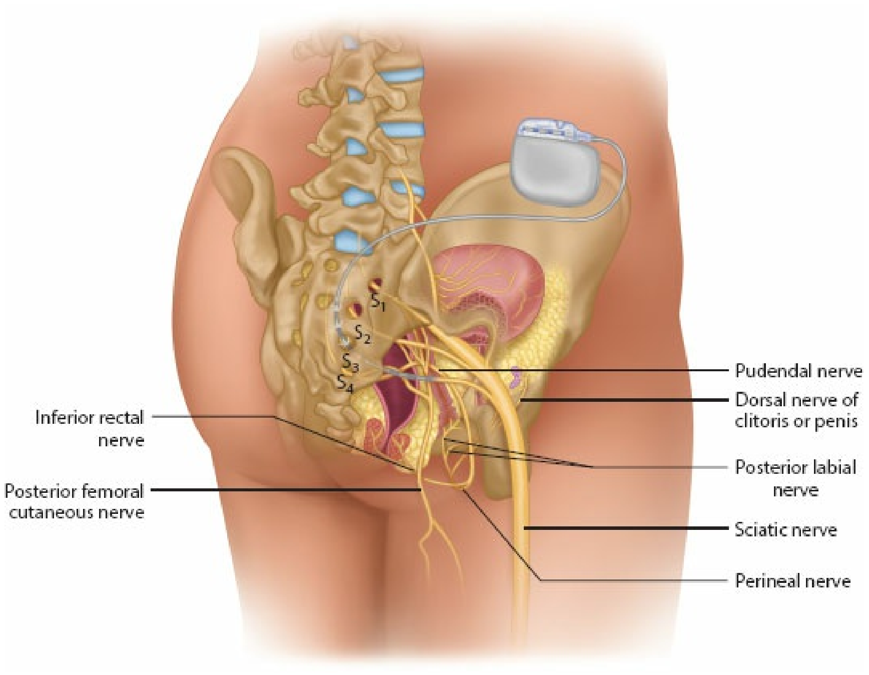


Figure 62.3 Relationship between position of sacral nerve stimulation device and relevant anatomy. (Courtesy of Medtronic, Inc., Minneapolis, MN Copyright 2010.)

A major advantage of SNM is that it involves placement of a temporary electrode, which can be used over a 1–4 week test period to measure response prior to embarking on surgical implantation of the permanent device. Following the initial trial, 60%–88% of patients proceed to permanent implantation [70–72]. A further advantage of SNM is that it does not involve any risk of direct surgical trauma to the sphincter mechanism itself. Morbidities associated with the procedure are less compared with other surgical techniques with a reported incidence ranging from 5% to 26% [62]. Such morbidities are usually minor and include pain at implant site, seroma, excessive tingling in the vaginal region, and superficial wound infection [62].

A meta-analysis published in 2011 of 665 patients who underwent SNM versus conservative treatment on patients with fecal incontinence found that the SNM group had reduced incontinence episodes, increased ability to defer defecation and improved quality of life scores [73]. A randomized controlled study by Tjandra et al. has demonstrated SNM to be more effective than optimal medical therapy, with the SNM group reporting significantly fewer incontinent episodes per week (from 9.5 to 3.1) and incontinent days per week (3.3 to 1) compared to controls (from 9.2 to 9.4 and from 3.3 to 3.1 respectively) [72]. Within the same institute and population sample, Chan et al. also demonstrated that SNM improved continence in patients with external anal sphincter defects of up to 120° of circumference [67].

Data on the long-term studies of SNM, with a mean follow-up of 51 to 74 months, have found a sustained improvement of fecal incontinence score and quality of life score [71,74,75]. In the national registry of the Italian group of sacral nerve stimulation, Altomare et al. [71] reported follow-up of 52 patients over a mean period of 74 months (range, 60–122). The group originally had 60 patients but 2 patients died of nonrelated disease to anal incontinence, and 6 had the device removed due to persistent complications or progressive failure of therapeutic efficacy within the first 2 years of follow-up. Hence 52 out of 60 (86.7%) patients were available for review. Out of 52 patients, 15 (28.8%) continued to suffer from complications, which included pain at site of implant (11.5%), electrode displacement (15.4%), and early battery rundown (1.9%). Functionally, by comparing Wexner scores at both baseline and follow-up for 50 patients, the mean score decreased from 15 to 5. In this study, 9 patients (18%) achieved 100% continence, 25 (50%) achieved at least 75% continence, and 37 (74%) achieved at least 50% continence. Matzel et al. [76] reported the follow-up of nine patients with a minimum of 7 years and mean period of 9.8 years (range 7–14). Compared to preoperative results, accidental loss of bowel content reduced from 40% to 0%, median number of incontinence episodes/week from 9 to 0.4 out of the 9 (44.4%) patients remained fully continent. A study carried out by Hollingshead et al. has even found no loss of efficacy in three patients after a 10-year follow-up [77].

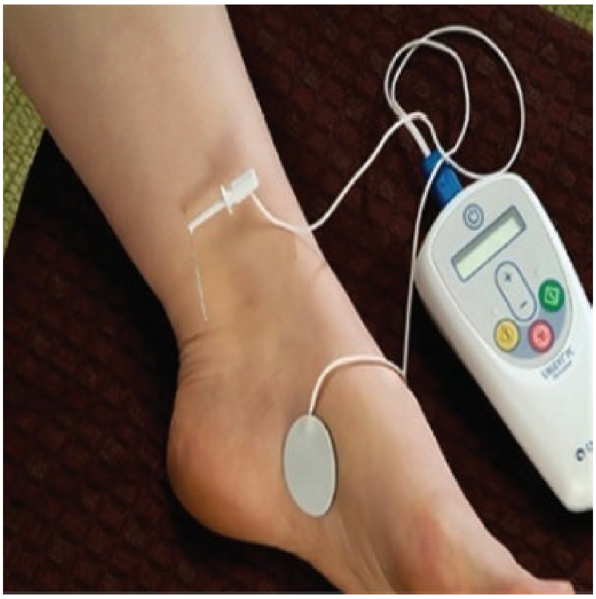


Figure 62.4 Positioning of posterior tibial nerve stimulation device. (By courtesy of Uroplasty, Inc., Minnetonka, MN, all rights reserved.)

Posterior Tibial Nerve Stimulation

Posterior tibial nerve stimulation (PTNS) (Figure 62.4) is an alternative technique of neuromodulation to SNM. It is a new concept that requires the application of electrical stimulation either percutaneously or transcutaneously, unilaterally over the posterior tibial nerve (located above and behind the medial malleolus). Currently, there are various protocols for the treatment with PTNS (e.g., one protocol involves 30 minutes per session, once a week for 12 weeks) [78–80]. Overall efficacy of PTNS ranges from 20% to 100%. Such wide range of results reflects on the heterogeneous nature of the study population, the different types of applications and the protocol used. Currently, a multicenter, randomized trial, CONFIDeNT (ISRCTN88559475), is ongoing with the primary end-point being a reduction in weekly fecal incontinence episodes and the secondary end-points being improvements in validated incontinence scores and disease-specific quality of life measures.

Neosphincters

Muscle Transposition

It is possible to augment the anal sphincter with another striated muscle. The muscles most commonly used are gracilis or gluteus but others such as obturator internus have also been employed [81]. Graciloplasty involves mobilization of the muscle from the inner thigh, which is wrapped around the anal canal and fixed to the contralateral ischial tuberosity. Continence is reliant upon the muscle wrap being tight enough to keep the anal canal closed, as coordinated voluntary contraction of the muscle itself is difficult. Gluteus transposition is a technically more demanding procedure but has the advantage that the muscles are easier to contract since the glutei are natural synergists of the anal sphincter. Results of unstimulated muscle transposition vary widely and it is now a rarely used technique. Bilateral graciloplasty may be useful where lack of local technical expertise or financial resources do not allow stimulated transposition.

Stimulated Muscle Transposition

The observation that by chronic stimulation muscle fibers could be converted from type II fast-twitch to fatigue-resistant slow-twitch fibers led to the development of the stimulated graciloplasty [82]. The mobilization of the gracilis muscle and wrap are similar to that for unstimulated graciloplasty but involve identification of the nerve to gracilis and implantation of a stimulating electrode around the nerve trunk or its branches. The stimulator is placed in a subcutaneous pocket in the abdominal wall and the electrode wires tunneled to it. After satisfactory healing, a period of muscle stimulation is commenced until continuous stimulation results in sustained muscle contraction. The patient switches off the stimulator to allow the muscle to relax and enable defecation [83]. Contraindications to stimulated graciloplasty include a history of perianal sepsis or Crohn's disease. In addition, as the stimulator may interfere with pacemakers and implanted defibrillators, the technique may not be appropriate in these patients.

In a study of 52 patients undergoing stimulated graciloplasty, 73% were continent after a median follow-up of 2 years and success was associated with improved quality of life [83]. Others have reported far less favorable results. Septic complications, hardware problems, and physiological imbalance have led to the high failure rates reported in some series [81]. Case selection is important; patients need to be well motivated and require careful preoperative assessment and counseling. The procedure has a recognized failure rate and may be associated with significant morbidity and scarring. In addition, patients may require significant input in terms of support for fine-tuning the stimulator.

Artificial Bowel Sphincter

When the sphincter muscles are irretrievably damaged or previous attempts at reconstruction have failed, the use of an artificial bowel sphincter may provide a simpler and less invasive approach than stimulated muscle transposition. The artificial sphincter prosthesis was developed from use in the treatment of urinary incontinence. It comprises a cuff that is implanted around the anus and a pressure-regulating balloon that is placed behind the rectus muscles and connected to a pump placed in the subcutaneous tissues of the labia. A temporary colostomy is not normally required. Cuff opening is controlled by squeezing the labial pump that then empties the cuff to enable evacuation; the cuff then slowly refills from the pressure-regulating balloon over a number of minutes to close the anal canal. Contraindications for artificial bowel sphincter include active sepsis, previous radiation, Crohn's disease, and poor-quality perineal tissue [84].

Early reports of the purpose-designed artificial bowel sphincter indicated that excellent functional results can be achieved both in terms of improving continence scores and improving anal canal resting pressures without adversely affecting rectal function [85]. An audit of the UK experience, however, showed that two-thirds of the sphincters implanted had required removal [86]. Infection was the predominant cause and methicillin-resistant *Staphylococcus aureus*, a common pathogen. Despite good functional outcomes in a proportion of patients, the future for the artificial sphincter remains uncertain. Early septic complications necessitate removal of the device in some patients and improvements in care directed at preventing infection are required. Long-term results reported by the Minnesota group demonstrated that only 49% of 45 patients achieved a functional artificial sphincter, with infection being the main reason for failure. Where implantation was successful, those patients did experience improved continence and quality of life [87].

Magnetic Sphincter

The use of a magnetic bead band for fecal incontinence aims to enhance the anal sphincter pressure by its weak magnetic force (Figure 62.5). During defecation, the increased intra-abdominal pressure allows the magnetic beads to separate, followed by reunion of beads to re-establish continence once stool is passed. The insertion of the titanium magnetic beads requires patient to undergo a general anesthetic. Under aseptic technique, an incision is made in the perineal body and a tunnel created along the circumference of the anal canal. The implant is then positioned after estimation with a sizing tool and secured by tying sutures together. Studies on its efficacy have so far been on either comparison study and case series [88,89]. In one comparative case-matched study, the magnetic anal sphincter was found to be as effective as the artificial sphincter in terms of improvement of incontinence and quality of life [89]. However, one case series reported suboptimal results with no patients reporting a clinical response (defined as >50% reduction in the Wexner score) and a morbidity rate of 57% [90]. Other case series found that some patients with an implanted magnetic anal sphincter can produce a sustainable result of up to 36 months [91]. Complications from magnetic bead sphincter include infection, bleeding, perianal swelling, separation at the suture connection, and pain [88–91].

Sphincter Augmentation

Endoscopic radiofrequency therapy (a.k.a. SECCA® procedure) aims to include fibrosis to the anal sphincter and thereby tightens its muscle fibers to improve fecal incontinence. It can be performed under general anesthetic or under sedation with a local anesthetic. Needle electrodes are guided to optimal position and deliver heat-generated radiofrequency energy at several sites of the anal sphincter with temperature monitoring to avoid excessive heat [92]. Although a good-quality trial is still awaited, several case-series studies have reported favorable short- and long-term results [93–95]. In terms of complications, there have been reports of secondary hemorrhage, constipation, anal pain, and mucus discharge after the procedure [96,97].

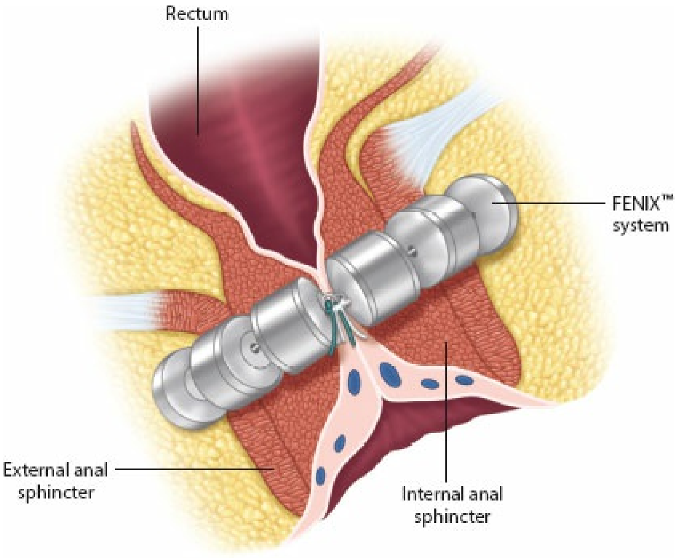


Figure 62.5 Magnetic sphincter augmenting the anal sphincter function. (Courtesy of Torax® Medical, Inc., Shoreview, MN. Copyright 2011.)

Injectable Bulking Agents

The use of injectable bulking agents was first described by urologists for urinary incontinence. The technique of mechanical bulking of the anal sphincter has been used for fecal incontinence since 1993 [98]. There are various injectable bulking agents: Coaptite (calcium hydroxylapatite ceramic microspheres), Contigen (collagen implant), Durasphere (pyrolytic carbon-coated beads), EVOH (Ethylene Vinyl Alcohol), polyacrylamide gel (Bulkamid), and PTQ (textured silicone particles). Injections are usually into the submucosal region or at the site of the sphincter defect. The morbidities described (generally low) range from pruritus ani, persistent anal discomfort to perianal sepsis [99]. A systematic review on the efficacy and safety of injectable bulking agents for passive fecal incontinence has found 13 case-series studies and only 1 randomized controlled trial. Although most studies reported statistical significant improvement in incontinence scores and quality of life, no statistical difference was found between the treatment and placebo arms in the randomized controlled trial [99].

Stomas

For some women who fail to respond to conservative or surgical treatments, a colostomy may be the only alternative to managing intolerable symptoms. In these individuals, a stoma should not be seen as a treatment failure and may allow many women to return to a near normal lifestyle. Colostomy irrigation is possible and may further improve their quality of life. Unfortunately, for a few women with a colostomy, persistent incontinence of mucus from the defunctioned rectum remains a problem and a proctectomy may be required.

SUMMARY

Careful assessment and investigation of anal incontinence can usually determine the underlying cause. Most women can be managed conservatively by a combination of dietary modification, medication, and biofeedback. Where conservative treatment fails, surgery may be considered. Women with identifiable sphincter defects may benefit from overlapping sphincter repair that offers good short-term functional results. Women should be counseled that longer-term results are less certain. When sphincter repair fails or where the sphincter itself is intact but weak, SNM and PTNS should be considered. Postanal repair, TPFR, and unstimulated muscle transposition offer short-term improvement for many women. Stimulated muscle transposition, artificial sphincters, magnetic bead band, SECCA® procedure, and injectables can provide a more satisfactory solution, but may be associated with associated morbidity. For a few women who have failed all treatment modalities, diversion stomas may be recommended.

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63 Constipation

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INTRODUCTION

"Constipation" is usually understood to imply infrequent bowel evacuations or difficult passage of feces persisting for a few weeks. It is one of the commonest medical complaints affecting patients of all ages, with an estimated UK prevalence varying from 8.2% to 52% [1]. Its incidence increases with age and is higher in those of lower socioeconomic class and with lower educational status [2].

The causes of constipation are multifactorial. These include dietary factors, toileting habits, medications, underlying medical conditions, psychological problems, organic diseases of the gastrointestinal tract (Table 63.1), and failures of the defecatory process [3]. Accurate history and clinical examination and investigations are essential in identifying a cause for each patient's symptoms.

PHYSIOLOGY OF NORMAL DEFECATION

Effective defecation requires coordinated efforts of colonic motility, intact rectal sensation, and pelvic floor relaxation. The primary function of the colon is the absorption of water from the small bowel effluent, leaving 100–150 mL of water in feces. A secondary function is to enable bacteria to ferment undigested fiber; the rectum stores feces until defecation takes place. Normal colonic transit varies from 24 to 96 hours [4].

The colon, rectum, and internal anal sphincter (continuation of the smooth muscle) are extrinsically innervated by the autonomic nervous system. The sympathetic innervation via the coeliac, superior, and inferior mesenteric plexus and hypogastric nerves (T11–L2) inhibits peristalsis and are sensitive to distension. The parasympathetic innervation by preganglionic vagal fibers and S2–4 splanchnic nerves increases peristalsis, contracts rectum, and relaxes internal anal sphincter to assist defecation. The intrinsic enteric nervous system (submucosal and myenteric plexuses) influences contractions and tone while the cells of Cajal are pacemakers. Local hormones also play a role.

CLASSIFICATION OF CONSTIPATION

The Rome consensus group published the Rome III criteria defining functional gastrointestinal disorders (Table 63.2). In order to be considered of medical significance, symptoms must be present for at least 3 months with onset of symptoms 6 months before diagnosis [5].

Subtypes of Constipation

Constipation can be divided into the following subtypes:

1. *Motility disorder*: Decreased high-amplitude peristaltic contraction causing slow transit constipation. Patients with severe colonic inertia may have a more diffuse motility disorder [6].
2. *Obstructive defecation syndrome* (ODS) *[7]* (also known as pelvic outlet obstruction, anismus, and pelvic dyssynergy): characterized by sensation of incomplete evacuation, prolonged straining and need for digital manipulation.
3. Irritable Bowel Syndrome with Constipation (IBS-C) associated with abdominal pain, irregular bowel habits, and pain relieved by defecation.

These subtypes of constipation can coexist.

HISTORY

"Constipation" implies different things to different people. An accurate history from the patient is important and should include size, consistency, and frequency of defecation and duration of symptoms.

In a UK-based population study, 99% of healthy individuals (*n* = 1455) had between three bowel motions per day to three times per week [8]. The Bristol stool chart is helpful in describing consistency [9]. The presence of mucus or blood in or on stool and history of abdominal or perianal pain should be ascertained as well as any difficulty in evacuation, need for perineal pressure, or digitation vaginally or rectally. Patients with slow transit constipation may complain of infrequent bowel movements and lack of urge to defecate despite laxatives. IBS patients may present with a chronic relapsing abdominal symptoms including abdominal pain and bloating associated with disturbed bowel habit [10].

If the patient has any of the red flag symptoms or signs (Box 63.1), they should be referred to a colorectal surgeon for further assessment to exclude colorectal cancer as per NICE guidance before proceeding to any further treatment [11].

Patients may have additional symptoms of urinary dysfunction or symptoms of uterine or vaginal prolapse, implying more global pelvic floor abnormality and dysfunction. It is important to ascertain if a patient has had a hysterectomy. Patients often date back the onset or exacerbation of symptom to that time [12]. A thorough obstetric history may reveal a history of obstetric trauma; high vaginal parity; prolonged labor, which may be associated with uterine prolapse; enteroceles; rectocele; and descending perineal syndrome. These conditions may present as symptoms of obstructive defecation such as prolonged defecation with sensation of anorectal obstruction and rectal fullness with tenesmus; as such these are also important screening parts of a urogynecological or urological history. Women sometimes use vaginal, anal digitation, or perineal pressure to aid evacuation.

Table 63.1 Causes of Secondary Constipation

1. General		
Poor diet ± lack of exercise		
Poor fluid intake/dehydration		
Old age		
Postoperative pain		
Hospital environment (lack of privacy/use of bed pan)		
2. Medication (BNF)		
Drug Group	*Condition*	*Examples*
Opiate	Pain control	Codeine, morphine, fentanyl
Antimuscarinic	Overactive bladder	Oxybutynin, solifenacin
	Parkinson’s disease	Procyclidine, benzhexol
	Asthma	Ipratropium
Tricyclic antidepressant	Depression	Amitriptyline, dothiepin
Antipsychotics	Schizophrenia	Chlorpromazine, clozapine
Parasympathomimetic alkaloid	Xerostomia/Sjögren’s	Pilocarpine
Vinca alkaloids	Leukemia/lymphoma	Vincristine, vinblastine
Calcium channel blocker	Arrhythmias/hypertension	Verapamil
Diuretics	Heart failure	Furosemide
Antacids	Indigestion	Calcium/aluminum + antacids
Supplements	Iron deficiency anemia	Ferrous sulphate
	Osteoporosis	Ergocalciferol
Nicotine replacement	Aid smoke cessation	Nicotine lozenges
3. Metabolic/endocrine conditions		
Amyloid		
Glucagonoma		
Hypercalcemia (hyperparathyroidism, milk alkali syndrome)		

    - Hypothyroidism
    - Hypokalemia
    - Panhypopituitary syndrome
    - Pheochromocytoma
    - Pregnancy
    - Porphyria
    - Arsenic/mercury/lead/phosphorus poisoning
    - Uremia

4. Bowel disorders
    - *Obstruction*: colorectal cancer, Crohn’s stricture, diverticular disease, volvulus
    - Pelvic mass (e.g., fetus, fibroid)
    - Fecal impaction
    - Megacolon/rectum
5. Neuromuscular conditions
    - *Central disorder*: tumors, trauma, cerovascular
    - *Peripheral disorder*: von Recklinghausen’s disease, multiple endocrine neoplasia
    - Spinal or pelvic nerve injury (e.g., obstetric trauma, surgery)
    - Aganglionosis (Hirschsprung’s and Chagas’ diseases)
    - Systemic sclerosis
    - Multiple sclerosis
    - Parkinson’s disease
    - Diabetic neuropathy
    - Pan gut dysmotility
6. Psychogenic
    - Anxiety/depression
    - Obsessional personality
    - Sexual/physical abuse
    - Immobility
    - Anorexia nervosa, bulimia, eating disorder

Source: Keighley MR and Williams NS eds., *Surgery of the Anus, Rectum and Colon*, Saunders Ltd., 2007.

Table 63.2 Rome III Criteria for Functional Constipation and Irritable Bowel Syndrome with Constipation

Functional constipation	**Irritable bowel syndrome**
Must include at least two of the following: • Straining[a] • Lumpy or hard stool[a] • Sensation of incomplete evacuation[a] • Sensation of anorectal blockage[a] • Manual manoeuvres to facilitate defecation [a]* (digital evacuation, support of the pelvic floor) • <3 stools per week Loose stools rarely present without the use of laxatives. Insufficient criteria for irritable bowel syndrome.	Recurrent abdominal pain or discomfort for at least 3 days/month in the last 3 months associated with at least two of the following: • Improvement with defecations • Onset associated with a change in frequency of stool • Onset associated with a change in form of stool IBS-C is a subtype of IBS with Bristol stool chart type 1–2 in ≥25% of defecations and type 6–7 in ≤25% of defecations.

Source: Tattersall MH, *Lancet Oncol*, 7(11), 886, 2006.

[a] At least 25% of defecations.

Box 63.1 Red Flag Symptoms and Signs of Colorectal Cancer

Change in bowel habit to looser stools or increased frequency and rectal bleeding (>40 years old)
Persistent rectal bleeding for 6 weeks without anal symptoms (>60 years old)
Change in bowel habit to looser stools or increased frequency for 6 weeks (>60 years old)
Palpable right iliac fossa mass
Palpable rectal mass (intraluminal)
Unexplained iron deficiency anemia (Hb < 11 g/dL for men and Hb < 10 g/dL in nonmenstruating women)

Initial treatment is based on lifestyle advice, and therefore, it is also mandatory to ascertain information on diet, fluid intake, exercise habits, and medical, surgical and drug histories, as drug side effects may precipitate symptoms.

Pelvic floor dysfunction is often associated with depression and anxiety, so questioning about additional contributing factors such as psychiatric illness and any history of sexual abuse may yield important information that may modify treatment regimens [13,14].

Patients with constipation may also report an increased incidence of history of sexual and physical abuse and a poorer health status than the general population [15]. In a study of 118 constipated patients, 32% reported physical abuse and 22% sexual abuse [16]. It is important that the issue of abuse is explored with appropriate backup from a safeguarding team where required. Patients often report that their bowel problems have adversely affected their family life, their relationships, work, and social life [16]. In a cross-sectional survey, Sun et al. [17] found that individuals with chronic constipation compared with matched controls were more likely to take sick leave and report general health impairment affecting work performance.

CLINICAL EXAMINATION

Abdominal examination may be unremarkable in most patients but it is important to rule out any intra-abdominal masses. Rectal examination is mandatory looking for skin tags, anal fissures, external hemorrhoids, and excoriation if present. Gaping of anal opening may suggest an underlying neurological problem or a full-thickness rectal prolapse. It is important to check for altered sensation around the perianal skin and perineum. A lack of reflex contraction of the external anal sphincter to perianal stimulation may indicate impaired pelvic innervation. Patients may demonstrate a full-thickness rectal prolapse, a bulge into the vaginal introitus indicating a rectocele, or bulging of the perineum below the ischial tuberosities indicating perineal descent. Digital rectal examination is performed systematically to assess resting anal tone; squeeze pressure by asking the patient to clench their anus on the examining finger. The finger is swept clockwise and anticlockwise to examine the entire circumference of the anal canal feeling for masses, ulceration, and tenderness. The puborectalis is examined by hooking the finger posteriorly over the coccyx. The puborectalis should be relaxed when the patient is asked to strain. In patients with anismus or dyssynergia, the puborectalis muscle often fails to relax or may be felt to contract when they strain. The sensitivity and specificity of diagnosing dyssynergia on rectal examination are 75% and 87%, respectively, when two or more of the following are identified on rectal examination: impaired perineal descent, paradoxical anal contraction, or impaired push effort [18]. Rigid sigmoidoscopy or proctoscopy examination in clinic can be a useful adjunct in assessing any mucosal abnormality in the anus and rectum as well as assessing rectoanal intussusception; mucosal folds may be visible when prominent. If there is a history of vaginal prolapse or obstructed defecation, vaginal/pelvic examination should also be performed.

INVESTIGATIONS

Systematic review looking at clinical utility of diagnostic tests for constipation however showed no clear evidence to support performing routine blood test, radiography, and endoscopy in patients with constipation without “red flag” symptoms [19,20]. So while screening for metabolic cause of constipation with full blood count and biochemistry including calcium and thyroid function test, this should be reserved for new patients presenting with constipation where there is a high index of suspicion or a relevant medical history. A meta-analysis of prospective cross-sectional surveys and cohort studies demonstrated no increase in prevalence of colorectal cancer in patients with constipation [21]. Patients with red flag signs or concerns about intraluminal cause for their symptoms should have endoscopic (flexible sigmoidoscopy/colonoscopy) or radiological examination (CT colonography/contrast study).

Additional investigations are reserved for patients who fail simple medical therapy. A modified algorithm of the management of constipation by the American Gastroenterological Association is shown in Figure 63.1 [22].

The following tests are useful in distinguishing between normal, slow-transit constipation, and ODS. Pros and cons of each investigation are summarized in Table 63.3 [19].

Diagnostic Studies to Evaluate Anorectal Function

Balloon Expulsion Test

This is a simple bedside test performed to assess the patient’s ability to expel an artificial stool. A balloon is placed in a patient’s rectum and filled with water. The patient is then asked to expel the balloon. Normal expulsion time is within a minute. Although a failure to expel a 50 mL balloon suggests dyssynergia, a normal test does not exclude the diagnosis [20].

Anorectal Manometry

This provides comprehensive information regarding rectal sensation, rectoanal inhibitory reflexes (RAIRs) and anal sphincter function. Anorectal manometry is a useful test for diagnosing dyssynergy (Figure 63.2) and altered rectal sensation and helps identify patients who may be suitable for biofeedback therapy [19]. A catheter-mounted balloon is inflated incrementally to

1. First constant sensation
2. Desire to defecate volume
3. Maximum tolerated volume

The three simple sensory thresholds described earlier cannot distinguish the factors influencing sensation including compliance and neural pathways [23]. Decreased sensation to distension is seen in obstructed defecation, but the evidence that this is due to parasympathetic nerve damage is debatable [24,25]. Damage to these nerves may be a factor in constipation following hysterectomy [26].

By using isobaric distension of a balloon, rectal compliance can be calculated as the steepest gradient of the curve plotting volume instilled divided by rectal pressure. Where compliance is high, greater volume needs to be instilled to achieve a given rise in pressure. This is the case in megarectum or in obstructive defecation. Decreased compliance (reduced laxity, increased hypersensitivity) is often found in inflammatory bowel disease or after pelvic radiotherapy.

RAIR is the reflex relaxation of the internal sphincter that occurs when a balloon is inflated in the rectum. Factors such as body position and consistency of “stool” play a role in one’s ability to expel stool. Up to 20% of asymptomatic healthy adults do not produce normal relaxation during attempted defecation [27]; hence, a finding of dyssynergia on anorectal manometry alone is not diagnostic. Electromyography (EMG) can also aid in the diagnosis of puborectalis syndrome where there is paradoxical or nonrelaxing puborectalis muscle.

Defecating Proctography

Defecating proctography is regarded as the gold standard investigation for evacuatory dysfunction. Contrast is inserted into the rectum, vagina, and small bowel to delineate each structure. The patient is asked to defecate on a commode under fluoroscopy to assess the process and effectiveness of defecation. Functional obstruction due to paradoxical contraction of puborectalis can be estimated by measuring the anorectal angle during defecation. Other causes of obstructive defecation such as rectocele, rectoanal intussusception, rectal prolapse, enterocele, sigmoidocele, vault prolapse, and excessive perineal descent can be identified. Small rectoceles may be physiological (Figure 63.3).

MR proctogram has the advantages of avoiding radiation and producing better anatomical and functional images of the pelvic floor anatomy, especially in patients who have had previous surgery [28,29] (Figure 63.4). A study comparing the results of defecating proctogram and MR proctogram in patients presenting with obstructive defecation symptoms found MR proctogram under reported pelvic floor abnormalities especially when there has been poor rectal evacuation [30]. This may be due to the fact that MR proctograms are often performed in a supine position with the patient defecating lubricating gel and patient found it difficult to evacuate in this nonphysiological condition [30].

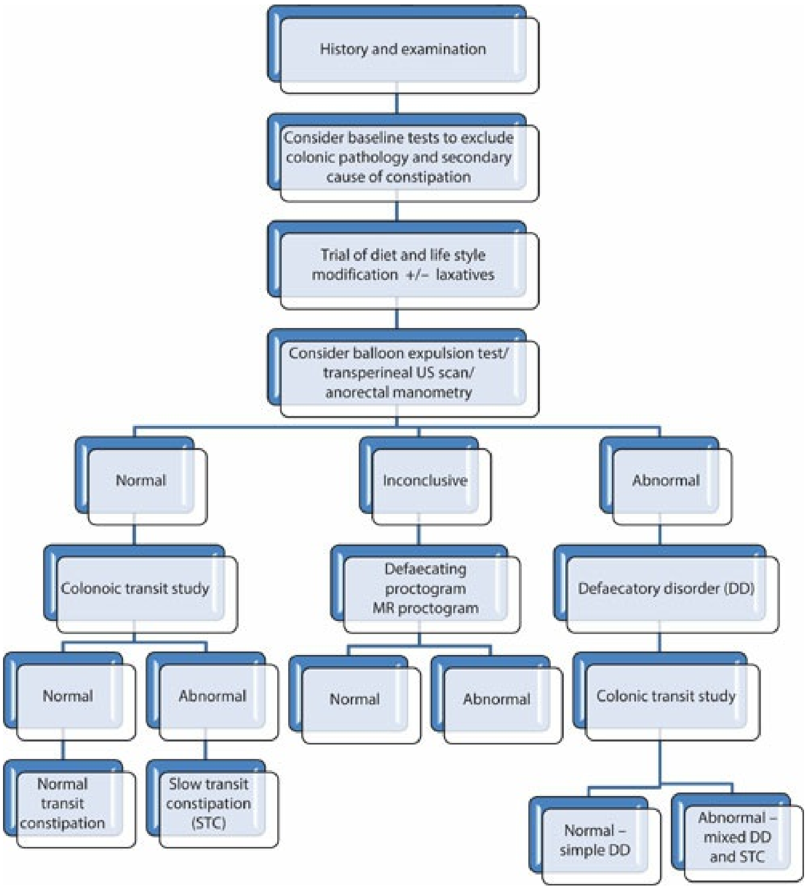
History and examination
Consider baseline tests to exclude colonic pathology and secondary cause of constipation
Trial of diet and life style modification +/– laxatives
Consider balloon expulsion test/ transperineal US scan/ anorectal manometry
Normal
Inconclusive
Abnormal
Colonoic transit study
Defaecating proctogram MR proctogram
Defaecatory disorder (DD)
Normal
Abnormal
Normal
Abnormal
Colonic transit study
Normal transit constipation
Slow transit constipation (STC)
Normal – simple DD
Abnormal – mixed DD and STC

Figure 63.1 Investigation algorithm for chronic constipation. (Based on American Gastroenterological Association et al., *Gastroenterology*, 144(1), 211, 2013; modified.)

An MR-based classification for ODS has been described by Piloni et al. based on combinations of abnormalities found (Table 63.4) [31].

Ultrasound Scan

Transperineal or translabial ultrasound scans allow multiplanar real-time imaging of the pelvis, providing important information on the dynamic functional anatomy of the pelvic floor. It is reported to have excellent tissue discrimination, allowing visualization of modern mesh implants that are difficult to see in other modalities [32]. Transperineal ultrasound scanning may compliment the aforementioned defecography by providing more information on rectal compliance and movement [33].

Diagnostic Studies to Evaluate Intestinal Transit

Since patient recall of bowel habit is often inaccurate, it is helpful to have an objective measure of transit. In the general population, the colonic transit time is normally less than 72 hours [34]. Various modalities are now available to determine gastrointestinal transit time [35].

Transit Study Using Radiopaque Markers

A capsule containing 24 radiopaque markers is swallowed and abdominal radiographs are taken at 12 and 120 hours. Normal colonic transit is defined as >20% markers at 12 hours and <80% at 120 hours [36]. Alternatively, different shaped radiopaque markers are ingested at 0, 24, and 48 hours and an abdominal x-ray is taken at 120 hours [37,38] (Figure 63.5). By counting the number of different shapes remaining, a special formula is used to estimate the transit time. Patients are asked to have high-fiber diet (20–30 g/day) and avoid laxatives, enemas, or medications that affect the bowel during the study. Excessive retention of markers in the rectum may infer outlet obstruction, rather than slow transit; 60% of patients with dyssynergic defecation have excessive retention of markers [39].

Table 63.3 Evidence-Based Summary of the Clinical Utility of Diagnostic Tests for Chronic Constipation

Test	Pros	Cons	Evidence	Recommendation
Abdominal x-ray	Simple, widely available to identify excessive fecal loading	Lack of standardization	Poor	C
Barium enema	Identify megacolon/rectum, stenosis, diverticulosis, intraluminal abnormality	Radiation exposure	Poor	C
Shapes transit study	Evaluate colonic transit, inexpensive	Inconsistent methodology	Good	B2
Colonic transit with scintigraphy	Evaluate slow/normal/rapid transit	Expensive, time-consuming	Good	B2
WMC	Evaluation of upper and lower GI transit, no radiation	Variable availability	Excellent	A1
Defecating proctogram	Identify dyssynergia, rectocele, prolapse, excessive decent, Hirschsprung’s disease	Radiation exposure, interobserver bias, inconsistent, embarrassment	Fair	B3
MR proctogram	Evaluates pelvic floor anatomy, sphincter morphology, and dynamic motion	Lack of standardization expensive, variable availability	Fair	B3
Anorectal ultrasound scan	Visualization of anal sphincters	Interobserver bias, variable availability	Poor	C
Anorectal manometry	Identify dyssynergic defecation, rectal hyposensitivity/hypersensitivity, impaired compliance	Embarrassment	Good	B2
Colonic manometry	Identify colonic myopathy, neuropathy	Invasive, variable availability	Good	B2
Balloon expulsion test	Bedside assessment of dyssynergic defecation	Lack of standardization	Good	B2

Source: Rao SS and Meduri K, *Best Pract Res Clin Gastroenterol*, 25(1), 127, 2011.

Notes: Grade A1: excellent; Grade B2: Good; Grade B3: Fair; Grade C: Poor.
Evidence in favor of the test with some evidence on specificity, sensitivity, accuracy, and positive predictive values.

Gastrointestinal Transit Scintigraphy

Scintigraphy can be used to assess the whole gastrointestinal tract or colonic transit [35]. Liquid or solid labeled with ^{111}In or ^{99m}Tc is ingested and scanned sequentially over hours to assess gastric emptying and small bowel transit [40,41]. Colonic transit scintigraphy is used to measure regional colonic transit by swallowing a pH-sensitive capsule containing ^{111}In absorbed on activated charcoal that is released in the terminal ileum. This will clarify if the patient has diffuse or localized dysmotility [42]. Scintigraphy can be useful when considering surgical treatment.

WMC

A SmartPill wireless motility capsule (WMC) is ingested with pH, temperature, and pressure sensors allowing a noninvasive method of measuring gastric emptying and small bowel and colonic transit [43]. WMC may reduce the need for further invasive motility tests [44,45].

Colonic Manometry

Colonic manometry catheters are placed using a colonoscope or via guidewire. A 24 hour recording allows complete assessment of overall motor activity in the colon at rest, during sleep, while walking, and after meals and medication, which may be helpful in diagnosing underlying myopathy or neuropathy, especially in children [46].

TREATMENT

The majority of patients presenting to their GP will respond well to simple conservative measures such as dietary and lifestyle advice and laxatives. Patients with persistent symptoms who are referred to the tertiary referral centers will benefit from investigation to identify those with slow transit constipation, obstructive defecation, or normal transit/IBS-C and to guide treatment.

CONSERVATIVE MANAGEMENT

Dietary and Lifestyle Advice

In contrast to the traditional advice to increase fiber intake (fruit, vegetables, or wheat bran), Tack et al. [47] suggested that patients with slow transit constipation (STC) are unlikely to respond to increased dietary fiber. In addition, Muller-Lissner et al. [48] highlighted that an increase in fiber intake may actually worsen the symptoms of chronic constipation by increasing fermentation in the gut causing bloating. The latest NICE guidelines recommend that patients with IBS-C reduce their intake of insoluble fiber (i.e., wheat bran) and increase the proportion of soluble fiber, i.e., oats [49]. There is minimal evidence to suggest that increasing fluid intake will increase transit times unless an individual is dehydrated, but fluid intake of 1.5 L/day is usually advised. One controlled trial has shown that higher fluid intake in the presence of a high-fiber diet can improve symptoms of chronic constipation [50].

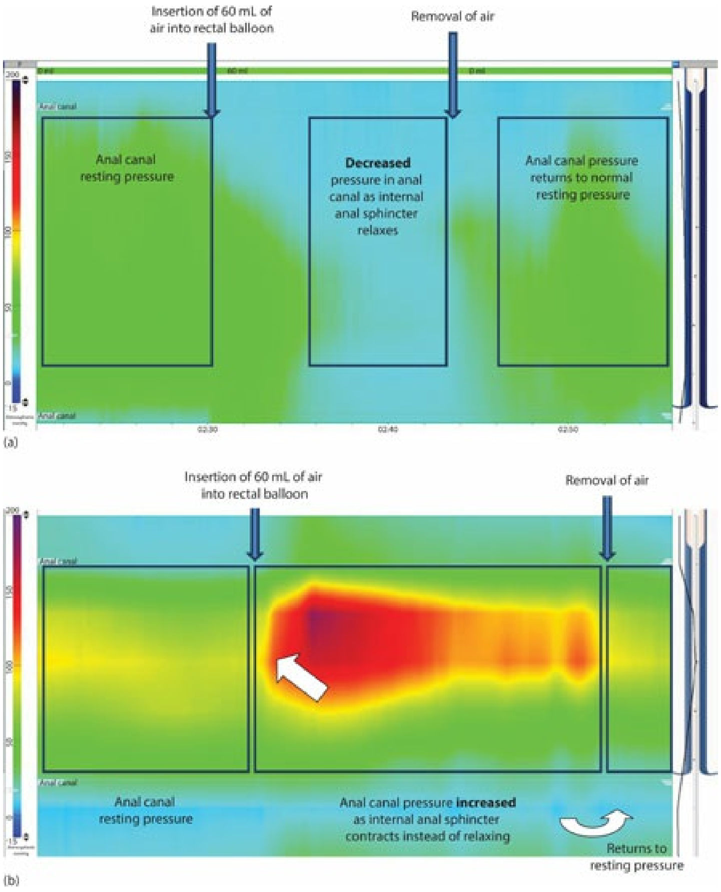
Insertion of 60 mL of air into rectal balloon
Removal of air
0 ml
60 ml
0 ml
200
Anal canal
Anal canal resting pressure
Decreased pressure in anal canal as internal anal sphincter relaxes
Anal canal pressure returns to normal resting pressure
-15
Anal canal
02:30
02:40
02:50
(a)
Insertion of 60 mL of air into rectal balloon
Removal of air
200
Anal canal
Anal canal
-15
Anal canal resting pressure
Anal canal pressure **increased** as internal anal sphincter contracts instead of relaxing
Returns to resting pressure
(b)

Figure 63.2 Anal manometry showing an example of a patient with normal rectoanal inhibitory reflexes (a) and anismus (b). (Courtesy of Mrs. Joanne Hayes, Clinicla Physiologist, UHB, Birmingham, U.K.)

It is unclear whether exercise is beneficial in treating constipation [51]. One small RCT reported that regular exercise decreases constipation as per Rome I criteria [52], whereas another study did not show any benefit [53]. However, exercise is to be encouraged if only for its other proven health benefits.

In addition, position when defecating is important and, in many societies, squatting is the normal posture used. The sitting position with a 90° posture is a relatively recent innovation used in Western toilets. This sitting position causes a narrow anorectal angle that increases straining needed to empty the rectum. A study designed to compare the straining forces applied when sitting or squatting looked at normal volunteers defecating in three positions: sitting on a standard-sized toilet seat (41–42 cm high), sitting on a lower toilet seat (31–32 cm high), and squatting [54]. Both the net time needed for sensation of satisfactory bowel emptying and the degree of straining were significantly less in the squatting position compared with both sitting positions ($p < 0.0001$). Thus, patients are advised to adopt a position where the knees are above the hips with feet flat on the floor. There are now several devices available to enable a squatting position to be adopted on a pedestal toilet.

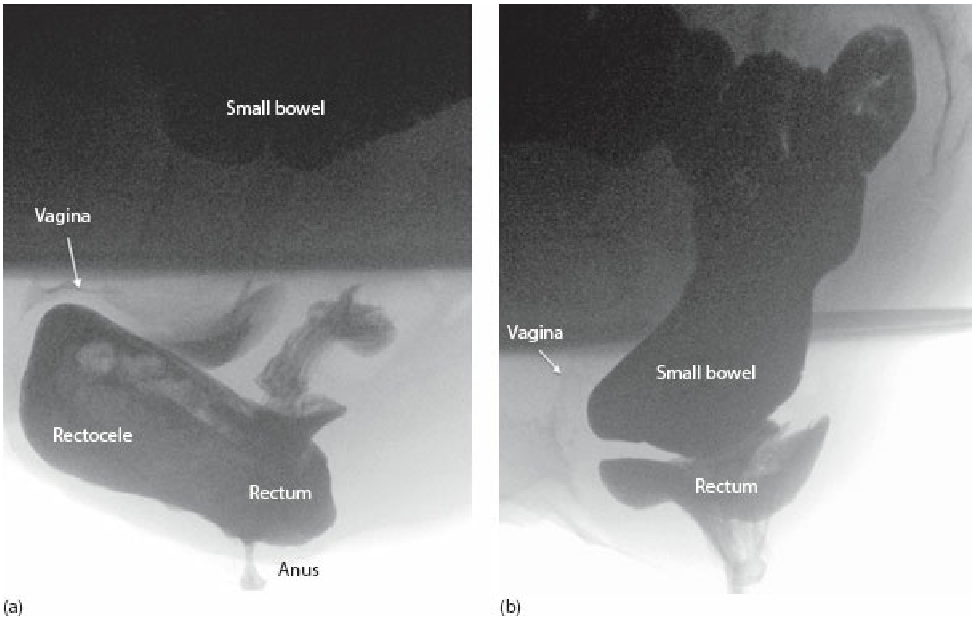

Figure 63.3 Defecating proctogram demonstrating large rectocele (a) and enterocele (b). (Courtesy of Dr. Peter Guest, Consultant Radiologist, UHB, Birmingham, U.K.)

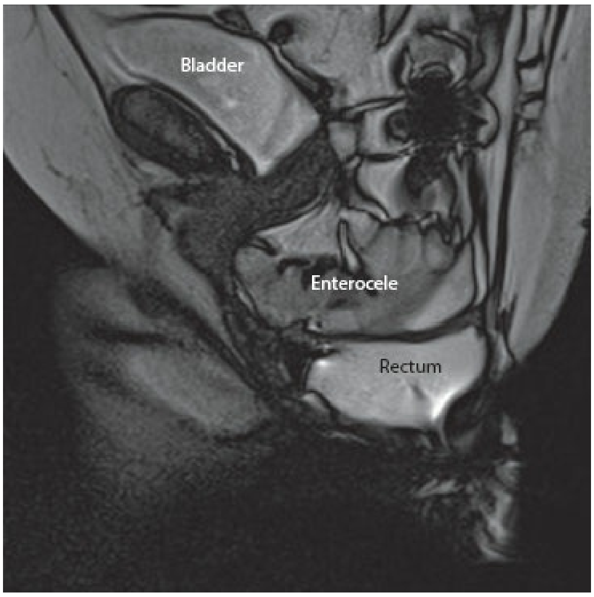

Figure 63.4 MR defecography showing an enterocele. (Courtesy of Dr. Arvind Pallen, Consultant Radiologist, UHB, Birmingham, U.K.)

Laxatives

A variety of laxatives are now available for treating constipation; all are more effective than placebo

[55]. The mechanism of each type of laxative will help to determine the most appropriate type of laxative for the patient's symptoms (Table 63.5) [56].

Bulk Laxatives/Fiber

Undigestible fiber is an important part of our diet to provide stool bulk. Bulk-forming laxatives attract water, forming larger and softer stool, which in turn causes colonic distension, stimulating peristalsis and effective propulsion of stool along the colon to rectum. It is useful to those patients passing small hard stools. It may cause symptoms of bloating but is usually well tolerated. Systematic review has reported that bulking agents induce an average increase of 1.4 bowel movements per week [57].

Osmotic Laxatives

Osmotic laxatives increase the amount of water in the colon. Lactulose (semisynthetic disaccharide, poorly absorbed sugar), macrogols (inert polymers of ethylene glycol), or magnesium salts retain fluid in the colonic lumen causing osmotic diarrhea. Absorption of magnesium is limited but caution must be exercised in patients with impaired renal function [58]. Lactulose is less effective than macrogols [59] and its use may be limited due to flatulence and bloating caused by bacterial fermentation. Phosphate enemas are also an osmotic laxative.

Table 63.4 MRI-Based Classification for Obstructive Defecation Syndrome

Grade	Category	MR features	Management
1	Simple functional	Puborectalis dyssynergia	Pelvic floor rehabilitation
		EAS dyssynergia	
2	Grade 1 + minor anatomical defect	Rectocele ≤ 2 cm	Pelvic floor rehabilitation
		First-degree intussusception	
		Mucosal prolapse	
		Focal LA defect < 1 cm	
3	Grade 2 + major anatomical defect of posterior compartment	Rectocele > 2 cm or trapping	Surgical (colorectal)
		2nd-/3rd-/4th-degree intussusception	
		Rectal floor descent > 5 cm below PCL	
		Focal LA defect < 1 cm	
4	Grade 3 + major anatomical defect in all three compartments	Multiple pelvic organ prolapse	Surgical (urogynecology)
		Multifocal LA defects > 1 cm	
		Detachment of endopelvic fascia	
5	Surgical failure	Anastomotic stricture/deformity	Multidisciplinary approach
		Reduced rectal capacity	
		Rectal pockets, sinus tract, granuloma	
		Persistent rectocele, intussusception	
		Difficult emptying/contrast retention	
		Distortion of vaginal shape	
		Pudendal nerve neuropathy	

Source: Piloni V et al., *Tech Coloproctol*, 17(5), 501, 2013.

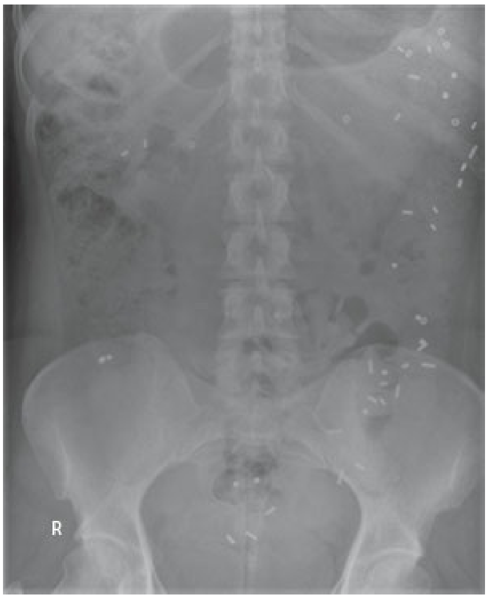

Figure 63.5 Shapes study of a patient with slow transit constipation taken at 120 hours. (Courtesy of Dr. Peter Guest, Consultant Radiologist, UHB, Birmingham, U.K.)

Stool Softeners

Stool softeners can be administered orally (liquid paraffin and docusate sodium) or rectally (arachis [peanut] oil and glycerol) to soften and lubricate the stool.

Stimulant Laxatives

Diphenylmethane derivatives such as bisacodyl, sodium picosulphate and anthraquinone derivatives such as senna are stimulant laxatives, which act on the enteric nervous system to increase intestinal motility but may cause abdominal cramps as a consequence. This can be managed by titrating the dose. Long-term use of anthraquinone-derived stimulants can generate brown discoloration of mucosa known as pseudomelanosis coli. Docusate sodium and glycerol are both stimulants and softening agents.

Parasympathomimetics such as neostigmine enhance parasympathetic activity in the gut and increase intestinal activity. It is rarely used for constipation. Neostigmine can be used in selected cases for the treatment of pseudoobstruction that has failed to settle with conservative management [60].

5-HT4 Receptor Agonists

Prucalopride is a selective serotonin (5-HT4) receptor agonist with prokinetic activity. NICE has recommended the use of prucalopride in women with chronic constipation who have failed to improve with at least two laxatives from different classes at the highest recommended dose for at least 6 months [61]. Efficacy of the treatment should be reviewed after a 4-week trial of the medication. In elderly patients, a reduced dose of 1 mg/day is recommended. The pivotal randomized double-blinded placebo-controlled trials carried out with a total of 1999 adults with chronic constipation (PRU-INT-6, PRU-USA-11, PRU-USA-13) showed that the proportion of subjects treated with prucalopride 2 mg/day who had three or more spontaneous complete bowel movements per week during weeks 1–4 ranged from 23.7% to 32.1%, compared with 9.8% to 11.5% for placebo (all $p \leq 0.001$) and during weeks 1–12 ranged from 19.5% to 28.9%, compared with 9.6% to 13.0% for placebo (all $p \leq 0.001$) [62–64]. Headache, nausea, and diarrhea were more common side effects with prucalopride compared to placebo [55]. A smaller study comparing efficacy of prucalopride on patients with different subtypes of constipation showed that all categories of constipation may respond to prucalopride [65].

Table 63.5 Summary of Laxatives

Laxative type	Examples of laxatives	Mechanism of action	Side effects
Bulk forming	Ispaghula husk,	Increase fecal mass	Bloating

	methylcellulose		
Osmotic	Lactulose, macrogols, magnesium salts	Increase water in colon	Flatulence, bloating Dehydration Electrolyte abnormality
Stool softeners	Liquid paraffin, docusate sodium	Luminal water binding, increases stool bulk	Abdominal pain and cramps
Stimulant	Bisacodyl, sodium picosulphate, senna	Increase intestinal motility	Abdominal pain and cramps
5-HT4 agonists	Prucalopride	Stimulates colonic and intestinal peristalsis	Nausea, vomiting, abdominal pain, dyspepsia, flatulence, headache
Colonic secretagogues	Linaclotide	Promoted fluid secretion into GI lumen	Diarrhea
Colonic secretagogues	Lubiprostone	Promoted fluid secretion into GI lumen	Nausea, vomiting, abdominal pain, dyspepsia, flatulence, headache

Source: Tack J et al., *Neurogastroenterol Motil*, 23(8), 697, 2011.

Colonic Secretagogues

Lubiprostone is a member of a new class of medication called prostones, which activate type 2 chloride channels (CIC-2) on enterocytes, and promote the secretion of chloride-rich intestinal fluid without altering the serum concentration of sodium or potassium. It is thought that by increasing the intestinal secretions, small bowel motility is increased, thereby increasing the passage of stool [66–68]. Three RCTs comparing lubiprostone 24 μg twice daily with placebo in 610 patients showed that lubiprostone significantly enhanced bowel movement frequency and relieved other constipation-related symptoms [68–70]. The most commonly reported side effects include nausea and diarrhea [55]. It is currently licensed for treatment of chronic idiopathic constipation. There are limited but supportive data on safety and efficacy of use of lubiprostone in the elderly population [71], constipated patients with Parkinson's disease [72], and treatment of opioid-induced constipation [73].

Treatment of Irritable Bowel Syndrome with Constipation

It is important to identify symptoms that are affecting the individual patient and tailor the treatment accordingly [10,49]. To treat their constipation, bulk-forming laxative, such as soluble fiber (ispaghula husk or oats), or osmotic laxatives (macrogol) are recommended. Antispasmodics or low-dose tricyclic antidepressants may ease abdominal pain associated with IBS.

Linaclotide is currently licensed for the treatment of moderate to severe IBS associated with constipation. It is a first-in-class, oral guanylate cyclase-C receptor agonist of enterocytes. It induces intestinal chloride and fluid secretion through cyclic GMP production [74]. Three RCTs comparing linaclotide with placebo containing 1582 patients showed that 290 μg once daily significantly improved abdominal pain, bloating, and constipation associated with IBS-C [75–77]. The most frequently reported side effect was diarrhea [78,79].

Biofeedback

Biofeedback is based on behavior modification and operant conditioning [80]. It teaches patients how to control a physiological function that is not usually under conscious control by using an instrument that provides visual and/or auditory feedback of an action. This therapy has been reported to be effective in both constipation and incontinence [81]. Three main methods of monitoring defecation and providing biofeedback to patients are EMG biofeedback, manometric biofeedback, and balloon sensory training [82]. None have been shown to be consistently more effective than any other method [83] but EMG biofeedback is the method most widely used [84].

Gut-directed biofeedback involves patients being taught to defecate successfully using bracing of the abdominal wall muscles and effective relaxation of the pelvic floor muscles [85]. This may be enhanced by use of a water-filled rectal balloon, which patients attempt to expel [86]. Patients are enabled to recognize the sensations associated with relaxation of the pelvic floor and anus together with correct use of abdominal muscles to create an effective pushing force and thus learn to defecate effectively. Patients may also be given basic instruction on gut anatomy and function to enhance their understanding, as well as behavioral advice about frequency and length of toilet visits, posture on the toilet, and dietary habits [87].

Numerous nonrandomized studies of biofeedback for idiopathic constipation have published positive results, suggesting that biofeedback is an effective intervention for constipation due to both slow gut transit [82,88] and evacuation disorders [89–92]. Biofeedback has been shown to be more effective than laxatives [93], relaxation training [89], and placebo [90]. A systematic review of seven trials, with a total of 413 participants, concluded that biofeedback conferred a sixfold increase in the odds of treatment success [84].

There is some evidence that evacuating regularly may also stimulate gut transit and so improve symptoms [86]. Whereas short-term results may vary from 60% to 90% improvement [94], long-term studies report sustained improvement in around 50% of patients [95]. As the treatment involves dedicated sessions with a single clinician, the development of that therapeutic relationship may also contribute to improvements in quality of life.

Psychological Therapy

Psychological therapies can improve symptoms without interacting with pharmacological treatments [96]. Additionally, they can improve patient's ability to cope with the symptoms thus improving quality of life. Discussion of symptoms with a supportive health-care professional who listens and responds appropriately can reduce feelings of isolation and shame. Some patients need more formalized psychological interventions, including counseling and cognitive behavioral therapy.

Rectal Irrigation

Rectal irrigation was originally used in clinical practice for children with spina bifida [97]. Indications were extended to adults with neurogenic bowel dysfunction after conservative management had failed [98]. It is now used in a wider variety of conditions such as rectocele, obstructed defecation, and other functional bowel problems [99]. It is taught to patients as a self-management method. Several products are available on the market; hence, the product can be chosen to suit individual patient's needs. They are designed to be used while sitting on the toilet to avoid accidents when transferring. Mini systems allow irrigation with up to 90 mL of water (Aquaflush Compact, Mini Qufora) and are used to aid initiation and completion of defecation, being helpful in patients with symptoms of ODS and incomplete evacuation [100,101]. The larger systems allow irrigation with a cone or balloon catheter, enabling instillation of larger quantities of water, used in patients with slow transit constipation or neurological abnormalities (Aquaflush Quick, Qufora, Peristeen).

In long-term follow-up of 169 patients over 56 months, rectal irrigation was found to be effective in 44% of patients with fecal incontinence and 62% of patients with defecatory disorders [24]. Collins and Norton retrospectively assessed 50 consecutive patients using the mini system and found that 62% improved or their symptoms completely resolved [102]. Absolute contraindications include stenosis, colorectal cancers, acute diverticulitis, and active inflammatory bowel disease. Most complications reported are minor and include abdominal cramps, minor anal bleeding, and leakage of irrigant after completion [99]. Introduction of a medical device and administration of water carry a risk of bowel perforation. In a consensus review of best practice, the perforation risk was estimated at 1 per 50,000 and was thought to be noncumulative [103]. For this reason, it is important that irrigation is taught by qualified experienced clinicians. Faaborg et al. have studied the long-term effects of using rectal irrigation in patients with functional bowel disorders and found that there was no long-term deterioration in anal sphincter function or rectal compliance [104].

Neuromodulation

PTNS

Percutaneous tibial nerve stimulation (PTNS) delivers electrical stimulation through an acupuncture needle placed medially above the ankle. It is postulated that stimulation of the tibial nerve in turn stimulates the sacral nerves thus neuromodulating bowel motility and/or sphincter function. The treatment is outpatient based and consists of 12 weekly 30 minute sessions. In a pilot study of 18 patients with constipation, the Wexner constipation and Patient Assessment of Constipation Quality of Life scores were significantly improved after a course of 12 treatments. Stool frequency also increased with a decrease in laxative use, although these results were not statistically significant [105].

SNS

There is growing interest in considering sacral nerve stimulation (SNS) as a first-line surgical intervention for constipation after incidental finding of increased bowel frequency and improvement in constipation of those who underwent permanent SNS for bladder dysfunction or fecal incontinence [106–111]. The latest review on the efficacy of SNS for constipation management in 225 temporary neuromodulations and 125 permanent implants showed more than 50% had objective evidence of improvement on bowel diaries on temporary neuromodulations and were maintained in approximately 90% of patients who subsequently underwent permanent implantation over medium-/long-term follow-up [112]. Subanalysis of the European trial data demonstrated improvement in both colonic transit and ability to evacuate as well as improvement in quality of life [113]. Improvement in defecatory frequency with temporary wire placement has been suggested as a good predictor of successful outcome with a permanent implant [108,112,113].

Complementary Medicine

Many patients resort to alternative medicine in desperation to find a solution to their symptoms. A small study of 30 patients with STC found that acupuncture leads to a decrease in the use of laxatives and improvement in symptoms [114]. There are no other robust studies available on the role of complementary therapies. Patients should be advised to exercise caution when considering other interventions.

SURGICAL MANAGEMENT

Surgery has a role in the management of carefully selected patients with chronic constipation who fail to improve with current conservative management [109–111].

Antegrade Continence Enema [50]

Antegrade continence enema (ACE) is considered as an alternative to colostomy in select patients with constipation or fecal incontinence. ACE surgery requires a continent connection to be created between the abdominal wall and cecum. Malone et al. [115] described the use of reversed appendix to maintain continence, which can now be performed laparoscopically assisted. If a patient has had previous appendicectomy or has an atrophic appendix, tubularized ileal or cecal conduits are used. Patients are taught to intubate the ACE with a catheter and perform antegrade colonic enema with irrigant, usually a mixture of water and phosphate enema. In general, success rates have been lower in adults than in children [110], but a Danish group has reported a favorable outcome in 69 adults who underwent ACE procedure with mean follow-up of 75 months [116].

Long-term complications include stoma stenosis, leakage, or failure to effectively treat the original symptoms requiring revision, reversal, or conversion to a stoma [7]. It is worth considering combining the ACE procedure with a colostomy in disabled patients and patients with persistent left colonic inertia despite retrograde irrigation [117].

Defunctioning Stoma

A stoma may be formed as definitive procedure, as guide to further treatment, or as salvage from failed alternative interventions [110]. In patients with slow transit constipation who have failed maximal conservative management, defunctioning ileostomy may be formed as a guide to colectomy [51]. Colectomy can be avoided in patients who have unsatisfactory ileostomy function or persistent abdominal symptoms such as pain or bloating.

Colectomy

Colectomy should only be considered as a treatment option for patients with diffuse slow colonic transit but normal gastric and small bowel transit [110]. Once a decision to resect has been made, then the next consideration is how much to resect. Two studies have reported good results by performing segmental resections or subtotal colectomies based on segmental transit time measurements [42,118]. However, limited subtotal colectomy with cecorectal or ileosigmoid anastomosis is generally reported as having an inferior functional outcome to ileorectal anastomosis [106]. The long-term results of surgery for slow transit constipation may be poor. However, a good outcome can be predicted in patients with slow transit constipation without impaired evacuation and overt psychological or psychiatric disease [119].

Surgical Treatment Options for Obstructive Defecation

Surgical repair of anatomical deformities identified in patients with ODSs should only be carried in those who have exhausted all conservative treatments. The aim of surgery is to correct anatomy with a relief of associated symptoms [120], although correction of anatomical abnormalities alone does not always lead to restoration of normal function [121]. To decide on the best treatment options, understanding the pelvic floor anatomy and the DeLancey level of pelvic organ support (Table 63.6) will help [122].

Rectocele

Surgical repair of rectoceles in patients presenting to the colorectal surgeon is usually recommended when they are 2 cm or more in depth with the need for patient to digitate to defecate and with evidence of significant trapping on defecating proctogram or MRI proctogram [123] via transvaginal, transperineal, transanal, or abdominal approaches. Transvaginal posterior colporrhaphy was found to have the lowest rate of recurrence of rectocele/enterocele in a Cochrane Review of all rectocele repairs [124]. Dyspareunia has been reported in up to 25% of women following posterior colporrhaphy. A systematic review of the use of biological materials in urogynecological surgery has shown that there was no additional benefit to the use of biological material in rectocele repair [125].

Stapled transanal rectal resection (STARR) involves resections of internally prolapsed rectum circumferentially using a circular stapling device. Jayne et al. reported 1-year outcome of patients who underwent STARR procedure for evacuation disorder on the European STARR registry. This showed significant improvement in symptom severity and quality of life score. However, 36% experienced complications including urgency, pain, urinary retention, bleeding, and septic events [126]. A consensus panel has developed a treatment algorithm for offering STARR by experienced surgeons for patients with evacuation disorder with a rectocele and/or intussusception [127].

Enterocele/Sigmoidocele

Enterocele or sigmoidocele occurs as a result of herniation of small bowel (enterocele) or sigmoid colon (sigmoidocele) through the uterosacral ligament at the vaginal apex into the pouch of Douglas, leading to separation of the rectovaginal septum. This can impede defecation leading to pelvic discomfort and perineal pressure with straining [128]. There are some physiological enteroceles, but if an enterocele or sigmoidocele impairs rectal emptying on defecating proctogram, then it is likely to be contributing to the patient's symptoms of ODS. Enteroceles can be repaired transabdominally laparoscopically (ventral mesh rectopexy and sacrocolpopexy) or vaginally in conjunction with pelvic floor repair (Table 63.6).

Table 63.6 DeLancey Level of Pelvic Organ Support

	Support	**Defect**
Level 1	Superior suspension of the vagina to the cardinal–uterosacral complex	Enterocele/sigmoidocele
Level 2	Lateral attachment of the upper two-thirds of the vagina	Rectocele
	Rectovaginal septum supporting posterior vaginal wall	Rectal intussusception
Level 3	Distal fusion of vagina into the urogenital diaphragm and perineal body	Supra-anal rectocele

Source: DeLancey JO, *Am J Obstet Gynecol*, 166(6 Pt 1), 1717, discussion 24–28, 1992.

Internal Intussusception/Rectal Prolapse

Surgically, the rectum is mobilized and returned to its correct anatomical position within the pelvis and many techniques have been described [120]. In suture rectopexy, the rectum is fully mobilized and sutured to the presacral fascia. In patients with redundant loop of sigmoid with preoperative symptoms of constipation, sigmoid resection may be considered. Laparoscopic resection rectopexy (Frykman–Goldberg procedure) has been shown to be safe with good long-term outcome [129,130]. The use of mesh has been introduced on assumption that a foreign body will produce stronger adhesions and fibrosis than dissection and suture alone. Various techniques have been described, including anterior sling rectopexy (Ripstein procedure), posterior mesh rectopexy (Well's posterior rectopexy), and use of fascia lata to fix the sacral promontory (Orr–Loygue procedure) with further modifications using different types of mesh. Systematic review on ventral rectopexy for rectal prolapse and intussusception showed that there appears to be a reduction in postoperative constipation if posterior rectal mobilization is not performed with division of lateral ligaments [131]. Current literature has shown modern nerve-sparing laparoscopic ventral mesh rectopexy that showed over 50% improvement in the short and medium term [132,133]. Robotic-assisted rectopexy has the advantages of 3D vision, a better view to identify and spare parasympathetic innervation to the rectum, and having flexible tips of instruments for suturing over laparoscopic approach. Recent literature supports safety and feasibility of robotic-assisted rectopexy [134]. There is limited evidence of the best mesh to be used. An expert panel (grade C evidence) has recommended the use of biological mesh in young women of reproductive age, diabetics, smokers, patients with history of pelvic radiation or IBD, or intraoperative breach of rectum or vagina [133].

Perineal procedures are considered in patients with full-thickness rectal prolapse who may not be fit for an abdominal procedure and may carry a higher recurrence rate [135]. Delorme's procedure involves transanal mucosal stripping with plication of the muscular wall of the rectum. The Altemeier procedure is transperineal resection of the rectosigmoid, which can be offered to frail patients with symptomatic large prolapse.

CONCLUSION

The management of constipation can be challenging. The majority of the patients can be managed conservatively with a multidisciplinary approach (see Chapter 65) in complex patients. Patients with idiopathic constipation can be managed conservatively without recourse to major surgical interventions. Surgery carries risks of serious morbidity and patient selection for surgical intervention must be carried out with caution. For a few, surgery can offer effective treatment with improvement in function and quality of life.

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64 Female Sexual Dysfunction

Seth D. Cohen and Irwin Goldstein

The objective of this chapter is to provide relevant evidence-based clinical information to help practitioners diagnose and treat specific biological-based sexual health pathophysiologies in women.

Female sexual dysfunction (FSD) is recognized as a common medical problem in all age groups. Data from the National Health and Social Life Survey, a study that describes both the distribution of sexual practices and the changes in these practices under current conditions, found that sexual dysfunction is more prevalent in women (43%) than in men (31%) [1]. Shifren et al. [2] evaluated data from the population-based Prevalence of Female Sexual Problems Associated with Distress and Determinants of Treatment Seeking study. This study estimated the prevalence of sexual problems and sexually related personal distress in U.S. women in addition to the prevalence of sexual disorders of desire, arousal, and orgasm. They concluded that about 40% of those with a sexual disorder of desire, arousal, or orgasm have concurrent depression. In 2014, there were over 25 FDA-approved drugs for men's sexual health; despite the significant number of women with bothersome FSD, there was only one drug that was FDA approved in women. This drug, ospemifene, is licensed to treat moderate to severe dyspareunia in menopausal women [3]. We feel that it is of vital importance to address female sexual problems systematically and will take you step-by-step through the presentation, diagnosis, and treatment of many FSD disorders in an organized and complete fashion.

A basic understanding of what sexual dysfunction means is a key for any clinician seeing FSD in their office. Based on the most current version of the DSM-V [4], sexual dysfunction is a heterogeneous group of disorders that are characterized by a clinically significant disruption in a person's ability to respond sexually or to experience sexual pleasure. In this, the recognized FSD disorders are female orgasmic disorder, female sexual interest/arousal disorder, and genitopelvic pain/penetration disorder.

To provide the best care to women struggling with FSD, clinicians must understand that sexual problems are commonly associated with significant personal distress including a diminution of self-worth and self-esteem, a reduction in life satisfaction, and a decline in the quality of the relationship with her partner [5]. Thus, to provide the best overall care for these patients, it is important for clinicians to be familiar with the basic aspects of appropriate women's sexual health-care delivery. "Sexual health" refers to a state of physical, emotional, mental, and social well-being related to sexuality [6]. Women have the right to a positive and respectful sexual relationship and to have pleasurable and safe sexual experiences, free of coercion, discrimination, and violence. Women have the right to sexual equity, the freedom from all forms of discrimination and violence. For sexual health to be arraigned and maintained, the sexual rights of all women must be respected, protected, and fulfilled [7].

To properly assess women with sexual dysfunction, it is necessary to take a biopsychosocial approach. To engage this method of diagnosis and treatment, a clinician may need to utilize multiple different health-care professionals from various fields in order to get to the root of the sexual dysfunction. This multidisciplinary methodology (Figure 64.1) has allowed us to have great success in diagnosis and treatment of difficult presentations of FSD.

VILLAGE

Despite the fact that female urology and urogynecology practitioners have a unique position to understand the anatomy and physiology of the peripheral genitalia and pelvic floor constituents, sexual medicine issues are usually highly complex and are, in general, secondary to interrelated psychological, physiological, and relationship issues molded with distinct couple dynamics. In most cases, women with sexual health concerns should consider undergoing concomitant psychological and physical therapy assessment and management by an appropriately trained specialist [7].

Traditional management of a woman with sexual health problems usually involves evaluation by a single provider with expertise in a specific discipline (i.e., medicine, psychotherapy, or physical therapy). Based on the outcome/initial diagnosis, the patient may be referred to a provider(s) in a different discipline(s). There are limitations to this traditional model: Sexual health is more than just the absence of symptoms. Expertise of the provider is often constrained by training and exposure as well as access to care by providers in different disciplines. There may be pelvic floor, psychological, or biological issues not addressed by this traditional model. Thus, at our institution, we have introduced a novel health-care technique that is able to assess these complicated issues in one patient visit; we call it the village health-care technique where multiple providers from various different backgrounds are able to take care of a single patient with complex disorders. We recognize that no one medical professional can take care of all sexual problems by himself or herself. This technique employs multiple different health-care specialists all of whom treat sexual dysfunction but whose expertise and training are unique to their specialty. In our office, a typical patient will be evaluated by a registered pelvic floor physical therapist, a sex therapist/sexuality educator, and a sexual medicine physician. If it is possible to recreate this office scenario in other offices, we feel that it has the highest yield for the proper diagnosis and treatment for FSD patients.

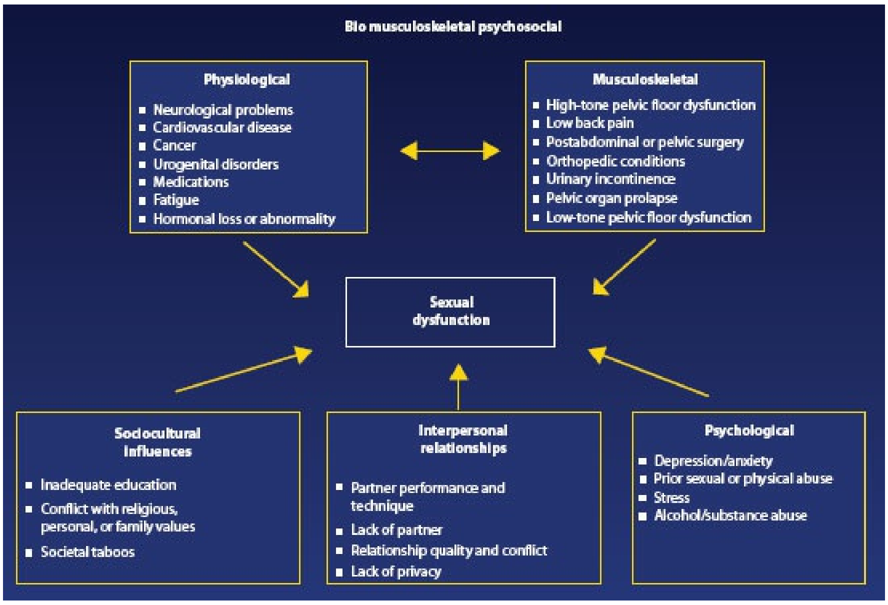

Figure 64.1 Stepwise, multidisciplinary approach to addressing female sexual dysfunction.

Psychosocial Assessment/History

It is not necessary to do an exhaustive sexual and family history for most evaluations. The patient’s description will indicate whether she experiences the dysfunction at all times or only under certain circumstances [8]. Identification of a precipitating factor will likely reveal a pattern within the mindset or experience of the patient, which would help explain the shift in sexual function, and it is helpful to establish if the change was preceded by or concurrent with major life stressor (breakup, death in the family, job problem, newborn in the house). In long-standing cases of primary dysfunction, it is more important to look for a precipitating cause with an emphasis on what is currently maintaining the dysfunction. For instance, if there was a traumatic or painful first sexual experience, is the woman still afraid that sex will hurt? Is fear or anxiety leading to painful pelvic floor muscle contractions during attempts at coitus?

The health-care provider should briefly screen all patients for obvious psychopathology that would impact the treatment algorithm for FSD. The health-care provider should investigate if the psychiatric symptoms are currently present or have been treated previously. These symptoms may be interrelated with the sexual disorder. This will help guide the clinician in defining goals and boundaries for the patient. Psychological factors [9] that can easily interplay with FSD include previous sexual trauma and abuse [10], depression [11], psychoses, anxiety, distraction, sexual neurosis, sexual inhibitions, and/or interpersonal relationship issues.

There is a statistically significant increase in depression for females with FSD. If the patient is depressed, then the severity of the depression should be clarified and documented accordingly. Furthermore, all patients who experience major depression should be questioned about suicide risk [11]. Thus, a close working relationship between the FSD clinician and sex therapist is typically warranted in cases of major/severe depressive symptoms.

Pelvic Floor Assessment in Women's Sexual Function

Overview

Normal function of the pelvic floor musculature is essential in maintaining appropriate sexual function. Both "low-tone pelvic floor dysfunction" and "high-tone pelvic floor muscle dysfunction" can be closely associated with women's sexual health concerns. Hypotonus of the pelvic floor muscles, secondary to childbirth, trauma, and/or aging, is related to urinary incontinence during orgasm, vaginal laxity, and/or thrusting dyspareunia secondary to pelvic organ prolapse. Hypertonus of the pelvic floor secondary to childbirth, postural stressors, microtrauma, infection, adhesions, and surgical trauma can contribute to symptoms of urinary retention, reduced force of stream, dysuria, urgency, penetrative dyspareunia, and/or vaginismus.

Assessment

The assessment of pelvic floor tone is determined by the woman's ability to isolate, contract, and relax the pelvic floor muscles. The pelvic examination should begin with a digital exam, which is performed by exerting light pressure on the lateral walls of the vagina to assess whether the woman can squeeze on the examining finger and elevate the pelvic floor without simultaneously contracting the abdominal, gluteal, or adductor muscle groups. If the patient is not able to produce sufficient muscle strength to compress the finger or is not able to sustain that pressure for several seconds, she may be exhibiting a low-tone pelvic floor dysfunction pattern. If, conversely, the woman experiences muscle tenderness or pain when pressure is applied to the lateral vaginal wall or during an attempted squeeze against resistance, she may be exhibiting a high-tone pelvic floor dysfunction pattern. A perineometer or an electromyography probe, designed to measure muscle activity, can verify these physical examination findings [12–15].

Hypoactive Pelvic Floor

Weakness and laxity of the pelvic floor muscles represent a spectrum of symptoms and conditions that include women with pelvic organ prolapse with or without urinary or fecal incontinence. Risk factors include age, heredity, trauma, menopausal status, and chronic medical conditions such as chronic obstructive pulmonary disease, obesity, and constipation. Stress incontinence that occurs with increased intra-abdominal pressure and maneuvers such as sneezing, coughing, and straining is related to abnormalities in urethral closure pressure and poor pelvic muscle support. Sexuality will often be adversely affected by a hypoactive pelvic floor since severe incontinence and prolapse symptoms are a source of anxiety and interfere with the overall sexual satisfaction experience. These women often express concern about feeling undesirable and fearing embarrassment [14–17].

Hypersensitive Pelvic Floor

Hypertonus of the pelvic floor musculature accounts for some of the concerns of female patients who present for evaluation of sexual health concerns. Hypersensitivity disorders involving the genitourinary tract represent a spectrum of symptoms and conditions that include chronic bacterial cystitis, urinary urgency and frequency, urethral syndrome, interstitial cystitis, vulvar pain, and perineal and pelvic pain. Sexuality is adversely affected for the majority of women with hypersensitivity disorders of the bladder, bowel, and vulva and high-tone pelvic floor dysfunction. Patients who can tolerate coitus often suffer a flare of their symptoms for days as a result of sexual activity, which then becomes a negative reinforcement for future sexual activity [14–17].

Physical Therapy Treatment

Although treatment regimens for high and low pelvic floor tone with resultant sexual dysfunction need a separate chapter, we will go over a few important tools that physical therapists use to treat the aforementioned disorders. Burning, stinging, irritating, raw, tearing, and searing pains are the most common complaints reported during and after vaginal penetration. If these symptoms are felt at the vaginal introitus and superficial structures such as the vulva, perineal body, posterior fourchette, and episiotomy site, then most likely the superficial muscle layers of the pelvic floor are implicated. If deeper vaginal pain occurs, restriction of the vaginal canal, levator ani and obturator internus muscle trigger points, or sacroiliac, symphysis pubis, hip, or lumbosacral joint dysfunction may be implicated [14].

Disorders of the female pelvic floor that result in bladder/urethra dysfunction and/or sexual dysfunction are common. Conservative therapies for hypersensitivity disorders of the pelvic floor are aimed at muscle reeducation. An individualized pelvic floor rehabilitation program aimed at facilitating sexual comfort and pleasure for patients can be designed. Massage of the pelvic floor can be performed to elongate shortened muscles and decrease high-tone spasm in such patients. Conservative therapies for low-tone pelvic floor dysfunction are also aimed at muscle reeducation. Pelvic floor muscle strengthening exercises, augmented with biofeedback and/or electrical stimulation to the pelvic floor, can be initiated [12,14,15].

Once the musculoskeletal diagnosis for vaginismus and dyspareunia has been established, treatment should include the following steps [8]:

1. Correct any joint malalignment to promote pain-free joint mobility.
2. Teach the patient self-correction joint techniques.
3. Inform about positions for sexual intimacy.
4. Eliminate tender trigger points in all of the muscles.
5. Eliminate or reduce scar adhesions and tissue restrictions.
6. Teach pelvic floor muscle awareness with a biofeedback device.
7. Reeducate the pelvic floor muscles to be relaxed upon penetration.
8. Stretch the muscles surrounding the vagina by combining down training with dilators.
9. Correct muscle imbalances by down training (relaxation) and up training (strengthening).
10. Correct muscle imbalances by teaching correct muscle timing and recruitment.
11. Educate about lubricants.

Sexual Health-Care Provider Assessment

Clinical History

There is limited consensus on management paradigms for the diagnosis of women with sexual health complaints. As it concerns the biological-based sexual dysfunction, the most relevant aspect of the diagnosis is the history and physical examination.

Clinical history taking centers on three components: sexual, medical, and psychosocial aspects. The sexual history should begin with the patient describing the sexual problem. The following questions may be utilized to help obtain maximal descriptive information. These are based on women presenting with sexual dysfunction rather than those presenting with combined incontinence problems, where the questions may be used as a modified basis to open discussions.

1. Do you ever experience problems with sexual interest, sexual arousal, and/or sexual orgasm?
2. Sexual problems are common in women who have urinary complaints. Do you have any urinary issues that bother you like frequency, urgency, or stress incontinence?
3. What is your current sexual function in terms of interest, arousal, and orgasm compared to when you were at your peak sexual function?
4. How long have you had the sexual problem? Timing? Frequency during the day, month, or year?
5. Does the sexual problem occur only during partner-related sexual activity or during manual manipulation?
6. In which situations is the sexual problem minimized? Maximized?
7. Is the sexual problem associated with any degree of discomfort, tenderness, soreness, or pain? If so, can you localize the site of pain in a schematic diagram of a woman’s genitalia?
8. What tests/evaluations have you already had in regard to your sexual health concern?

The medical history should include focused questions on any accompanying medical/surgical illnesses and/or the use of medications [16]. Urogynecologic history taking such as incontinence [17–20], frequent urinary tract infections, interstitial cystitis [21], pelvic surgeries, childbirth [22,23], abortions, episiotomy, sexually transmitted diseases [24], pelvic inflammatory disorder, endometriosis, fibroids [25], hysterectomy with or without oophorectomy, and menopausal status [26] should all be obtained.

Topics of importance in the medical history should include a cursory history of the use of various birth controls the patient has taken and the timing of the sexual dysfunction in relation to starting and stopping them and neurological diseases like a spinal cord injury or trauma to the pudendal nerve and its branches. Chronic diseases like diabetes, anemia, hyperlipidemia, coronary artery disease should also be addressed including medications taken for these chronic illnesses. A history of holistic and integrative medications and vitamin supplementation is warranted to better understand the extent to which the severity of the illness has driven the patient to such ailments. Over-the-counter and illicit drug use like cocaine, marijuana, and ecstasy should be addressed in the history.

Since the endocrine system, including the sex steroids, plays a pivotal role in genital function, a complete evaluation of the endocrine function is warranted. We check nine lab values for all women who present to our institute with sexual dysfunction: estradiol [27,32], progesterone, testosterone [28–30] and calculated free testosterone, prolactin, sex hormone–binding globulin (SHBG), thyroid-stimulating hormone (TSH) [31], luteinizing hormone, follicle-stimulating hormone (FSH), and dihydrotestosterone (DHT). Along with the hormone evaluation, the medical history should routinely probe and evaluate for estrogen deficiency [32,33] such as vaginal dryness, vaginal bleeding with minimal vaginal manipulation, hot flashes and night sweats, and other symptoms of menopause. Symptoms of androgen insufficiency (i.e., menopause or a girl taking birth control pills) would include fatigue, lack of energy, diminished skeletal muscle mass and strength, depressed mood, lethargy, insomnia, hypersomnia, and lack of interest in sexual activity [34–36].

It is relevant to inquire about the sexual heath of the patient’s partner. For women in a relationship with men, male sexual dysfunction such as erectile dysfunction, early ejaculation, or an anatomical concern such as Peyronie’s disease may exist and need to be addressed by a urologist.

Finally, an important caveat to history taking in women with sexual health concerns is that history taking may be viewed in some women as actually the beginning of their treatment. Women are often empowered following a detailed discussion about their sexual health concerns. Women who have undergone a detailed medical background interview have initiated the first step in overcoming past failures to take action in this area. It is not uncommon for the discussion with the health-care clinician to expose a breadth of important information that will be vital in the overall treatment plan.

Validated Questionnaires

Validated, reliable, standardized self-rated questionnaires [32–35] are useful to assist in identification of the presence or absence of the various domains of women’s sexual dysfunction, such as sexual desire, sexual arousal, orgasm, and/or sexual pain. The most common of such questionnaire is the female sexual function index [36,37]. This self-reported patient screening tool is used to score symptoms against normative values for populations of women with and without sexual dysfunction. As in all areas of clinical medicine, the use of screening tools for clinical diagnosis has recognized limitations. The determination of particular psychological contributors or confounds, contextual conditions, and other features and characteristics that affect an individual women requires a more traditional assessment through structured history and physical examination.

Physical Examination

The physical examination for a woman with sexual health concerns should be tailored to the sexual medicine complaint obtained on history taking. For example, if during history taking genital itching is a major sexual health problem, a careful assessment would follow for the presence/absence of a genital dermatitis condition [38]. If a woman with sexual health problems is under the age of 50 and has sexual pain, a careful physical examination should evaluate for the presence of hormonally mediated vestibulodynia vs. neuroproliferative vestibulodynia [39,40]. Similar complaints of sexual pain in a woman over 50 years of age should assess for the presence of vaginal atrophy with dryness, loss of rugae, mucosal thinning, pale hue, and lack of shiny vaginal secretions; all are indications of menopausal hormonal status [32,33].

The physical examination should be performed ideally without menses and without intercourse or douching for 24 hours before the exam. If dysfunction occurs at a specific time, such as mid-cycle dyspareunia, the physical examination should be scheduled at the time of the sexual problem. The genital-focused examination should be considered routine in the diagnosis of women's sexual health problems, but its personal character demands that a rational explanation exist for its inclusion in the diagnostic process. A focused peripheral genital examination is recommended in women with sexual dysfunction for complaints of dyspareunia, genitopelvic pain/penetration disorder, genital arousal disorder and combined arousal disorder, orgasmic disorder, pelvic trauma history, and any dermatologic disease affecting genital health such as herpes or lichen sclerosis. The examiner may also assess for anal and vaginal tone, voluntary tightening of anus, and bulbocavernosus reflexes in women with suspected neurological disorders [41].

Patient consent to examination is particularly important. It is vital that the patient is aware of the purpose of the exam and understands that she has the final authority to terminate the physical examination, to ask questions, to have control over who is in attendance, and to understand the extent of the assessment. Inclusion of the sexual partner, with permission of the patient, is advantageous and provides needed patient support. Allowing the patient to observe any pathology via digital photography is often therapeutic, allowing, for the first time in many cases, an illustration and connection of a detected physical abnormality with the sexual health problem. If a genital sexual pain history exists, the patient should point with her finger to the location/s of the discomfort during the physical examination [34].

Independent of the gender of the examining health-care clinician, it is strongly recommended that a female chaperone the health-care clinician during the entirety of the examination. If a chaperone is declined then this should be documented contemporaneously, preferably with witnessing. The patient should wear a sheet to cover her lower torso. The patient should be placed in the lithotomy position and the examining health-care clinician should use vulvoscopy (Figure 64.2) with magnified vision and a focused light source [34]. In addition, warming the room creates a more relaxed environment in which the patient will feel more comfortable.

External Examination

The first part of the examination involves inspection of the vulva and labia majora. Two gloved fingers are placed on either side of the clitoral shaft, and using an upward force in the cephalic direction, the prepuce is retracted to gain full exposure of the glans clitoris, corona, and right and left frenulum emanating at 5:00 and 7:00 from the posterior portion of the glans clitoris (Figure 64.3a and b). The labia minora are inspected for labial resorption and for their ability to meet at the midline posterior fourchette (Figure 64.4a and b). The maximal labial width is recorded to compare pre- and posthormone supplementation. Inspection of the urethral meatus is performed (Figure 64.5a) and any erythema, stenosis, or meatal prolapse (Figure 64.5b) is noted. Using gauze to maximally retract the labia minora, the labial–hymenal junction (Hart's Line) is identified. The Q-tip cotton swab is placed at multiple locations on the vestibule, which is defined as the tissue medial to Hart's line (Figure 64.6). A Q-tip cotton swab test is performed, gently applying pressure on the minor vestibular glands (Figure 64.7a), documenting the quality (0–10 pain scale works well here) of the discomfort or pain or erythema (Figure 64.7b) in a clockwise fashion.

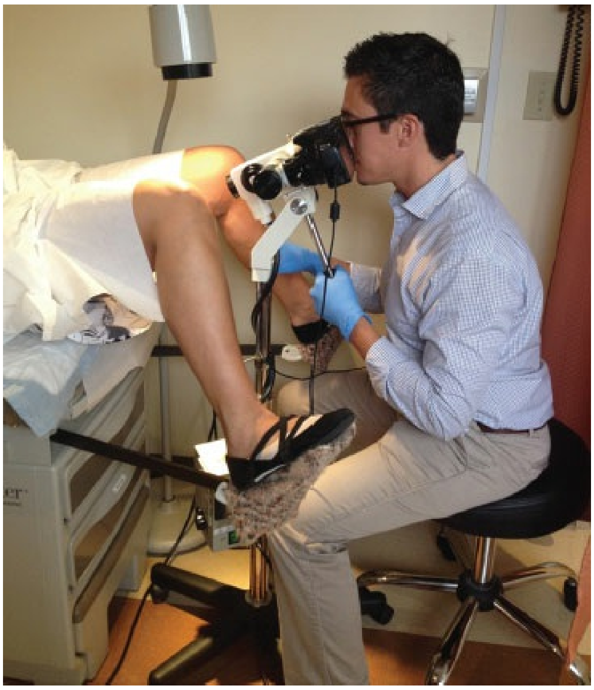

Figure 64.2 Vulvoscopy. The examining health-care clinician should use vulvoscopy with magnified vision and a focused light source. The patient should be placed in the lithotomy position and wear a sheet to cover her lower torso.

Internal Examination

For the speculum examination, a warm, lubricated speculum is used. The periurethral tissue or G-spot region is inspected (Figure 64.8) by lateralizing the arms of the speculum instead of the more common anterior–posterior approach. The vaginal wall is examined for the presence of vaginal rugae (Figure 64.9a and b), inflammation, discharge, color and thickness of the vaginal walls, and any vaginal lesions. Vaginal smear and wet mount is obtained. Vaginal pH is recorded. Single-digit palpation is achieved by gently placing a finger into the vaginal opening and depressing the bulbocavernosus muscle. Two fingers are placed against the lateral walls of the levator and underlying obturator muscles, which are assessed for tenderness. A rectovaginal and bimanual examination can be performed if indicated [34,47].

Neurourological Testing

Neurourological examination consists of sensory and reflex testing [47]. The sensory neurological exam evaluates the integrity of the three branches of the pudendal nerve including the dorsal nerve of the clitoris (sensation from the glans clitoris and clitoral shaft), the perineal nerve (sensation from the perineum and labia), and the inferior rectal nerve (sensation from the perianal skin). Testing is performed by assessing light touch (cotton ball or Q-tip) (Figure 64.10a) and pin prick (sterile needle) (Figure 64.10b). Testing sites include the right and left sides of the clitoral area, labia majora, labia minora, and perianal areas. The motor portion of the pudendal nerve is derived from the pelvic floor muscles. Sacral reflexes include the bulbocavernosus reflex and the anal wink reflex, and both sensory and motor arms of these reflexes are branches of the pudendal nerve. The afferent arm of the bulbocavernosus reflex is the dorsal nerve of the clitoris, and the efferent arm is the perineal nerve. The index and middle fingers are placed along the posterolateral aspect of either the right or left vaginal wall overlying the bulb of the clitoris, surrounded by the bulbocavernosus muscle. A gentle pinch of the glans clitoris with the opposite hand will elicit contraction of the bulbocavernosus muscle (Figure 64.11). The examination is repeated with the examining fingers facing the opposite vaginal wall. The afferent and efferent arms of the anal wink reflex both arise from the inferior rectal nerve. The anal wink reflex is performed using the wooden shaft end of the Q-tip and is assessed by touching the perianal skin, about 1 cm from the anus at the 3 o’clock and the 9 o’clock positions. Visible contraction of the anal sphincter will be noted after touching the skin [47].

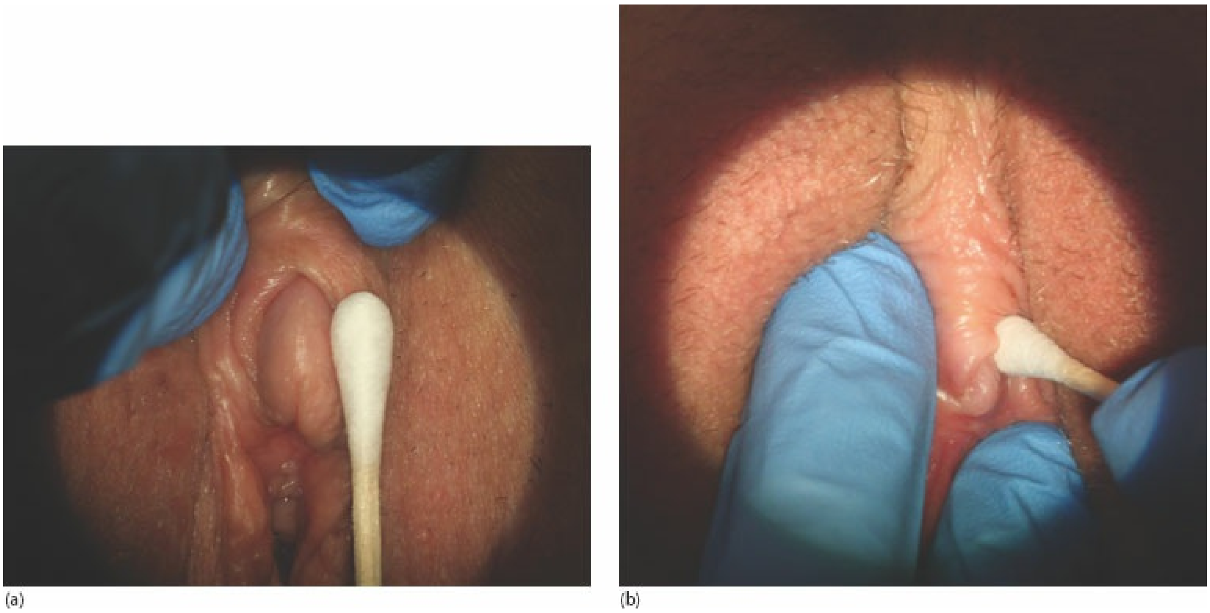
(a) (b)

Figure 64.3 (a) The prepuce is retracted to gain full exposure of the glans clitoris, corona, and right and left frenulum emanating at 5:00 and 7:00 from the posterior portion of the glans clitoris. The normal size is estimated to be about the diameter of a Q-tip. (b) Vulvoscopic view of moderate clitoral phimosis.

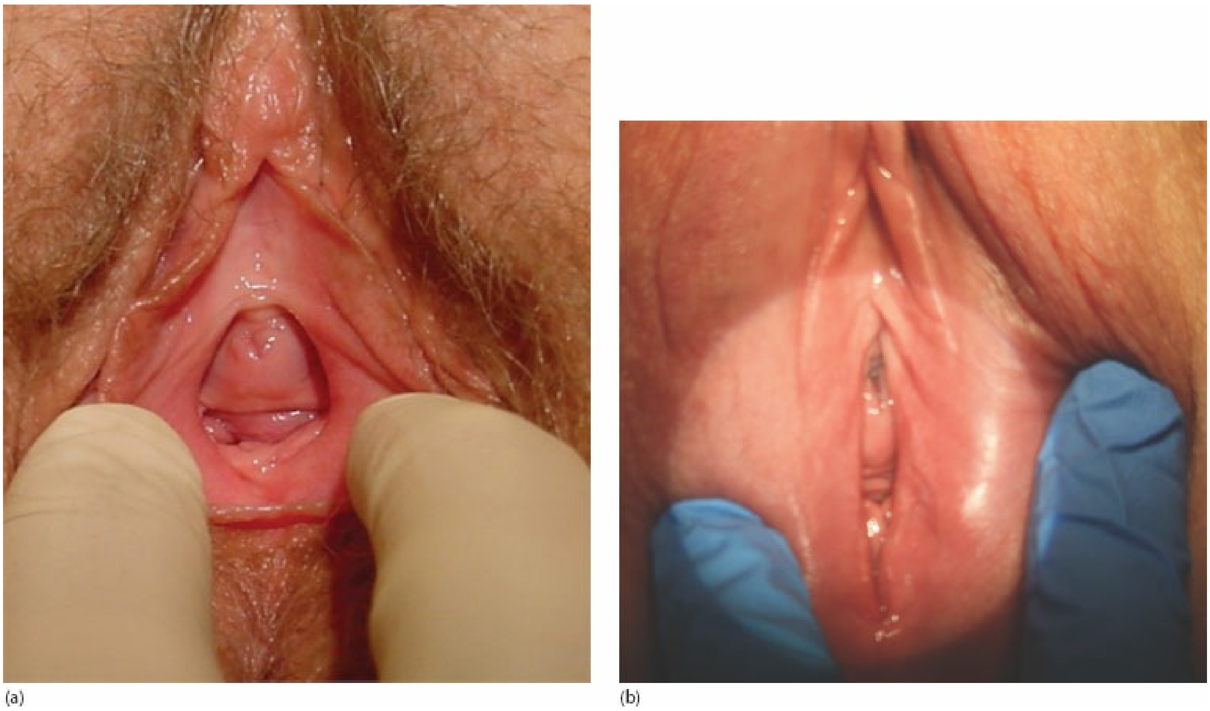
(a) (b)

Figure 64.4 (a) The labia minora are inspected for labial resorption and for their ability to meet in the midline posterior fourchette. (b) Vulvoscopic view of labial resorption.

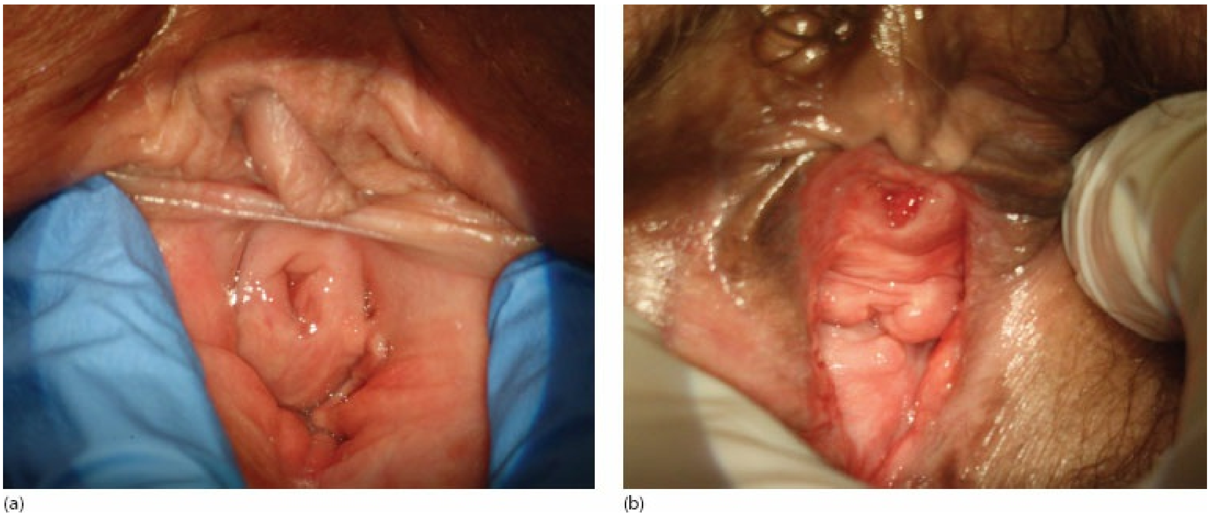
(a) (b)

Figure 64.5 (a) Inspection of the urethral meatus is performed. (b) Mild urethral prolapse in a woman with genitourinary syndrome of menopause.

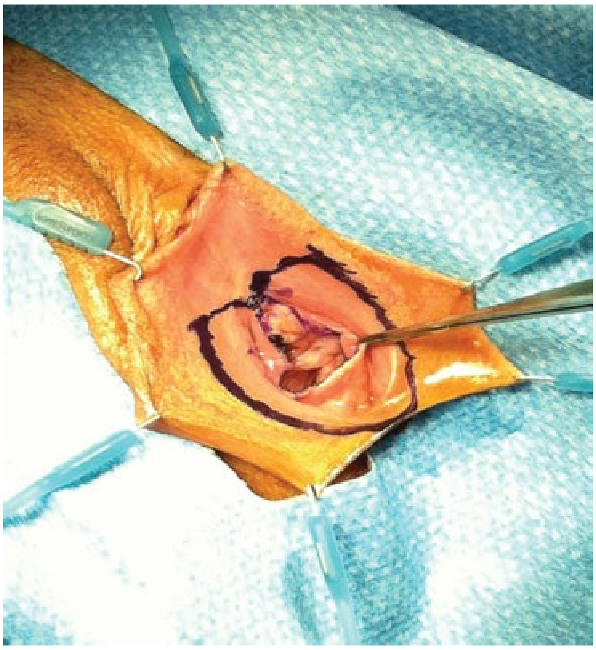

Figure 64.6 Hart’s line (here, outlined in blue ink at the beginning of a vestibulectomy).

Neurophysiological tests are not yet consensed so the history and physical examination remains the best methodology to screen for neurological causes for FSD. Objective sensory nerve testing may be performed with a biothesiometer (Figure 64.12a). This quantitative sensory test measures vibratory perception thresholds (expressed in volts) and values are obtained in a nongenital reference site (pulp index finger) as well as in multiple genital sites such as the glans clitoris (dorsal nerve of the clitoris) and the right and left labia minora (the perineal nerve). Other quantitative sensory testing involves determination of hot and cold perception threshold values in these test sites (Figure 64.12b) [34].

The health-care clinician may also perform a complete physical exam, such as examining for a thyroid goiter, to rule out other comorbid conditions that might be causing sexual dysfunction. A general physical exam is highly recommended in women with chronic illnesses and as part of good medical care, including a detailed breast exam and evaluation of blood pressure and heart rate.

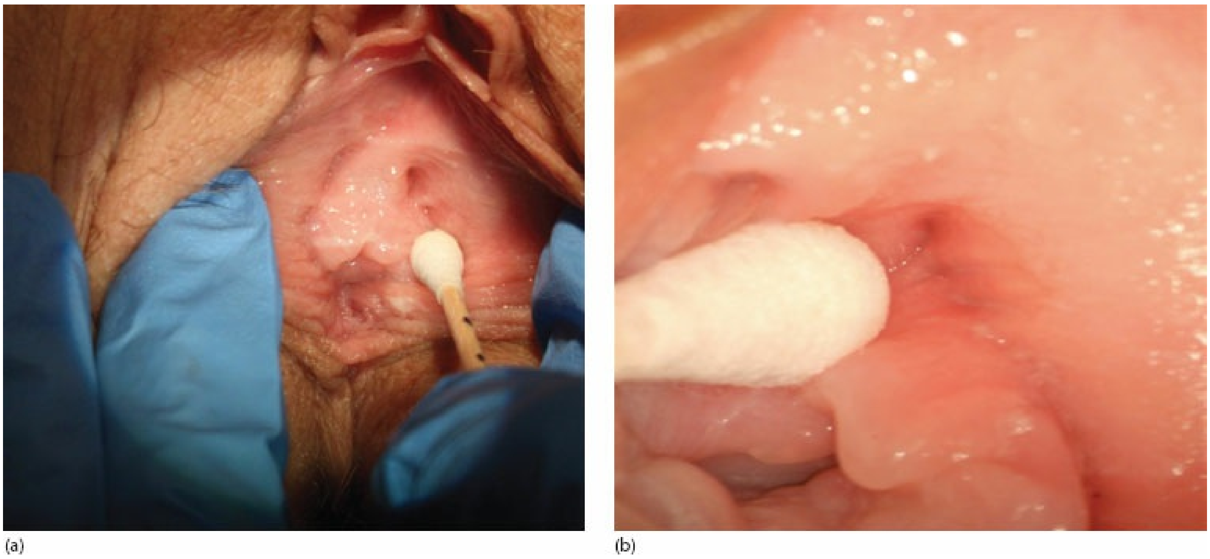

Figure 64.7 (a) A Q-tip cotton swab test is performed, gently applying pressure to the minor vestibular glands. This woman has no pain and no erythema overlying the minor vestibular glands. (b) This woman had pain, discomfort, and erythema overlying minor vestibular glands.

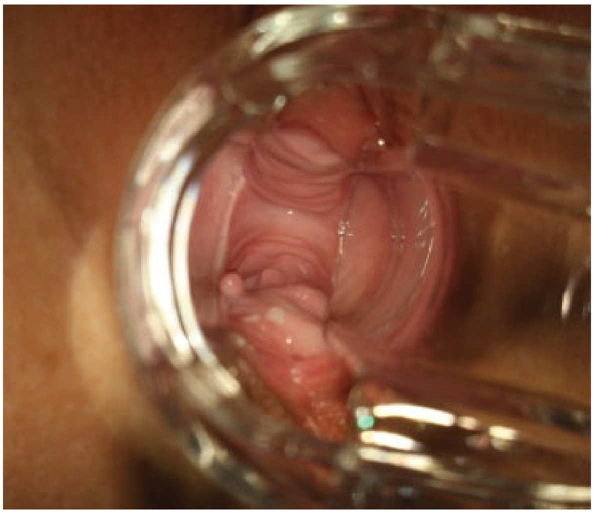

Figure 64.8 With the speculum turned horizontal, the periurethral tissue and G-spot region are inspected.

Laboratory Testing

There is no consensus on recommended routine laboratory tests for the evaluation of women with desire, arousal, and orgasm sexual health concerns. Blood testing should be dictated by clinical suspicion, especially from the results of the history and physical examination. If appropriate, the health-care clinician may assess multiple androgen and estrogen values [34] such as (nine hormone values) total testosterone, free testosterone, SHBG, DHT, estradiol, and progesterone. Pituitary function may be measured by obtaining luteinizing hormone (LH), FSH, and prolactin. TSH should be measured to exclude subclinical thyroid disease [34].

There are multiple concerns with the determination of serum hormone levels, especially testosterone [34–36]. The normal ranges of testosterone concentration values for women of different age groups without sexual dysfunction are not well defined. Testosterone levels reach a peak during the early follicular phase, with small but less significant variation across the rest of the cycle. Testosterone assays are not uniformly sensitive or reliable enough to accurately measure testosterone at the low serum concentrations typically found in women. Free testosterone is clinically more important than total testosterone in sexual function because the vast majority of testosterone is bound to SHBG and only a small amount of total testosterone is biologically available. The measurement of SHBG is relatively simple to perform with good reproducibility. Equilibrium dialysis is a highly sensitive assay for free testosterone; however, this method is not feasible for clinical practice. Measurement of free testosterone by analogue assays is unreliable. Free androgen may also be calculated using the free androgen index, defined as total testosterone (nmol/L) divided by SHBG (nmol/L). Calculated free testosterone may be determined and takes into account total testosterone, SHBG, and albumin. A calculator for the free testosterone is available online at http://www.issam.ch/freetesto.htm.

Androgens, including testosterone, not only are necessary for reproductive function and hormonal balance in women but also represent important precursors for the biosynthesis of estrogens. Historically, androgens were identified predominantly with male sexual function, contributing to a lack of recognition of the effects of androgens in women. We know that androgens have multiple biochemical effects in the body including but not limited to sexual desire, bone density, muscle mass and strength, mood, energy, and psychological well-being. However, sex steroid hormone actions are quite complex and involve critical enzymes and critical hormone receptors that also determine tissue exposure, tissue sensitivity, and tissue responsiveness.

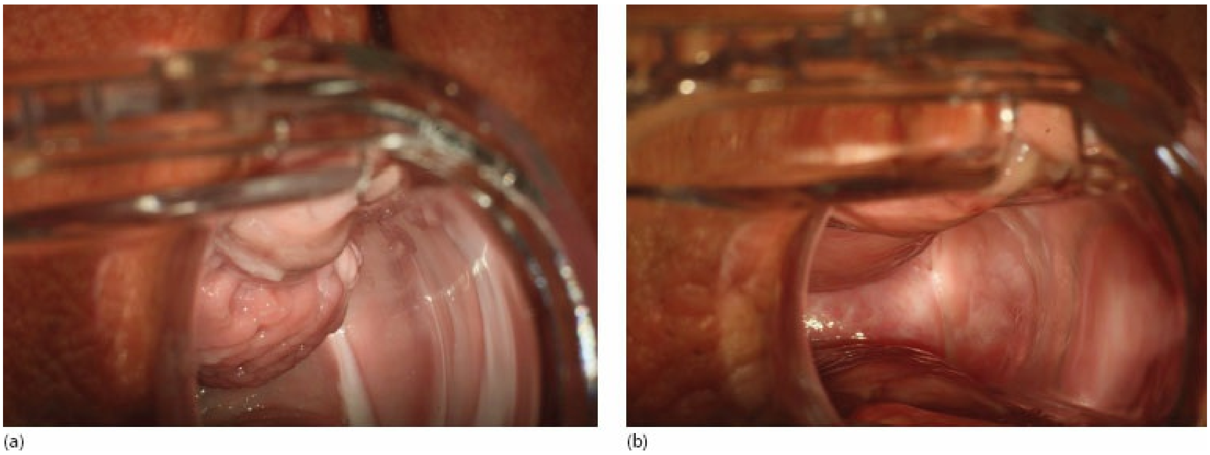
(a)
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Figure 64.9 (a) The vaginal wall is examined for the presence of vaginal rugae. (b) Absent vaginal rugae in a woman with genitourinary syndrome of menopause.

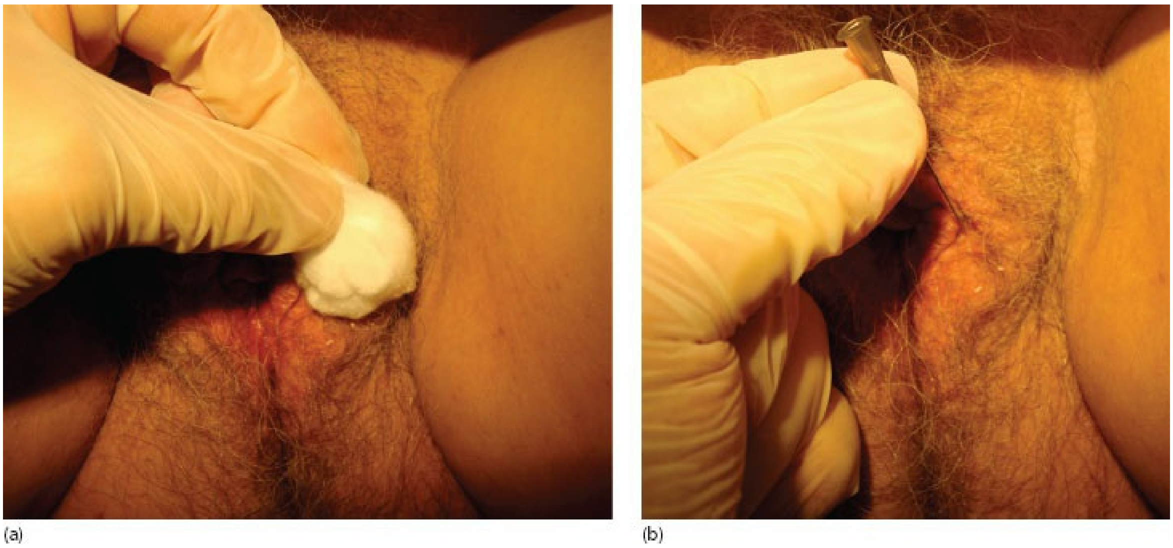
(a)
(b)

Figure 64.10 (a) Neurological testing is performed by assessing light touch (cotton ball or Q-tip). (b) Neurological testing is performed by assessing the pain response to pinprick (sterile needle).

For example, in individuals, there are variations in the amount and activity of critical enzymes such as the 5-alpha-reductase enzyme, which is important in converting free testosterone into DHT. In our office, we have located a small subset of women who do not respond to typical doses of testosterone

(1/10 the dose for men), and we hypothesize that they have a deficiency in the 5-alpha-reductase enzyme [42]. We performed an IRB-approved retrospective chart review of 17 women examined between 2007 and 2013 who presented with persistent sexual side effects despite being treated with testosterone replacement therapy (TRT). Data collected included DHT, testosterone, SHBG, and calculated free testosterone values. The duration of use and duration of persistent side effects were recorded. Data from psychometrically validated questionnaires were assessed for parametric data analysis. Treatment regimens used in this study to achieve a free testosterone of 0.8 ng/dL were testosterone pellets labeled Testopel. The mean age of all 17 women was 57 years old. The mean pretreated testosterone values were 18.55 ng/dL; mean free testosterone values, 0.19 ng/dL; and mean DHT values, 10 ng/mL. After initial treatments with one testosterone pellet, the mean treated testosterone values increased to 141.89 ng/dL, mean free testosterone values to 1.40 ng/dL, and mean DHT values to 13.21 ng/mL. Since these patients continued to have persistent sexual side effects, we increased treatment in the 17 women to two pellets. The mean testosterone values increased to 174.50 ng/dL, mean free testosterone values to 1.61 ng/dL, and mean DHT values to 23.63 ng/mL with subsequent improvement in symptoms. No major adverse side effects were encountered in this study; however, two patients did experience mild acne and hair growth, which were both treated with local skin care. The mechanistic hypotheses to describe this phenomenon include persistent endocrine and epigenetic gene expression alterations of the 5-alpha-reductase enzyme. To improve symptoms in these patients, we have found that increasing the serum free testosterone levels above 0.8 ng/dL slowly drives DHT levels to the upper tertile of the normal range. Patients should be informed of possible persistent side effects of TRT and the need to drive testosterone values higher to see improvements in sexual side effects.

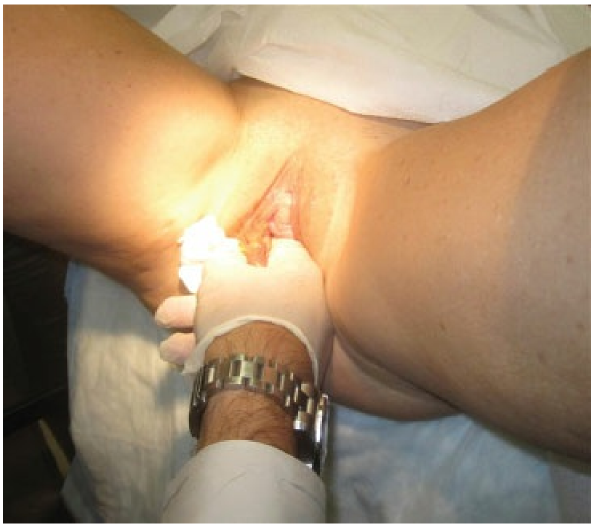

Figure 64.11 The afferent arm of the bulbocavernosus reflex is the dorsal nerve of the clitoris, and the efferent arm is the perineal nerve. The index and middle fingers are placed along the posterolateral aspect of either the right or left vaginal wall overlying the bulb of the clitoris, surrounded by the bulbocavernosus muscle. A gentle pinch of the glans clitoris with the opposite hand will elicit contraction of the bulbocavernosus muscle.

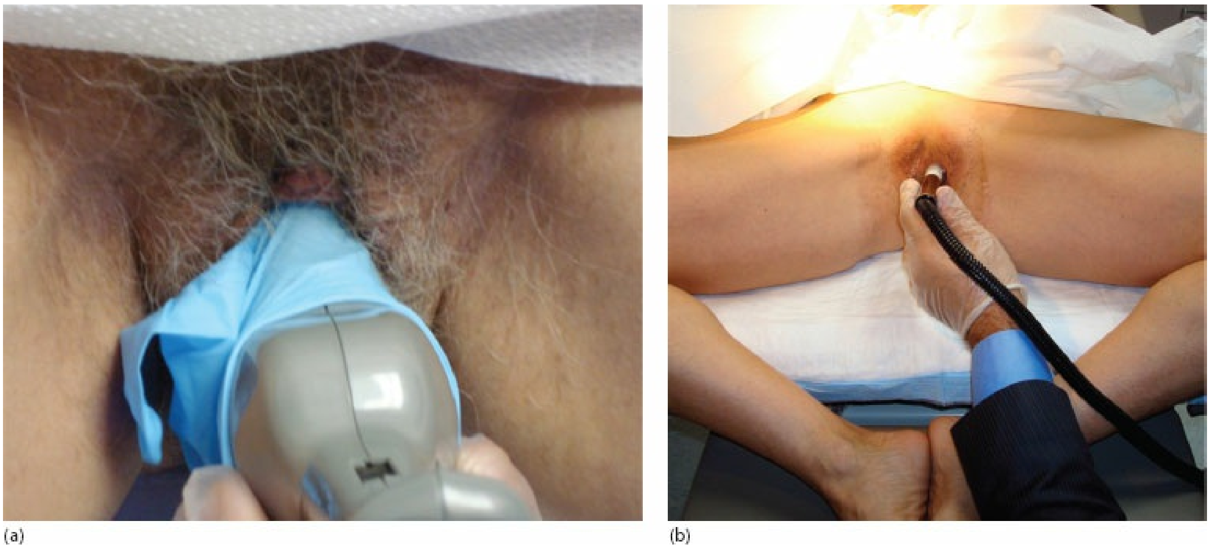

Figure 64.12 (a) A biothesiometer measures vibratory perception thresholds (expressed in volts) on a genital reference site (index finger) as well as in multiple genital sites such as the glans clitoris (dorsal nerve of the clitoris) and the right and left labia minora (the perineal nerve). (b) Quantitative sensory testing involves determination of hot and cold perception threshold values in the same test sites as the biothesiometer.

In addition, individuals have variations in individual sex steroid hormone receptor sequencing. Thus, independent of the values of sex steroid hormones, the unique individual variations in critical enzymes and sex steroid hormone receptors result in individual differences in tissue exposure, tissue sensitivity, and tissue responsiveness. More research is needed in the blood testing of sex steroid hormones in women with sexual health concerns.

Although there is a lack of clinical consensus as to the value, specificity, and sensitivity of individual hormone blood tests, there are evidence-based, placebo-controlled, double-blind data supporting the efficacy of exogenous sex steroid hormone treatment in women with sexual health concerns [34–36,43,44]. It is important to discuss with the patient the strategy of serial blood test surveillance testing to address safety concerns during such treatment.

Typical FSD Patient Assessment and Treatment Algorithms

Phase 1 (Local Tissue Hormone Supplementation)

It is important to emphasize that no single type of hormonal intervention or regimen will be effective in all women with desire, arousal, and orgasm sexual health concerns [34]. The hormonal abnormalities that are identified will determine which of the following biological treatment options women are offered in Phase 1.

Based on the history and physical examination, local estrogen treatment may be achieved with vestibular estradiol alone, intravaginal estradiol alone, or a combination of both. Local estrogen and testosterone, in the form of estradiol 0.03% + testosterone 0.1% in hypoallergenic base, improves vaginal perfusion, lubrication, tissue tone, and elasticity and restores the normal vaginal pH and vaginal health [32,33,45–49]. Vaginal estradiol also relieves dyspareunia, atrophic vaginitis, and vaginismus. Some systemic estradiol absorption occurs with all local vaginal estrogens, and regular estradiol blood testing may be necessary in some women. Daily application of a film of vestibular estrogen is recommended as well, because it promotes the health of the frenulum (the most sensitive part of the external genitalia), labia minora, urethral meatus, hymenal tissue, and vestibular glands [32,33,56–58].

The human vagina consists of three layers of tissue: the epithelium (composed of squamous cells), the lamina propria, and the muscularis (inner circular and outer longitudinal smooth muscle) [32,33]. The epithelium undergoes mild changes during the menstrual cycle. The lamina propria is replete with tiny blood vessels that become engorged with blood during sexual arousal, leading to lubrication. The smooth muscle of the muscularis enables the vagina to dilate and lengthen during penile penetration. Relaxation of that muscle leads to arousal. These three layers of tissue may function in an interrelated way. It is hypothesized that the blood vessels in the lamina propria that allow for lubrication are dependent on growth factors and that the growth factors are derived from the muscularis. Postmenopausal atrophy of vaginal tissues may be due to decreased synthesis of these growth factors resulting in a diminished number of critical blood vessels in the lamina propria [32,33].

Increased vaginal blood flow is an indicator of sexual arousal [50]. Genital swelling and lubrication are responses to increased clitoral and vaginal perfusion; increased length and diameter of the vaginal canal and clitoral corpora cavernosa; engorgement of the vagina wall, clitoris, and labia major and minora; and transudation of lubricating fluid from the vaginal epithelium. In animal studies [59], blood flow to the vagina was greatly reduced in the oophorectomized rats compared with the intact rats. Contrary to what one might expect, subphysiological doses of estradiol increased vaginal blood flow in oophorectomized rats more than either physiological or supraphysiologic doses. Ovariectomy-deprived estradiol values caused the vaginal epithelium to thin down to a single layer. Subphysiologic doses of estradiol increased the thickness of the vaginal epithelium the most because the oophorectomized rats had more estrogen-alpha receptors in the epithelium than the intact animals. A small amount of estradiol delivered to tissue with many estrogen-alpha receptors produced a huge response. Thus, estradiol regulates estrogen receptors through a negative feedback system. The muscularis, the muscle that enables the vagina to lengthen and widen during sexual arousal, also atrophies without estrogen. In postmenopausal women who do not take hormone therapy, the vaginal epithelium, lamina propria blood vessels, and muscularis all decrease. Like the epithelium, the muscularis responds to estradiol by increasing in thickness [59].

Women with sexual dysfunction who are placed on Phase 1 treatment (local estrogen/testosterone to the vestibule and into the vagina) need to undergo surveillance blood tests after 3 months of therapy to monitor the patient’s levels of estradiol, progesterone, DHEA, testosterone, androstenedione, DHT, FSH, LH, prolactin, and TSH as indicated. Women with desire, arousal, and orgasm sexual health concerns whose symptoms of distress are not resolved satisfactorily with Phase 1 treatments may consider progressing to Phase 2 treatments.

Phase 2 (Bioidentical Systemic Hormone Supplementation)

In Phase 2, women receive systemic estrogen and/or systemic testosterone (no FDA-approved testosterone replacement exists for women). Several clinical trials have shown that the distressing symptoms of vaginal atrophy associated with low-estrogen states are ameliorated after systemic estrogen therapy [34,54,56]. Low doses of systemic bioidentical nonsynthetic 17-beta-estradiol reduced vaginal atrophy compared with placebo in healthy menopausal women [34,54,56]. Systemic estrogen therapy can also successfully improve hot flushes, night sweats, and sleep disturbances that negatively affect body image, mood, and sexual desire. All efforts are made to keep serum estradiol levels between 30 and 50 ng/dL. The concept of maintaining estradiol values at low levels is to reduce the side effect risk while achieving a minimum efficacious dose [34]. Risks of systemic estrogen use should be discussed at length with the patient; they include breast cancer, heart attack, and stroke. In women with an intact uterus, systemic estrogen should always be opposed by a progestogen. All efforts are made to use bioidentical nonsynthetic progesterone and keep values in the range of 1 ng/dL [34].

Systemic testosterone (no FDA-approved testosterone replacement exists for women) has gained increased interest and use amongst clinicians treating FSD in their practice. The simple reason is that systemic testosterone supplementation can help alleviate a whole host of symptoms from dyspareunia in hormonally mediated vestibulodynia to low mood, desire, and libido. Systemic testosterone can be administered via transdermal application or intramuscular injection or with a pellet inserted into the adipose tissue of the buttocks. The dose for any systemic testosterone given to women is at one-tenth the dose administered to men. When checking laboratory values, it is important to keep women in a range of free testosterone between 6–8 ng/dL. In addition, we check a DHT value, which we aim to keep in the upper tertile range, since on occasion women with a free testosterone between 6–8 ng/dL may still be symptomatic. In that scenario, we hypothesize that there is a downstream abnormality or deficiency in the 5-alpha-reductase enzyme, and thus, the testosterone value will have to be increased to offset the lower DHT. Finally, if side effects like male pattern balding or facial hair or acne become a problem, low dose 5-alpha-reductase inhibitor (finasteride 1 mg) once to twice a month can be administered.

Systemic androgens (systemic DHEA and/or systemic testosterone) have been shown to improve mood, energy, stimulation, sensation, arousal, and orgasm in women with sexual health concerns.

Limited clinical trials have examined the effects of systemic DHEA therapy on sexual function in women [51–53]. Baulieu and colleagues [56] administered systemic DHEA (50 mg) or placebo to 140 women between the ages of 60 and 79 years for 12 months. Systemic DHEA treatment produced approximately a doubling of serum total testosterone concentration and also significantly increased skin hydration and bone density. Libido was increased after 6 months of treatment; sexual activity and sexual satisfaction were both increased after 12 months [56]. One benefit of administering systemic DHEA and systemic testosterone is that these hormones will endogenously aromatize to estradiol, thus relieving hot flashes and night sweats without the administration of systemic estrogen [34].

Systemic testosterone has been used to treat women with sexual dysfunction since the 1940s [54]. Transdermal patches or gels or subcutaneous pellets are being studied for their safety and efficacy in reducing sexual symptoms associated with testosterone insufficiency [34–36]. Transdermal testosterone patches have been compared with placebo in estrogenized women who had undergone oophorectomy and hysterectomy. One study [55] showed that the 300 μg testosterone patch was significantly more effective than the 150 μg patch or placebo in improving frequency of sexual activity, pleasure, and fantasy during a 12-week period.

Phase 3 (Nonhormonal Medication)

In phase 3, attention is given to the possible role of dopamine agonists (only one FDA-approved nonhormonal medication exist) in facilitating desire and orgasm sexual responses [56–58]. Sexual motivation is encouraged, sustained, and ended by a number of central nervous system neurotransmitter and receptor changes induced, in part, by the action of sex steroids, androgens, estrogens, progestins, and the central neurotransmitter dopamine [60]. The activation of dopamine receptors may be a key intermediary in the stimulation of incentive sexual motivation and sexual reward. These neurotransmitters and receptor changes in turn activate central sexual arousal and desire. Contemporary animal research reveals that dopamine neurotransmitter systems may play a critical intermediary role in the central regulation of sexual arousal and excitation, mood, and incentive-related sexual behavior, in particular, in the motivational responses to conditioned external stimuli. In summary, the complex central neurochemical actions of neurotransmitters stimulate sensory awareness, central sexual arousal, mood, and reward, which relates to relevant individuals' sexual experiences involving a partner, a place, and an action [60].

Bupropion, which is a noradrenaline and dopamine reuptake inhibitor with nicotinic antagonist properties originally marketed as an antidepressant, may have a beneficial effect on women with hypoactive sexual desire disorder [34,57,58]. In a placebo-controlled trial [62], bupropion produced an increase in desire and frequency of sexual activity compared with placebo. Traditional dosing starts at 150 mg twice a day; we have found that low dose of 75 mg twice a day achieves an optimal improvement in sexual dysfunction symptoms. Other dopamine agonists used are cabergoline administered at 0.5 mg up to three times per week, and ropinirole 0.25 mg administered daily [56]. Oxytocin lozenges, linked to improved arousal and desire, are administered at 250IU sublingual 30 minutes to 1 hour before sexual activity. Research with oxytocin has shown marked improvement in a number of components of sexual function, including libido, erection, and orgasm [59]. Amphetamines like Adderall and other drugs used to treat attention deficit disorder have been increasingly useful in helping women to concentrate and thus improving orgasmic response and intensity [60].

Currently, there is one drug that is FDA approved, flibanserin, which is a drug that clinically has been shown to improve hypoactive sexual desire disorder. Specifically, flibanserin works by diminishing serotonin release by serotonin 1A agonism and also inhibits binding to the serotonin 2A receptor involved in inhibitory cortical outflow. It further acts to increase dopamine and noradrenalin [61].

Vasodilators

Basic science studies [62,63] investigating the physiology of sexual function utilizing female animal models support the role of nitric oxide cyclic guanosine monophosphate phosphodiesterase type 5 pathways in the peripheral arousal physiology of the clitoral corpus cavernosum, corpus spongiosum, vaginal epithelium, and vaginal lamina propria.

There have been several clinical studies [64–66] on selective phosphodiesterase inhibitors (PDE5i) over the last few years, conducted with either premenopausal or postmenopausal women with arousal sexual health concerns as well as healthy women without sexual dysfunction. Many studies did not take into account the hormonal milieu of the subjects in the inclusion and exclusion criteria. An important point in treating women with arousal sexual health concerns is that an adequate sex steroid (androgen and estrogen) hormonal milieu is critical for benefits from selective phosphodiesterase inhibitor treatment.

One study, a double-blind, crossover, placebo-controlled safety and efficacy study [70] with selective PDE5i, was performed in premenopausal women with normal ovulatory cycles and normal levels of steroid hormones who were affected by female sexual arousal disorder without hypoactive sexual desire disorder. Subjects were observed to benefit from treatment with the active selective PDE5i, showing improvement in sexual arousal, orgasm, frequency, and enjoyment of sexual intercourse versus placebo. Nurnberg found that sildenafil significantly improved sexual function, especially orgasm in women whose free testosterone values were in the normal range and also in women who developed sexual health problems following use of selective serotonin reuptake inhibitors [71].

Sexual Pain Management

Biological pathophysiologies resulting in women's sexual health problems associated with sexual pain may occur in the clitoris, urethra, bladder, vulva, vestibule, vagina, and pelvic floor muscles.

Clitoris, Prepuce, and Frenula

In women with focused clitoral pain, clitoral itching, or clitoral burning, careful inspection of the glans clitoris should be performed [67]. Failure to visualize the whole glans clitoris with the corona is consistent with some degree (mild, moderate, or severe) of preputial phimosis, based on the elasticity of the prepuce and its ability to retract on examination. Since phimosis may create a closed compartment, phimosis is often the underlying pathology in clitoral glans balanitis associated with recurrent fungal infections. Initial treatment may be conservative with topical estrogen and/or testosterone creams to see if the prepuce can be made more elastic and retractile. Topical antifungal agents such as nystatin or oral antifungal agents such as fluconazole may be considered. Infections can also be related to herpes virus, with appropriate treatment administered such as acyclovir. If conservative treatment fails due to the phimotic prepuce, surgical management by dorsal slit procedure should be considered [72].

Urethral Meatus

Gentle retraction of the labia minora should provide full view of the urethral meatus. Prolapse of the urethral mucosa out of the urethral lumen is highly associated with estrogen deficiency states such as following bilateral oophorectomy, natural menopause, or following chemotherapy for malignancy. Clinical symptoms include urgency, frequency, and discomfort on urination as well as spotting of blood, which may be observed on the toilet paper after wiping following voiding. The abnormal voiding history is often accompanied by a unique sexual history. Women with urethral prolapse often have the ability to have full sexual pleasure and satisfaction during self-stimulation of the clitoris; however, during sexual activity with the partner or with a mechanical device, she experiences pain and/or urgency to urinate and/or inability to have orgasm secondary to distracting pain. Conservative treatment options include topical or systemic estrogens, although the risks and benefits of estrogen treatment need to be fully discussed.

Vulva/Vestibule

Genital sexual pain in the vulva/vestibule may be related to varied specific disorders [40,68,69]. The treatment of any genital sexual pain disorder involves the multidisciplinary team approach, and this is especially true for the disabling condition of vestibulodynia. Patient management includes education and support, especially regarding avoidance of contacts and practice of healthy vulval hygiene, pelvic floor physical therapy treatment, management of concomitant depression, and management of any associated neurological, dermatological, gynecological, orthopedic, or urological conditions.

HORMONALLY MEDIATED VESTIBULODYNIA

Hormonally mediated vestibulodynia symptoms are similar to those of neuroproliferative but seen more commonly in young girls who have been exposed to birth control pills or menopausal women. Symptoms include vaginal dryness, dyspareunia, itching, burning upon palpation of the vestibule. On physical exam, the vulva may appear atrophic and resorbed, the clitoris can be shrunken, and the telltale sign of hormonally mediated vestibulodynia is an inflamed and painful vestibule and periurethral glands. These are provoked with a Q-tip and are graded on a 0–10 pain scale. The hormonally depleted vagina typically has lost the rugae, has a pale complexion, has a lack of lubricating substance, and will bleed with minimal contact. On wet mount, the microscopic examination reveals parabasal cells and increased white blood cells. The vaginal pH is typically elevated to 6.0–7.0 (normal 4–4.5). Conservative treatment begins with local topical and intravaginal estrogens. Important, however, is to address the testosterone receptors within the vestibule as this tissue is derived from the endoderm compared with the estrogen-rich ectoderm of the vulva and the vagina-derived mesoderm. We routinely will have these patients apply a compounded 0.01% testosterone + 0.3% estrogen cream to the vestibule and into the vagina.

NEUROPROLIFERATIVE VESTIBULODYNIA

Neuroproliferative vestibulodynia is a disorder seen more commonly in younger women who has either been living with vestibular pain since they can remember (congenital) or developed symptoms over time, consistent with neuroproliferative vestibulodynia. Typically, these women have failed conservative management first: physical therapy, hormone replacement (if necessary), medical management like tricyclic antidepressants or gabapentin, topical xylocaine/lidocaine, and positive VAT. When the VAT is positive, the patient is offered a complete vestibulectomy (Figure 64.13a and b), which is a surgical procedure in which the entire vestibule and associated glands are surgically excised.

Dermatological Conditions

Lichen Sclerosis

Lichen sclerosis [44] (Figure 64.14) is a chronic genital dermatitis condition that is associated with varying intensity of symptoms including vulval itching and/or burning and various degrees of vulval scarring leading to narrowing of the introitus and with subsequent dyspareunia. The typical presentation of burning and itching symptoms can be so intense as to severely interfere with sexual activity, day-to-day activities, and even sleep. If the scarring of lichen sclerosis involves the perianal area, the patient may also complain of perianal fissuring and painful defecation. The diagnosis of lichen sclerosis is suspected by physical examination showing a white color genital, vulval, and vestibular tissue with paleness, loss of pigmentation, and characteristic “cigarette paper” wrinkling. Classically, the genital tissue changes do not involve the inside of the vagina, and if they involve the perianal area, there is a traditional “figure of eight” extension. The lichen sclerosis condition commonly involves the vestibule with associated labia minora atrophy and the vaginal introitus with loss of elasticity and narrowing [44]. Diagnosis is confirmed with a biopsy of the affected areas. Once a diagnosis is made, treatment with clobetasol 0.05% topical cream is applied to all affected areas daily for 12 weeks and then decreased to 3 times a week. For more severe disease, 10% hydrocortisone acetate is compounded in a vaginal cream, and 3–5 g (300–500 mg) is inserted nightly for 2 weeks and then decreased to Monday, Wednesday, and Friday. There are no safety data on these products and local atrophy may occur. Yeast infections must be suppressed using fluconazole 150 mg weekly. Adrenal axis suppression can occur with prolonged use [70]. Failure to respond may require more specialist gynecological, dermatological, or plastics support.

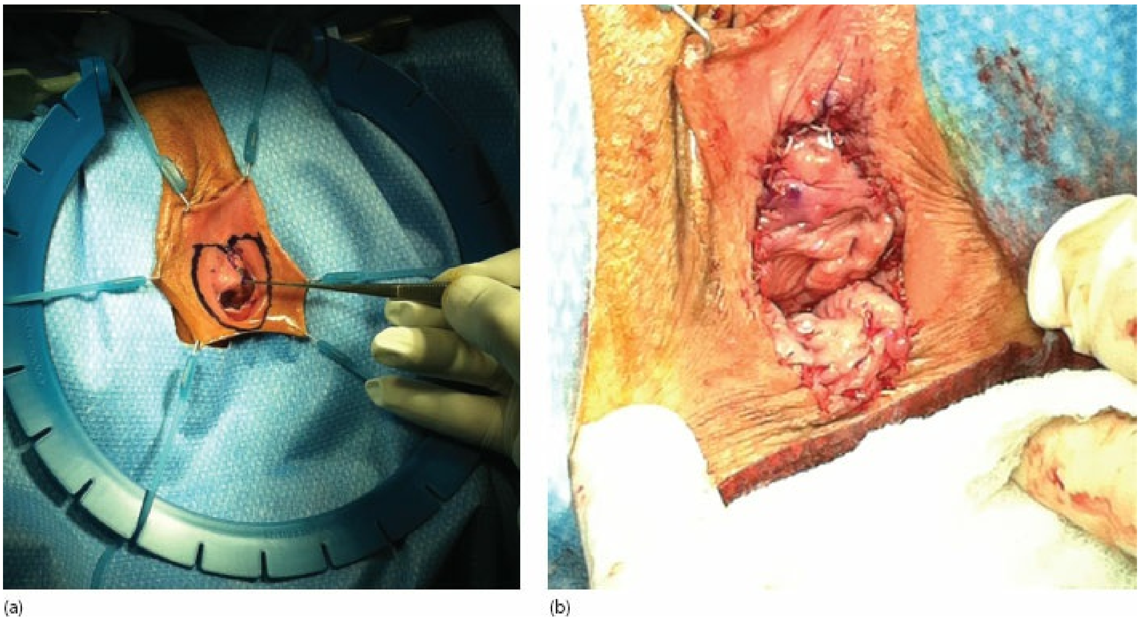

Figure 64.13 (a) Complete vestibulectomy with vaginal advancement flap includes excision of the vestibular mucosa adjacent to the urethral meatus/Skene's glands region anteriorly. (b) Picture from the end of a vestibulectomy. All vestibular mucosal tissue has been removed, laterally and posteriorly, with reconstruction including the posterior vaginal flap advancement.

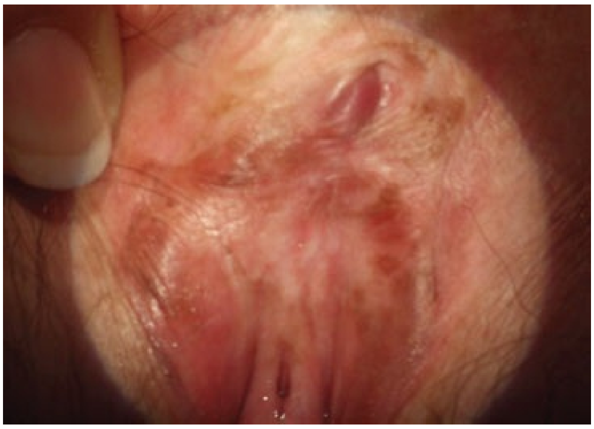

Figure 64.14 Lichen sclerosis is diagnosed by physical examination. The typical presentation is genital, vulval, and vestibular tissue with paleness, loss of pigmentation, and characteristic "cigarette paper" wrinkling. Classically, the genital tissue changes do not involve the inside of the vagina. Lichen sclerosis commonly involves the vestibule with associated labia minora atrophy and the vaginal introitus with loss of elasticity and narrowing.

Lichen Planus

Lichen planus is another chronic genital dermatitis condition, which is likely to have a pathophysiology related to varied altered immunological disorders, and as a result, the presenting symptoms may vary widely. Lichen planus may occur secondary to drugs, such as antihypertensives, diuretics, oral hypoglycemics, and nonsteroidal anti-inflammatory agents. One presentation is primarily associated with itching and does not result in scarring. Another is erosive and destructive. Overall, patient complaints may include severe vulval itching, pain, burning, and irritation similar to lichen sclerosis. Dyspareunia occurs secondary to vaginal introital scarring. Some types of lichen planus, unlike lichen sclerosis, may involve the vaginal mucosa. If there is vaginal involvement, a purulent malodorous discharge may be noted. Findings on physical examination of women with lichen planus vary widely. The pruritic type of lichen planus is associated with a purple color and multiple papules and plaques on the vulva and vestibule. The erosive type is associated with vestibular ulcers, scarring, clitoris and labia minora atrophy, and occasionally destruction of the vagina has been reported [44]. Similar to lichen sclerosus, biopsy proven disease with lichen planus is treated similarly with a topical steroid, clobetasol 0.05%. Daily treatment may be needed for 8–12 weeks to gain adequate control. Education is very important here. The patient needs to know exactly where to apply the ointment and how much. A diagram is very useful and a clinical photograph of the female patient's affected area is even better. For long-term use consider intermittent application, such as treatment on Monday, Wednesday and Friday, or switch to a low potency steroid. If there is concern about recurrent yeast infections prescribe oral fluconazole 150 mg weekly for suppression.

DIV

Women who present because of a qualitative or quantitative alteration in vaginal discharge should be evaluated by clinical examination and appropriate laboratory tests, such as pH and microscopy. Bacterial vaginosis, vulvovaginal candidiasis, and trichomoniasis vaginitis are the most common causes of vaginal discharge in premenopausal women. When these conditions have been excluded, other causes of vaginal discharge must be considered in the differential diagnosis of women with vaginal complaints. Desquamative inflammatory vaginitis (DIV) (Figure 64.15a and b) is a chronic clinical syndrome of unknown etiology. Most investigators believe that it is primarily an inflammatory vaginitis of noninfectious etiology, with secondary bacterial microbiota disruption [71].

DIV is characterized by pain (dyspareunia, vaginal/introital pain, burning) with diffuse exudative vaginitis and epithelial cell exfoliation, resulting in profuse vaginal discharge (usually yellow but may be gray or green). In a large series of 98 patients diagnosed with DIV (mean age 49.6 years), 70%–90% had purulent vaginal discharge, dyspareunia, and vaginal inflammation [72]. Treatment is aimed at alleviating the chronic discharge with various compounded mixtures of antibiotics, steroids, and hormones applied topically to the inside of the vagina as a suppository. Currently, we use a compounded vaginal suppository of 10% hydrocortisone + 2% clindamycin + 0.02% estradiol. Anytime a treatment regimen involves a strong steroid like hydrocortisone or clobetasol, antifungal should be used since resultant yeast infections can be common.

Surgery

Surgical Treatment for Neuroproliferative Vestibulodynia

Surgical intervention for management of women with neuroproliferative vestibulodynia is offered to those who have failed initial conservative medical, psychological, and/or physical therapy focused treatment. Surgery is based on the hypothesis that the pathophysiology of neuroproliferative vestibulodynia is associated with inflamed, irritated, and hypersensitive vestibular glandular tissue and related increased nerve density in the vestibular mucosa. Surgical success is therefore based on excision of this abnormal glandular and nerve tissue in the vestibule. In women with neuroproliferative vestibulodynia, the procedure entitled complete vestibulectomy with vaginal advancement flap includes excision of the vestibular mucosa adjacent to the urethral meatus/Skene's glands region anteriorly, excision of vestibular mucosa laterally, and posteriorly to the hymen with reconstruction including the posterior vaginal flap advancement (Figure 64.13a and b). This procedure is usually performed under general or regional anesthesia.

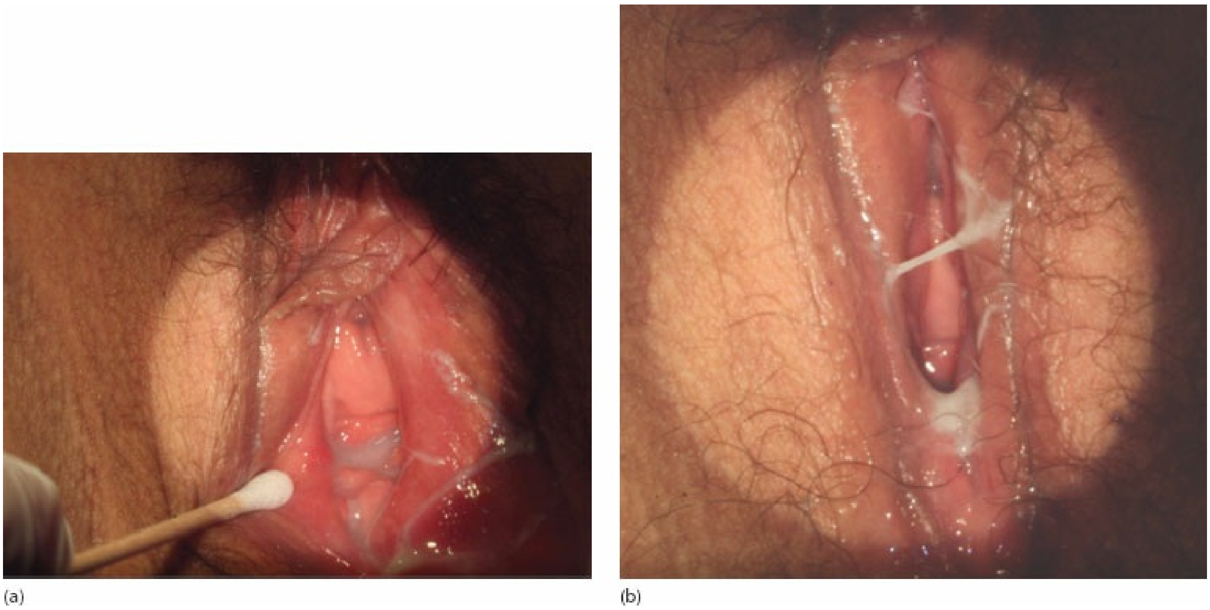

Figure 64.15 (a and b) Desquamative inflammatory vaginitis. Copious yellow discharge, usually described by patients as “dries like glue” and “sticks to underwear.” Under microscopy, we see leukorrhea and parabasal cells.

Complications include bleeding, infection, increased pain, hematoma, wound dehiscence, vaginal stenosis, scar tissue formation, and Bartholin duct cyst formation. During vestibulectomy, the vaginal advancement may cover the ostia of the Bartholin glands; however, the risk of postoperative Bartholin gland cyst formation is only 1%. As always with surgery, the risk of these complications can be reduced with appropriate surgical techniques. Various closure techniques have been described to minimize the risks of postoperative complications. Specifically, the vaginal advancement flap should be anchored by multiple interrupted horizontal mattress sutures of 3-0 Vicryl placed in an anterior–posterior direction. The remaining mucosal flap is then approximated to the perineum with interrupted stitches of 4-0 Vicryl. Intraoperative bupivacaine extended-release liposome is applied conservatively to the dissected tissue to aid in 72 hours of postoperative recovery. Postoperative care includes oral opioid pain medications for the first few weeks, including warm baths nightly. At 6 weeks postoperative follow-up, we will (1) perform vulvoscopy and a vaginal ultrasound to determine for the presence or absence of Batholin’s cysts and (2) perform a Q-tip test to see if any recurrent glands are causing pain. Ultrasound allows visualization of Bartholin cyst formation. We have found that cysts >10 mm, when painful, are easily drained via intraoperative marsupialization.

CONCLUSIONS

In a comprehensive textbook on *female urology and urogynecology*, it is important and appropriate to have a detailed chapter on the biologically focused management of women’s sexual health concerns. In the twenty-first century, in medicine, increasing numbers of health-care clinicians will need to be able to manage women with sexual health concerns since more and more women will expect and demand such management. In addition, those health-care clinicians who want to maximize overall women’s health-care delivery will increasingly engage in the management of women’s sexual health concerns, in addition to the traditional focus on continence and urological conditions. The need to address these issues is such that in future it will be increasingly more difficult for female urologists and urogynecologists to not provide at least first-line sexual health care to women.

The basic premise of biologically focused management of women’s sexual health concerns is that the normal physiological processes regulating sexual activity can be altered by biological pathology. How each specific medical condition modulates women’s sexual health requires increased intensive basic science investigation. From the perspective of biologically focused clinicians, identification of the underlying pathophysiology of the sexual dysfunction is essential. If the biological basis of the sexual health concern can be diagnosed by history and physical examination and laboratory testing, management outcome may be successfully directed to the source pathophysiology. Of the many challenges facing health-care professionals today, the first is to improve the ability to accurately diagnose women with sexual health concerns, and the second is to ensure that women receive the best evidence-based available management options. The biologically focused clinician needs to have access to new developments in evidence-based, state-of-the-art data concerning biologically focused management strategies for women's sexual health concerns. As stated earlier, membership in specialized societies such as the International Society for the Study of Women's Sexual Health (ISSWSH) will help the interested clinician achieve this goal.

ISSWSH

Clinicians who are particularly interested in women's sexual health or want to improve their clinical management skills may wish to become members of the ISSWSH, an international, multidisciplinary, academic, clinical, and scientific organization. The purposes of the ISSWSH are to provide opportunities for communication among scholars, researchers, and practitioners about women's sexual health; to support the highest standards of ethics and professionalism in research, education, and clinical practice relative to women's sexual health; and to provide the public with accurate information about women's sexual health. Interested health-care professionals should visit the organization's website: http://www.isswsh.org.

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65 Multidisciplinary Team

Kaori Futaba, Simon Radley, and Matthew Parsons

MULTIDISCIPLINARY TEAM

Pelvic floor pathology in women encompasses a wide spectrum of functional, anatomical, neurological, hormonal, and neoplastic conditions that may be associated with symptoms of bowel, urinary, and/or sexual dysfunction [1]. The realization that the pelvic floor does not exist in isolation is an important concept that must be explored [2]. Functionally, the pelvis is multicompartmental, and so it is important to ask the right questions to assess patients. A review performed by Davis and Kumar in 2003 found that patients only reported their most severe symptoms and often did not report symptoms of incontinence or sexual dysfunction as they felt it was not worthy of attention. Patients often volunteered limited information due to shame, cultural beliefs, stereotyping, and self-blame [3]. Many symptoms of pelvic floor dysfunction are of a personal and sensitive nature and use of a self-completed questionnaire may be a valuable method of assessment to obtain accurate information on symptoms that are important to the patient [4]. Patients can complete the questionnaires in private and take as long as required.

Questionnaires can be used as a screening tool to carry out a comprehensive assessment of the whole pelvic floor to identify patients who may have more than one compartment symptomatology and who may benefit from a multidisciplinary assessment and treatment. The Birmingham Bowel and Urinary Symptoms Questionnaire (BBUSQ-22) is a 22-item questionnaire encompassing all aspects of pelvic floor function including constipation, evacuation, incontinence, and urinary symptoms in women [1]. The electronic personal assessment questionnaire-pelvic floor (ePAQ-PF) is a one-item-per-page touchscreen questionnaire with interaction allowing detailed questioning and skipping. It comprises four dimensions: 35 urinary, 33 bowel, 22 vaginal, and 28 sexual items. Each domain is scored 0–100. ePAQ-PF also scores how much each symptom bothers them on a four-point scale producing a one A4 page summary providing an overview as well as details of the pelvic floor problems [5]. There are many individual symptomatic severity scores and quality of life assessments available as summarized in Table 65.1. They may be useful for assessment pre- and posttreatment.

There are many benefits in developing a pelvic floor multidisciplinary team (MDT). The Calman–Hine report, published in 1995, proposed an MDT approach for the management of colorectal cancer, which is now well established [21]. MDT working already plays a key role in the management of benign diseases such as inflammatory bowel disease. The pelvis has been anatomically and functionally divided into an anterior compartment (the bladder), a middle compartment (the vagina), and a posterior compartment (the rectum), each compartment cared for in isolation. It has been suggested for over two decades that pelvic floor disorders would be better managed through the collaborative efforts of gynecologists, urologists, colorectal surgeons, psychologists, physiotherapists, neurologists, and radiologists [22].

Patients with complex pelvic floor conditions can be discussed with the members of the MDT, particularly when more than one compartment is affected. The team can share ideas and experiences to reach a consensus on the best treatment options, some of which may involve combined operating. It is estimated that one in nine women will undergo surgery for pelvic floor disorders during their lifetime and that 30% of these patients will require further surgery for the same condition [23]. With pelvic floor disorders, the correlation between structural abnormality and function is not always straightforward [24]. Organ-specific approach in the management of pelvic floor disorders may result in partial treatment of their global pelvic floor dysfunction, leading to high recurrence rate [25]. Harold Drutz, the ex-president of the International Urogynecological Association, at the 21st annual clinical meeting in Vienna in 1996, commented that “we have done women a tremendous disservice by fractionating health care for pelvic floor disorders and that there needs to be increasing dialogue, not monologue, between urologists, urogynecologist, gynecologists and colorectal surgeons” [26].

The interdisciplinary, multiprofessional pelvic floor MDT meeting provides an excellent environment for the team to develop expertise collectively and encourage best evidence-led practice, improving patient care and satisfaction [27]. It provides a valuable way of managing difficult cases as well as streamlining management [24]. Cross-specialty MDT allows decisions to be made about patients without the need for face-to-face consultations in each case. Patients for surgery can be discussed to ensure that the right operation is being offered to the patient, but the MDT meeting can also help in discussing complex patients in whom we may not be able to offer a surgical solution for their symptoms. These patients, knowing that their cases have been discussed with all members of MDT, may accept such a decision more readily. It will also allow standardization of care across different units, building a link between different specialties and simplifying referral pathways. It is important to appreciate that the pelvic floor MDT is not just about meeting once a month but is integral to patient care.

The pelvic floor MDT meeting also allows an opportunity to discuss important topics, which may be suitable for a cross-specialty audit or to carry out clinical trials to improve patient care. Comparison of studies in the literature carried out by different specialties for the same condition in the past has been difficult as there has been lack of uniformity in assessment and scoring, for example, different descriptions and grading of prolapse [28].

Table 65.1 Severity Score and Quality of Life Questionnaires

Severity score	**Quality of life score**
Urinary incontinence (UI) [6]	
Incontinence Severity Index [7]	Incontinence Quality of Life Questionnaire [8]
Stress-related leak, Emptying ability, Anatomy, Protection, Inhibition, Quality of life, Mobility and Mental Status Incontinence Classification System [9]	Bristol Female Urinary Tract Symptoms Questionnaire
Urinary Incontinence Severity Score [10]	Stress and Urge Incontinence and Quality of Life Questionnaire [11]
International Consultation on Incontinence Questionnaire (ICIQ)-UI [12]	ICIQ-UIqol
Vaginal symptoms (VS)	
ICIQ-VS [13]	ICIQ-VSqol
Bowel symptoms (BS)	
ICIQ-BS	ICIQ-BSqol
	Gastrointestinal Quality of Life Index
Constipation	
Constipation Assessment Scale [14]	
Wexner Constipation Scoring System [15]	
Patient Assessment of Constipation-Symptom [16]	Patient Assessment of Constipation-Quality of Life [17]
Modified Obstructive Defecation Syndrome Longo Score	
Fecal incontinence	
Wexner incontinence Grading Scale [18]	Fecal Incontinence Quality of Life Scale [19]
St. Mark’s Incontinence Scores [20]	EQ-5D

In Birmingham, the pelvic floor MDT meeting takes place on a monthly basis with sufficient time set aside to discuss the cases. Online patient records and radiological imaging allow us to discuss patients and their imaging and investigations. An attendance register is kept. Minutes are kept from each meeting, and letters detailing discussion and decisions are written to the patients’ primary care physician and other involved parties. Copies of the correspondence are usually also sent to the patients.

The pelvic floor MDT needs to be inclusive of all the members and should include the following [25,27]:

Urogynecologists: To offer specialist input into the investigation and management of conditions affecting the anterior and middle compartment.

Colorectal surgeons with specialist interest in pelvic floor disorders. To offer specialist input into the investigation and management of conditions affecting the posterior compartment.

Urologists with specialist interest in pelvic floor disorders. To offer specialist input into the investigation and management of conditions affecting the anterior compartment.

Specialist radiologists and radiographers: Expert interpretation of specialized investigations such as transit study, defecating proctogram, and MR proctogram.

Medical gastroenterologists with interest in dysmotility. Gastroenterologists play a key role in the medical management of patients with functional bowel disorders. Most male and nulliparous women present through the medical clinic.

Physiologist: Carries out GI physiology investigations including endorectal ultrasound scans and anorectal physiology. They may also be involved in programming and follow-up of patients with sacral nerve stimulators.

Midwives: Midwives with specialist expertise in managing patients who have sustained previous obstetric sphincter injuries. They play an important role in supporting patients at a challenging time post obstetric injuries but also in counseling patients who has had previous obstetric injury decide how to deliver with subsequent pregnancies.

Specialist nurses: Nurse specialist with interest in managing pelvic floor dysfunction such as urinary or fecal incontinence. Plays a key role in providing patients support, education, and teaching patients how to perform some of the conservative treatments such as self-catheterizations and rectal irrigations. Helps to reinforce the advice given by the rest of the MDT in clinics.

Physiotherapists: Offers postpartum pelvic floor rehabilitation, as well as targeted biofeedback sessions for patients with incontinence.

Dieticians: Offers patients advice on dietary intake, which may have a profound effect on their abdominal and bowel symptoms.

Clinical psychologists: Some patients may have complex psychological issues, who would benefit from combined treatment with psychologists. Behavioral modification techniques are just as important as surgical treatments [26].

Chronic pain specialists: Patients with chronic pain, not managed by simple measures, may benefit from assessment and other alternative treatments by the chronic pain team.

The clinician in charge of the patient’s dominant symptom usually coordinates assessment and treatment. In some units, patients with pelvic floor disorders are managed in a combined pelvic floor clinic allowing patients to be assessed by different specialties in one clinic. A dedicated specialist led pelvic floor clinic offers several advantages including key members of the MDT to be present in one clinic and adequate time available for comprehensive clinical assessment, review, and discussion of results to decide on the best treatment. It also offers a comprehensive training opportunity for trainees. It is essential as a unit to decide on how patients are identified, who would benefit from a review in the combined pelvic floor clinic, and which members of the MDT should attend. The MDT meeting provides the ideal filter for the combined clinic. Decisions can be made as to which women will specifically benefit from a combined clinic appointment. While the benefits of a combined clinic may seem evident, such clinics are necessarily labor intensive and not necessarily cost effective in overall health-care delivery. More than one senior clinician can spend a considerable length of time with an individual patient and this is clearly not achievable for all. However, joint clinic may allow patients to be managed efficiently avoiding multiple trips to different hospitals for investigations and clinic appointments, waiting several weeks in between each episode. A telephone survey performed on 165 patients’ experience with the multidisciplinary pelvic floor clinic in Canada showed that the majority of patients were satisfied and accepting of a multidisciplinary approach to pelvic floor dysfunction [29].

In Birmingham, patients who have sustained obstetric third- or fourth-degree tears are routinely reviewed 12 weeks postpartum in the Obstetric Anal Sphincter Injury Services clinic once a month. Patients are assessed by midwives, urogynecologists, and colorectal surgeons [30] according to their symptoms. Most will not require any interventions other than advice and reassurance regarding subsequent deliveries. Many are happy that we offer an opportunity for cesarean delivery in future pregnancies if they prefer; most choose vaginal birth that is appropriate in the majority of cases. Identifying symptomatic women in the combined clinic allows them early access to investigation and treatments (most of which are nonsurgical) as well as appropriate support and counseling as required. New women are seen by a clinician who completes a standard proforma. This ensures all the appropriate questions are asked to identify symptoms. It also provides a useful audit tool.

Adjacency of clinic rooms means that advice is readily available from the subspecialists present as required. Lower urinary tract symptoms and minor anal (other than incontinence) or vaginal symptoms are particularly common in this group of women [31].

The delivery of a modern pelvic floor service is more demanding and complex than ever. An effective service requires a group of enthusiastic clinicians and allied health-care professionals with an interest in managing patients with pelvic floor disorder to work in tandem. We believe that there is a role for a combined clinic, but the use of the MDT meeting and global symptoms scoring system allows us to identify which patients will derive most benefit from such a clinic. The unit also requires the basic diagnostic infrastructure and provision of a comprehensive range of treatments. Patients can be diagnosed accurately, and treatment options can then be discussed with adequate information on realistic outcomes and possible complications. The spectrum of therapeutic options in pelvic floor conditions has increased enormously in the last decade, offering an exciting challenge for the future [27].

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66 Multidisciplinary Clinic: Urology and Urogynecology

Pallavi Latthe

INTRODUCTION

Functional disorders account for a large amount of the medical activity, including in urology. The decreased quality of life due to lower urinary tract symptoms (LUTSs) requires prompt management with primary assessment preferably in the community. Referral to a specialist is required when simple management has failed and whenever any of the following coexists: hematuria, recurrent urinary infection, prolapse, masses, or neurological conditions [1].

The concept of multidisciplinary specialty clinics has evolved in order to provide comprehensive, coordinated, and the best possible care for patients with complex diseases or where these cover more than one traditional service boundary. These models have repeatedly been shown to improve clinical outcomes in a variety of conditions [2].

A multidisciplinary team (MDT) is the key to accurately assess patients with regard to their bother and handicap, therefore offering the most appropriate conservative, medical or surgical management [3]. An MDT discussion provides a forum wherein specialists can engage in patient selection, match the patient to the appropriate therapy, and consider patients for enrolment in clinical trials. When there is controversy or no clear evidence-based guidance, productive MDTs will reach consensus and can often revisit challenging cases for the continuum of care [4]. In our experience, the establishment of an MDT has been the first step in establishing joint services and this underpins the subsequent outpatient and surgical services.

The core training in obstetrics and gynecology has undergone tremendous change over the last decade. More and more information must be assimilated in a shorter time. The need for competent pelvic surgeons remains clearly important but the integrated structure to achieve this goal remains elusive.

The female urinary tract consists of the kidneys, ureters, bladder, and urethra. The former two organs are exclusively within the remit of the urologist, but there is an overlap between the female urologist and urogynecologist in the management of disorders of the bladder and urethra. Most urologists do not deal with pelvic organ prolapse and concomitant gynecological conditions if any, and this has traditionally been the remit of gynecologist and more latterly of urogynecologist (particularly in the United Kingdom with the advent of special interest and subspecialty training). With this, there has been a greater recognition of what situation is appropriate and more importantly what is not appropriate to be undertaken in isolation.

Recognizing the strengths, limitations of services, and skills required provides the second step to why joint or synchronized clinics may be important and why a joint clinic service delivery model may be the ideal setting to ensure that patients with complex LUTSs receive seamless care and a better patient experience with input from urogynecologists and urologists. This service incorporates specialist urology input along with urogynecology, physiotherapy, and nursing involvement. In a perfect setting, a pain physician and psychologist would also attend periodically for input into selected cases.

The aims of specialized clinic in neurourology, functional urology, and urogynecology are to further investigate the underlying disorder responsible for the urinary symptoms and prevent urinary tract complications. Patients benefit from the joint expertise. In our setting of university teaching hospital, patients who have been seen by the urogynecologists locally or in the surrounding hospitals in the region are seen in these joint clinics. They can have upper or lower urinary tract conditions resistant to the usual treatment regimen offered.

The multidisciplinary joint urology clinic provides

- Diagnostic evaluation and/or treatment
- Coordinated, comprehensive care

- Follow-up and monitoring
- Information, education, and reassurance
- Access to specialty medical care as required

The services offered depend not only on the individual training and expertise of the doctor but also on the resources, availability of equipment, and referral pathways. The urologists perform urinary diversions, urethroplasty, treatment of stones, sacral neuromodulation, and fistula repairs besides managing other LUTSs. In addition, they manage the rapid access hematuria pathways for patients, which incorporate one-stop flexible cystoscopy clinics. The urogynecologist offers concomitant prolapse and incontinence surgery, conservative therapies, as well as simultaneous treatment of any coexistent gynecological problems. This ensures that patient is managed holistically and has a better range of treatment options made available to them.

A joint urology–urogynecology service was set up at the author's hospital to enhance the scope of services provided through a collaborative approach to treatment. It has the following aims:

1. To deliver an excellent experience that exceeds patients' expectations
2. To develop an exceptional organization where people achieve their potential
3. To work with our partners to maintain and develop our service, academic, and research standing
4. To offer an efficient tailored service whereby a patient whose problems overlap both specialties can be seen by both specialists simultaneously allowing a comprehensive management plan
5. To provide a better service for PAG and pediatric urology patients in transition to adult services

The objectives are to offer innovative diagnostic and therapeutic strategies specific to each individual patient's problems and to facilitate the gathering of multiple opinions from various clinical specialists.

Team members include urogynecologist, adult ± adolescent urologist (who attends as required periodically), specialist urology and urogynecology nurses, physiotherapist, and trainees/fellows from urology, urogynecology, and allied professions. The team can access input from other subspecialties (pediatric–adolescent gynecologist) as and when required.

To audit the efficiency of the service, the following outcome data are collected:

- The provision of a multidisciplinary individualized management plan to be shared with the family doctor
- Patient experience/satisfaction through undertaking patient questionnaires—friends and family test [5]
- Objective measures like patient global impression of improvement and disease-specific quality of life questionnaire, e.g., electronic personal assessment questionnaire (ePAQ) pelvic floor [6,7]
- Reduced patient journey—comparison between the length of time and resources spent before (seeing two different specialists in their respective clinics, investigations, and then treatment) and what is now being achieved by consultation in a joint setting

The joint operating sessions generally have patients who benefit from the dual expertise. Some examples include urethral diverticulectomy, vaginal fistula repairs, urethroplasty, pubovaginal sling, neuromodulation, removal or excision of the eroded sling/mesh into the bladder/urethra, and elective abdominal delivery for patients with history of complex reconstructive urological surgeries. There are cases of feminizing genitoplasty, gonadectomy, etc., that are done in conjunction with the pediatric urologist. One might also encounter stigmata or complications from surgeries done in infancy (e.g., girl with CAH who presented with pain after having had clitoral reduction and pull-through vaginoplasty in infancy—see Figure 66.1).

Since its inception, a joint clinic is conducted every 2 months preceded by a MDT meeting where the patients and their management plans are discussed. The data collected prospectively suggest that the joint clinic works well for a reduction in the use of resources (clinic times, waiting times, duplication of investigations, and treatment).

A further review of patient satisfaction was undertaken using the friends and family test [5]; it was apparent that the patients were quite satisfied with the setup and the service provided. When the patients were asked how likely would they recommend this clinic to a friend or family member if they needed similar care or treatment, 10/11 commented that it was extremely likely and 1/11 said it was likely on the 5-point Likert scale ranging from extremely likely to extremely unlikely; 9/11 also thought that everything was done quite well when asked what went well. There were no adverse comments.

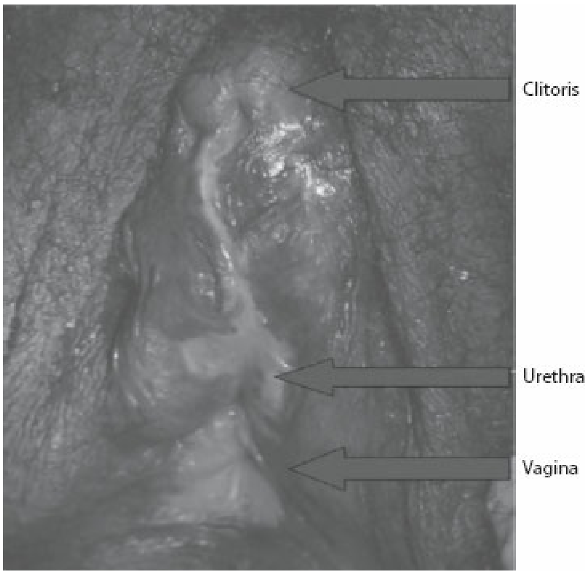

Figure 66.1 Scarring from infant genitoplasty. (Reproduced from Breech LL, Complications of vaginoplasty and clitoroplasty, in Teich S and Caniano DA, eds., *Reoperative Pediatric Surgery*, Totowa, NJ: Humana Press, 2008, pp. 499–514. With permission.)

The standard of care for all patients with urinary problems in the joint clinic is evidence based, guidelines driven, and provided by board-certified or accredited specialists. At the core of the exceptional patient and family experience is a respectful partnership based on enabling them to participate in their plan of care.

JOINT UROLOGY CLINIC FOR SPINA BIFIDA AND EXSTROPHY OF WOMEN

In the care of complex congenital conditions, urological management need to be cohesive to ensure they are effective. All youth must transition from pediatric to adult-centered medical care. This process is especially difficult for youth with special health-care needs. Many young women do not receive the age-appropriate medical care they need and are at risk during this vulnerable time [9]. Young people with chronic illness are significantly more likely than healthy peers to develop emotional difficulties requiring psychological support. The challenge for health services, however, is that the psychological difficulties that young people present with are intimately related to their physical condition rather than being traditional anxiety or depression. Young people worry about their most intimate body parts and about how these parts both look and function.

Table 66.1 Issues Faced by the Young Person and Their Family When Moving from a Family-Based Care Structure to Independent Management

The young person	Transition coincides with other major life changes.
	Greater opportunity to participate in risk-taking behavior.
	Neurodevelopment incomplete; may be perhaps limited by underlying condition.
	May have poor health literacy leading to difficulty implementing treatment information.
	Not likely to prioritize care for medical condition.
	May not be ready to assume responsibility for good urological care.
	Can access many sources of potentially conflicting information.
	Often geographically distant from clinician and medical team.
The family	Parents may no longer had a direct relationship with the clinician.
	Limited recognition of legal status within the doctor–patient relationship.
	Dance of independence with young person.

	Conflict between caregiving and promoting young person's autonomy.
	Advocating for young person versus impeding confidentiality.

For many, these worries only surface as the reality of a future becomes tangible. From mid- to late adolescence, the reality of leaving home and developing independent lives can impact overall adjustment and well-being.

The focus of transitional care is often on the move from one service to another, but it must be underpinned by acknowledging the changing developmental needs of adolescents and young adults. In the transition phase where responsibility for care, interventions, and decisions will shift from parents to the patient, the importance of maintaining attendance and compliance needs emphasis. A young adult will be experiencing many changes: a shift to university or working life, new relationships, and increased personal/fiscal responsibility. It is easy to imagine when someone who is asymptomatic would chose to put a visit to a urologist, gynecologist, or nephrologist far down on their list of priorities (Table 66.1).

We also see patients referred from the pediatric services including the disorders of sexual development (DSD) clinics. The pediatric urologist, endocrinologist, and psychologist provide input into this clinic on a regular basis. The author is a urogynecologist as well as a pediatric adolescent gynecologist who attends the DSD clinics regularly. It provides continuity of care to then review these girls in the joint urology clinics or joint endocrinology clinics as appropriate.

Bladder Care

Bladder reconstruction in childhood creates a lifelong contract between the patient and his/her medical team. Long-term management involves surveillance of functional, symptomatic, and metabolic/renal status [10]. Patients must be under the care of an MDT capable of providing appropriate advice and support in all areas. It is common for issues such as catheterization and bladder emptying to engender resistance in an adolescent patient.

Psychological Care

Female sexual function in DSD like congenital adrenal hyperplasia also generates controversy when surgery is discussed. Outcome data for surgery are lacking. Some significant publications have attempted informing a debate about early surgery, evaluating outcomes, and questioning necessity in infancy and potential benefits (or disadvantages) of early surgery [11,12]. This ultimately relates to potential balance of parental versus patient consent in elective procedures. It is important that decisions surrounding surgery in all these patients regardless of their age are made as part of an MDT to ensure all options and implications have been considered [13].

Adolescent Gynecology

By adolescence and early adulthood, it is important to ensure a conduit for menstrual flow, an introitus and vagina for sexual intercourse, and normal sensation to allow sexual pleasure. It is essential to discuss contraception if sexually active [14,15]. In conditions such as exstrophy, prolapse may be a concern and difficult to treat.

Emptying the bladder with catheterization and emptying the bowels with an enema or suppository will increase the likelihood of “accident-free” sex. After sexual intercourse, the woman should again empty her bladder to decrease the risk of a urinary tract infection. For women who do not catheterize, they could urinate before and after sex. If they still have significant urinary leakage during sex or frequent urinary tract infections, urinary retention should be considered.

Since sexual arousal may not always induce vaginal lubrication, a lubricant may be needed. Other women may have difficulty with intercourse due to physical restrictions from problems with the bones, joints, and/or muscles that affect movement of the hips and legs.

Obstetric Care

Combined clinics also allow a smooth integration into other services, and many young women with spina bifida (SB) and/or hydrocephalus are able to become pregnant.

Changes in the pelvic nerves and muscles mean that pregnancy for women with SB is more challenging than in the general population and should be managed by a team skilled in neurological and urological screening to ensure the pregnancy is not adversely affecting a shunt or their kidneys. The type of delivery depends on multiple physical factors, including sensation level, ability to push with pelvic muscles, size of the pelvis, and flexibility around the hips and knees. The more conducive these factors are to the birthing process, the more likely a vaginal delivery can be achieved.

If it appears that the baby will not be safely delivered via the birth canal, a cesarean section will be recommended. In this case, the urinary tract should be evaluated for reimplantations, diversions, or conduits to make sure they are avoided during the delivery incision. It is best to deliver in an environment experienced in high-risk pregnancies, with urologist available; integration allows these to be planned appropriately and the patients to be familiar with all aspects of their care and the care providers.

Women with bladder exstrophy have a median gestation at delivery of 37 weeks, with 26% at <37 weeks, and generally have cesarean performed with general surgeons or urologist present. In the series reported by Dean et al. [16], 12% of women experienced major birth-related complications such as ureteric transection, fistula, and postpartum hemorrhage. Joint urology clinics provide a good setting to plan these complex deliveries.

CONCLUSION

Fully integrated services with combined MDT reviews have underpinned the development of combined clinics. This has led to an increased collaboration between services and an increase in both patient and health-care professional satisfaction in care provided. In addition, we have noticed a significant improvement in the transitional care of patients leaving children’s services and integrated the care for aspects that have not traditionally been part of pediatric services such as future reproductive health.

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67 Multidisciplinary Clinics: Specific Considerations for Elderly Care

Claire Sutton and Philip Toozs-Hobson

INTRODUCTION

Life expectancy has increased over the last 50 years by a decade from 71 to 81 [1]. With this, there are increasing demands placed on health services by the challenges where elderly patients may represent a different set of physiological responses that may require a different approach to management. This trend in life expectancy is likely to continue and the impact of concurrent conditions, and their treatments will increasingly need to be considered as they affect or modify the symptoms or treatments of incontinence. Many patients may age without problem and therefore can be treated in the same way as younger patients, others may develop a number of age-related conditions that impact on each other, and it is this later group that will benefit from a multidisciplinary approach.

In essence, these changes can present patients and their carers with one or both of two challenges: First, continence is a key issue facing older people and as such is often referred to as one of the geriatric giants [2]. Problems with urinary incontinence increase with age and are particularly common in the hospitalized and institutionalized elderly, affecting up to two-thirds of elderly inpatients and those in nursing homes [3,4]. Second, health-care professionals dealing specifically with incontinence are going to need to have a better understanding of the problems specific to aging that represent important cofactors in continence.

Currently, despite the increased prevalence and awareness, many older patients accept incontinence as part of normal aging and as such the complaint is underreported. Unfortunately, it is well recognized that incontinence in older people has far-reaching consequences including social isolation, depression, falls, and pressure sores [5–7]. It is also a common “tipping point” for an individual to move into a care home setting. Carer strain caused by trying to manage relentless incontinence should also not be underestimated [8].

A main drive of caring for the elderly has to be to increase efforts to raise general standards of continence care. This chapter will set out our approach to the multidisciplinary clinic for women with particularly complex multiple problems. It will also outline some of the physiological changes associated with aging. Finally, it will propose a functional approach to the assessment of the potential confounding factors associated with age and basic strategy to dealing with them.

Aims of the Joint Clinic

1. To offer assessment and management advice to patients with incontinence affected by complex comorbidities in a manner acceptable to general practitioners (GP)
2. To offer continence assessment and management to patients with complex medical conditions who have refractory incontinence
3. To have a reductionist approach to polypharmacy
4. To work in partnership with patients, relatives, and health-care professionals providing day-to-day care [9,10] in setting management plans
5. To feed into other health-care resources as appropriate to improve overall treatment/management for patients

Philosophy

The service is commissioned as a multidisciplinary service with additional funding per consultation offset by the reduction in cost from different constituent service appointments. By definition, all women are tertiary referrals as the only route into the clinic is through the care of the elderly service or urogynecology service.

Appointments are deliberately longer and patients are encouraged to attend with relatives or main health-care providers. Consultations take place with both consultants in elderly care and urogynecology, with the support of specialist nurses. All modalities of both services are available to all patients (albeit modified) so that no patient is excluded from any part of the service based on age or disability alone.

Effects of Aging on the Bladder

Through life, the muscle (detrusor) suffers repeated small insults that continually cause damage and replacement of the muscle fibers with collagen. As a result, the bladder becomes stiffer than it was as collagen is less distensible than detrusor, and second, it contracts with less force as there is less muscle. In addition, there are changes to the nerve supply that are discussed in more detail in the following.

Effects of Aging on the Bladder

The combination of these two events, described earlier in small repeated insults over time during events such as pregnancy and childbirth or as a result of infections or distension, results in delayed sensation from the nerve changes and reduced capacity from the increased stiffness. Over time, cumulative small injuries such during pregnancy, infection or distension, cause nerve damage resulting in delayed sensation and reduced capacity increase the possibility of urgency and urgency incontinence occurring. A further effect of the replacement of the muscle fibers with collagen is reduced efficiency of contraction leading to incomplete emptying and a reduction in the functional bladder capacity as a consequence from the failure to empty to completion.

These effects are mirrored in the urethra, where a replacement of muscle with collagen makes the urethra less compliant. This change is seen as a reduction of the maximal urethral closure pressure (potentially increasing risk of “failure” of the sphincter) and second a reduction in distensibility during voiding reducing the urinary flow rate.

Retention

Management of the condition as early as possible and prior to crisis if achievable is important to ensure the best clinical outcome for the woman. Management includes treating allied conditions known to be associated with voiding dysfunction such as constipation and treating conditions that may contribute to complications such as atrophic vaginitis.

Acute retention itself, however, requires catheterization and attempts to improve voiding with cholinergics have proven disappointing.

Specific Effects of Urinary Retention: Physiology and Effects of Distension

The bladder is designed as a compliant organ with small pressure changes for a large change in volume. The bladder spends 99% of its time in a storage function and 1% in voiding. Normal storage pressures run between 0 and 10 mmHg with voiding pressures of up to 25 mmHg and pressures above 10 mmHg are enough to suppress bladder wall perfusion. If this occurs for extended periods of time, the bladder will undergo ischemic changes to the wall.

Such a situation may occur when the bladder is over distended and if it is stretched past the normal elastic limit (plastic distension). The bladder does not immediately recover to contract and empty. If managed immediately and carefully, this effect is almost always reversible.

Effects of Distension Injuries

Short-term injuries may be reversible or result in damage, depending on whether the bladder tissue stretches past the elastic limit into plastic deformity. This in turn causes the bladder to empty inefficiently. Once overdistension raises intravesical pressure beyond 7–10 mmHg, there is a reduction of the oxygen supply [11], resulting in ischemic tissue damage. One consequence of this is an alteration in the nerve supply to the bladder, making the muscle more sensitive to the neurotransmitters [12] in the nerve endings and also a change in the nerve type.

Animal models have demonstrated two effects of ischemia. First is that the bladder loses its ability to empty (although this will usually recover with time) [13–15]. Second, there is also evidence that reperfusion may add a second layer of injury onto the bladder [16], and as a result of this oxidative stress, the ability of the bladder to produce nerve growth factor is reduced after repeated insults [17].

The changes in the bladder's nerve supply leads to an increase in the so-called "nonadrenergic noncholinergic" fibers, otherwise known as the adrenergic fibers [18].

A second insult can occur with reperfusion leading to oxidative stress. This results in the production of nerve growth factor. Repeated insults do reduce this recovery response, and it is probably repeated distensions that create a chronic problem rather than isolated incidents.

The resultant changes mean, with time, that the bladder becomes less compliant with filling (reduced capacity) and also has reduced contractility (poorer emptying).

The result of these episodes is a replacement of the injured detrusor muscle fibers with collagen. Collagen is a structural protein that, depending on the degree of cross-linking having flexible characteristics, is not a muscle fiber and does not demonstrate the same ability to distend in a compliant manner as detrusor fibers or more importantly to contract. The net effect of this is the bladder starts to lose the elasticity required for compliant distension. Second, the loss of muscle leads to a net reduction in contractile force so the ability to empty may reduce.

The second effect is a gradual change in the autonomic nerve supply from the traditional adrenergic and cholinergic fibers of the sympathetic and parasympathetic nervous system to nonadrenergic noncholinergic fibers that use a purinergic transmitter more commonly thought of as secondary messengers such as ATP.

Impact of Voiding Dysfunction

Many women will have suboptimal voiding, but this remains subclinical until symptoms reach the tipping point. The implications for women are threefold. First, symptoms of frequency, urgency, poor stream, double voiding, and nocturia develop related to reduced flow, poor contractility, and delayed/reduced sensation. Second, difficulty with conventional treatment for urgency may occur as the reduction in cholinergic fibers may reduce the effectiveness of anticholinergics, while increasing side effects. This can manifest with elevated postvoid residuals as demonstrated in studies. As such, the introduction of mirabegron, a beta-3 agonist, gives a medication that has different side effect profile and potentially less impact on voiding function.

Finally, problems may develop with sequelae of the poor emptying, such as urinary tract infections (exacerbated by atrophic vaginitis), which can be complicated by upper urinary tract infections and a subsequent effect on renal function.

Precipitating Factors

Situations affecting voiding include concomitant conditions such as constipation and urinary tract infections as well as comorbidities such as diabetes. Various medications can also impact on bladder function such as antihypertensives including rapid-acting diuretics leading to rapid fill and calcium channel antagonists affecting the sensory thresholds. There are also a host of medications with anticholinergic side effects.

Urinary Tract Infection

Urinary tract infections may precipitate retention/voiding difficulties or be sequelae of it. It is important to examine for this and also to send a sample for culture and sensitivity. The importance of microbiology becomes more relevant in chronic conditions and gives evidence as to whether infections are recurrent (as in frequently occurring) or whether they are resistant to clearance, as a result of altered virulence, e.g., as part of a biofilm on a catheter or stone, or by becoming intracellular.

Voiding problems may occur with prolapse and occasionally presents directly as bladder symptoms such as urgency or voiding difficulties but more commonly subclinically, due to the more direct symptoms of a lump/bulge in the vagina. All patients presenting with prolapse should be asked about voiding function prior to surgery. If there is any doubt, then the minimum of a postmicturition residual should be performed, or in more complex cases, urodynamics may be indicated. If poor voiding is identified, then the option of a suprapubic catheter may be considered at the time of surgery being performed for other conditions that may affect mobility.

It is, however, important to recognize that older people are a heterogeneous group, many aging with minimal comorbidities and retaining a good level of independence. Others do not age so successfully and develop multiple conditions, requiring many pharmacological interventions, and are less independent. This latter, frailer group poses a significant challenge, and it is vital to take a holistic approach to their continence assessment and management [19]. It is also important to recognize the common coexistence of the key geriatric conditions, such as incontinence, immobility, falls, and cognitive impairment, as managing one will undoubtedly require recognition and optimization of the others.

EFFECT OF COMORBIDITIES

Aging is commonly associated with the development of multiple comorbidities, many of which may impact on the occurrence and management of incontinence in conjunction with the aging urinary tract. Cardiovascular conditions such as heart failure can lead to fluid overloaded states contributing to nocturnal polyuria and incontinence.

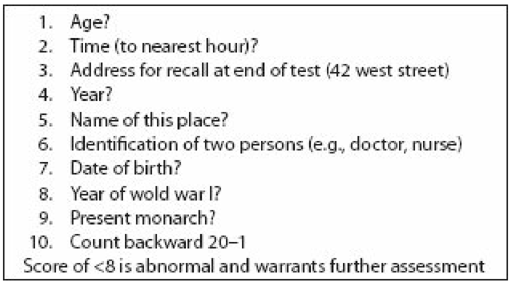
Optimization of the underlying heart failure may, therefore, ameliorate the symptoms. Treatment options for symptomatic relief of excess fluid may paradoxically involve the use of loop diuretics, e.g., furosemide or bumetanide (fast-acting loop diuretics), or slower-acting thiazides that act by inhibiting sodium reabsorption by the distal loop. ACE inhibitors and angiotensin receptor blockers are common first-line therapies with evidence to increase survival. Alcohol is a commonly consumed “social” diuretic that inhibits vasopressin. Diabetes can impact via a variety of mechanisms such as polyuria due to hyperglycemia or functional difficulties such as immobility and ability to self-toilet due to peripheral neuropathy and/or visual impairment from diabetic retinopathy or cataracts. There are a plethora of therapeutic options available to manage diabetes from diet alone to complex regimens including insulin and oral hypoglycemic agents. More recent advances include the use of “gliptins,” e.g., sitagliptin. These drugs block the enzyme that breaks down incretins. Incretins help boost insulin production. Side effects can include nasopharyngitis and so induce a cough worsening stress urinary incontinence (SUI). In the setting of the joint clinic, it would be prudent to assess the control of diabetes by checking a long-acting biomarker such as HbA1c. Elevated levels suggest that management of hyperglycemia is suboptimal, and appropriate diabetes services may need to assess the patient.

Neurological conditions such as stroke, Parkinson’s disease, and spinal cord pathologies can affect continence and are more common in older people, as described in Chapter 51. Incontinence and overactive bladder (OAB) post stroke is common and a poor prognostic marker; further guidance can be found in the Royal College of Physicians (RCP) stroke guidelines. Cognitive issues are common in older people with neurological conditions, and this should be borne in mind when choosing to treat OAB pharmacologically as discussed further in the following text. Musculoskeletal conditions, such as osteoarthritis and rheumatoid arthritis, and previous hip fracture can also impact on functional status and hence continence and are worthy of informal if not formal assessment as a part of the functional review.

Constipation is a common problem in frail older people, especially the hospitalized and institutionalized. This may impact on maintenance of continence by precipitating urinary retention and is often associated with fecal incontinence due to overflow leakage. Continence assessment in older people should, therefore, always include an enquiry into bowel habit, the exclusion of constipation, and usually a digital rectal examination. Enquiry into diet and fluid intake will of course be relevant to constipation and should be considered with bowel care in mind. Encouraging the individual to respond to “the call to stool” and drinking sufficiently may be enough to alleviate mild symptoms. In those with firm stool, a softener should be used such as docusate sodium. Reduced bowel motility usually responds to stimulant laxatives such as Senna or bisacodyl. Impaction is usually ameliorated by way of a strong osmotic laxative such as Laxido. Once the acute constipation is relieved, a bulking agent such as Fybogel should be introduced. Lactulose should generally be avoided and reserved for patients with liver disease. Detection of constipation may be improved with the use of screening questionnaires.

Dementia

This requires particular consideration as it is also often under recognized and/or accepted as part of aging. A continence assessment in an older individual should always include a cognitive screen. A simple question such as the following is a useful start: “have you or your family had any concerns about your memory in the last 12 months?” [20]. If the answer is “yes,” consider completing an abbreviated mental test score (Figure 67.1) [21] and asking the GP to refer to a local memory service for assessment. If the patient is already diagnosed with dementia or dementia is suspected, exploration as to how that impacts on continence is necessary. Cognitive impairment may lead to an unreliable history, reduced fluid intake, or rarely excessive fluid intake. The individual may not consistently remember to take their medication or may become disorientated as to where the toilet is situated, particularly in a novel environment. It may be that the impact is often on the carer rather than the patient; an example is when the patient forgets that he or she has been to the toilet, so having a coping strategy to manage the repeated requests to visit the toilet or conversely putting in a plan for regular toileting to avoid incontinence may be important. Similarly, anticholinergic medication may have an impact on cognitive function [22], and the OAB medication should be chosen with caution. Oxybutynin, in line with National institute of Clinical Excellence (NICE) guidance [23], should be avoided in frail elderly patients including those with cognitive impairment. Agents such as trospium chloride (which is less absorbed across the blood–brain barrier), tolterodine/fesoterodine (bladder specific), or solifenacin/darifenacin (which are more M3 rather than M1 specific) tend to be well tolerated with respect to cognition. Betmiga (being an adrenergic drug avoids muscarinic effects) has evidence supporting a lack of cognitive side effects and is an alternative in patients who either fail first-line therapy or in whom an anticholinergic is contraindicated. Management plans in such cases will inevitably involve support from carers/family and as such they will usually need to be involved in the assessment. Optimizing a continence-friendly environment is also important in patients with dementia. Signage of toilet facilities and contrasting toilet seats can be effective [24].



1. Age?
2. Time (to nearest hour)?
3. Address for recall at end of test (42 west street)
4. Year?
5. Name of this place?
6. Identification of two persons (e.g., doctor, nurse)
7. Date of birth?
8. Year of wold war I?
9. Present monarch?
10. Count backward 20–1

Score of <8 is abnormal and warrants further assessment

Figure 67.1 Abbreviated mental test score.

POLYPHARMACY

Many older people take multiple medications to treat their many diseases. These may both impact on continence and also need to be considered if continence-specific pharmaceuticals are to be initiated. See Table 67.1.

Table 67.1 Medication and Effect on Continence

Class of drug	Effects on incontinence
Alpha adrenergic agonists, e.g., midodrine, clonidine	Increased smooth muscle tone in urethra urinary retention.
Alpha adrenergic antagonists, e.g., doxazosin	Reduce smooth muscle tone in urethra leading to stress incontinence in women.
Angiotensin-converting enzyme inhibitors, e.g., perindopril, ramipril	Side effects include cough that can exacerbate stress incontinence.
Anticholinergics, e.g., oxybutynin	Retention, incomplete bladder emptying, constipation, cognitive impairment all impact on incontinence.
Calcium channel blockers, e.g., amlodipine, diltiazem, verapamil	Retention, incomplete emptying, constipation contributing to urinary incontinence. Side effects include ankle edema that can lead to nocturnal polyuria.
Cholinesterase inhibitors, e.g., neostigmine, rivastigmine	Increase bladder contractility that may lead to urge incontinence.
Diuretics, e.g., bendroflumethiazide, furosemide	Increased diuresis may precipitate incontinence.

Lithium	Lithium therapy may lead to diabetes insipidus and polyuria. It is also associated with urgency.
Opioid analgesics	Commonly lead to constipation, confusion, and urinary retention that can lead to incontinence.
Psychotropic drugs, e.g., haloperidol	Can lead to sedation, confusion, and impaired mobility impacting on continence.
Selective serotonin reuptake inhibitors, e.g., citalopram, fluoxetine	Increase cholinergic effect hence may lead to incontinence.
Gabapentin, glitazones, NSAIDs	Can cause edema leading to nocturnal polyuria.

Source: DuBeau CE et al., Incontinence in the frail elderly, in *Fourth International Consultation on Incontinence*, 4th ed., July 5–8 2008, Paris, France, 2009.

Aging itself also has an impact on pharmacology. Older people tend to experience more side effects and to suffer more drug interactions. The effects are often underestimated or not recognized as the frail elderly are seldom the focus of pharmaceutical studies due to the number of confounding factors such as comorbidities, and therefore, robust evidence is not always available in this population. It is well recognized, for example, that older patients are more sensitive to anticholinergic side effects (dry mouth, blurred vision, constipation, confusion); it is quite possible that some of this is also a dose effect as relatively higher doses may be required due to the change in nerve supply to the bladder discussed earlier, making the lower dose more refractory. Side effects in general tend to be more common and more severe than in younger, fitter patients, and the mantra of start low and go slow is important to adhere to. The clinician must bear this in mind when treating older patients [25,26].

Pharmacokinetics

Absorption of medication: With aging, GI motility, blood flow, and gastric secretions reduce. Additionally, PPI and antacids are commonly prescribed in the elderly and as a consequence the stomach pH increases [27].

Aging can be associated with a decrease in the functional reserve if multiple organs. As a consequence, they also often take medication for multiple conditions. First-pass metabolism has decreased, and so drugs that are normally rapidly cleared may persist as a result of both the decreased liver mass (with its decreased perfusion) and the increased metabolic activity of multiple medications [28]. Hepatic clearance as a result may decrease by up to 30% and CYP metabolism may also reduce (more so for phase 1 reactions than phase 2). The bioavailability of drugs also may increase. Lipophilic drugs may increase the volume of distribution, with an increased half-life, while water-soluble drugs may do the reverse. As a result, conversely, some lipophilic drugs such as propranolol may have increased first-pass clearance [29].

Finally, with renal function decreasing by up to 50% with age, the excretion of drugs or their metabolites may be reduced. Concurrent hypertension and cardiac disease may place further strain on the renal function.

FUNCTIONAL ASSESSMENT

A comprehensive geriatric assessment of a frail older person presenting with incontinence should always include a history of mobility and ability to get to and use the toilet. Enquiry as to how difficult it is to mobilize and situation of toileting facilities within the domestic situation can be very revealing. An occupational therapist may be required to optimize the ability to use the toilet or may provide an alternative solution or assistive equipment. A physiotherapist may be able to improve mobility allowing the patient to get to the toilet more quickly and safely. Social services may also need to become involved; if it is possible, additional care may be necessary.

CONCLUSION

The increase in life expectancy over the last 50 years has changed how we need to approach medicine. Changes in physiology, comorbidity, and polypharmacy all impact on the delivery of high-quality continence care and need to be considered in the management strategies for elderly patients.

In our experience, the development of joint services has led to better and more appropriate utilization of the services available and increased patient satisfaction.

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Section VII

Surgery for Urinary Incontinence

68 How and Why Incontinence Surgery Works

Mauricio Plata, Nicolas Fernandez, David James Osborn, and Roger R. Dmochowski

INTRODUCTION

Stress urinary incontinence (SUI), as defined by the International Continence Society (ICS), is the involuntary leakage of urine on effort or exertion or on sneezing or coughing [1].

Surgical procedures are considered the most durable treatment for the majority of women with moderate and severe SUI. The history of SUI surgery has seen a broad variety of surgical procedures described based upon the theories regarding the causation of incontinence in vogue during each period of time. Although several risk factors for SUI have been identified such as aging, obesity, pregnancy, and delivery, the pathophysiology of SUI remains poorly understood.

This chapter will review the history of urinary incontinence theories and its relation to the development of surgery through the anatomic landmarks and the proposed mechanisms underneath the procedures performed for SUI.

MECHANISM OF CONTINENCE

The primary principle of any surgical procedure for SUI is to provide urinary continence without disrupting micturition and with an acceptable rate of complications.

Current and past surgical procedures have failed in achieving universal success in urinary continence outcomes. Approximately 30% of the surgical procedures done for SUI are done on patients with recurrent SUI [2]. These failure rates vary depending on the way continence is measured or defined; however, the failure rates are reflective, in part, of the shortcomings in understanding of the pathophysiology of SUI [3].

The physiology of continence depends on central and peripheral mechanisms. There are multiple central input centers such as the cerebral cortex, midbrain, and spinal cord. There are also peripheral control mechanisms that involve not only neuromuscular elements but also myofascial support structures. The coordination of these mechanisms contributes to overall continence status.

Urinary continence during stress maneuvers is maintained by several mechanisms. It is the result of a combination of passive anatomical coaptation and active muscle tone. It depends on the intrinsic properties of the urethra and sphincter, as well as the anatomic support of surrounding tissues. The urethra is normally composed of three layers: the mucosa, spongy vascular submucosa, and the outer muscle layer. The mucosal layer plays an important role due to its coaptation effect upon the urethral lumen. Mucosal secretions increase surface tension, which makes coaptation even more effective. The spongy vascular submucosal layer contributes a compressive effect by vascular perfusion and vasodilatation. Estrogen stimulation loss associated with menopause reduces secretions and vascularization and may contribute to SUI. The outer muscle layer is a very complex mechanism. It is composed of the internal smooth muscle sphincter, which anatomically is not a real sphincter because component fibers are not completely circular. This layer has also longitudinal fibers that emanate from the ureters and trigone and end at the proximal third of the urethra. The external sphincter is composed of striated circular muscle with its thickest part at the middle third of the urethra. The striated sphincter has two different types of fibers: the slow twitch fibers, which create a continuous contraction and keep the urethral lumen closed, and the fast twitch fibers, which contract voluntarily with increases in abdominal pressure.

The anatomic support of the urethra, bladder, and other pelvic organs is provided by the muscles and fascial layers of the pelvic floor. The pelvic diaphragm is composed of the levator ani muscles and coccygeus muscles. The levator ani consists of three muscle layers with a natural hiatus where the vagina and urethra exit the true pelvis. The fascial layers are composed of connective tissue. The endopelvic fascia and arcus tendineus play a critical role in continence and pelvic floor support (Figures 68.1 and 68.2).

Passive transmission of abdominal pressure to the proximal urethra compresses the anterior urethral wall against the posterior urethral wall. Also, the guarding reflex, which results from increasing contraction of the striated muscle of the external urethral sphincter in response to increases in abdominal pressure during Valsalva maneuvers, contributes to continence [4]. Another mechanism that is also additive to continence during stress is the active compression of the urethra against the pubic bone during bladder filling and straining as a consequence of the active tone of the pelvic muscles and their associated ligaments. The role of the urethral smooth muscular sphincter in promoting continence was first described by McGuire in the early 1990s [5]. During videourodynamic studies, urethral mucosal coaptation, either at rest or in the presence of minimal physical stress, was observed to play a key role in the maintenance of continence.

THEORIES OF INCONTINENCE AND ITS RELATION WITH SURGICAL PROCEDURES

Knowledge regarding the pathophysiology of incontinence and its treatment has been in continuous evolution. Since the beginning of the twentieth century, multiple authors have described new concepts in order to better understand this condition.

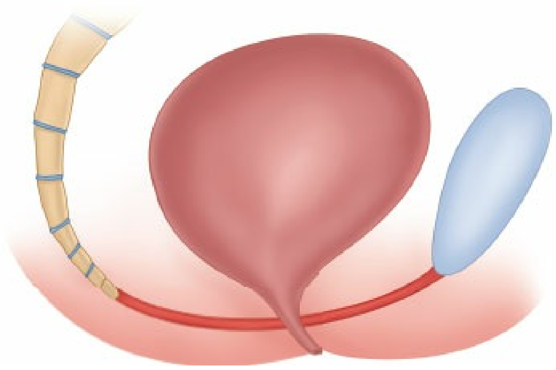

Figure 68.1 Teoria A.

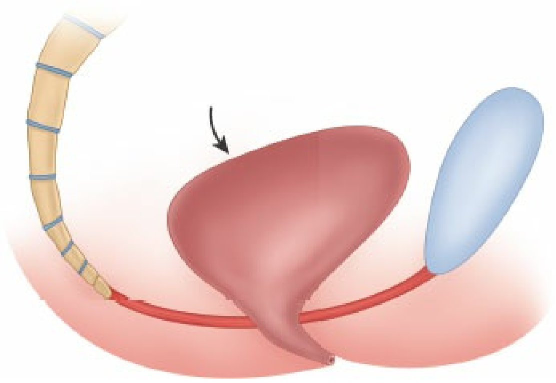

Figure 68.2 Teoria B.

Anatomic Theories

Howard Kelly, a gynecologist at Johns Hopkins, was one of the first authors to describe urethral lumen dysfunction, observed during cystoscopy, as the cause for SUI [6]. Given these findings, he proposed a procedure to narrow the bladder neck in order to improve incontinence—now known as the Kelly plication. He proposed that the incontinence depends not only on the urethra but also on bladder neck compression and that an imbrication of the bladder neck and urethra would reestablish continence.

Bonney, in the early 1920s, described the loss of paraurethral support as a contributing cause of incontinence that resulted from a sudden and abnormal displacement of the urethra and urethrovesical junction immediately inferior to the pubic symphysis [7]. The author described a procedure with the underlying rationale of restoring the urethrovesical junction to a more supported and elevated position above the urogenital diaphragm and providing a restored backboard against which the urethra could be compressed during increases in abdominal pressure. The effectiveness of this depended on the quality of the juxta-urethral supportive structures.

Kennedy demonstrated the contributing importance of the levator ani muscle fibers posterior to the symphysis pubis as supportive elements (15). These results led Aldridge, in 1946, to describe the association between pelvic floor injury after childbirth and urinary incontinence [8]. Damage to either the pelvic floor musculature (levator ani) or pubourethral ligaments was posited to result in descent of the proximal urethra such that the intra-abdominal position of this structure was lost with resultant abdominal pressure transmission directly to the urinary outlet, resulting in urinary incontinence. Repositioning of the urethrovesical junction and proximal urethra into an abdominal position with the aim of equilibrating the transmission of abdominal pressure to the bladder and the urethra became the cornerstone concept for all retropubic procedures such as the Marshall–Marchetti–Krantz (MMK), Burch colposuspension, and later modifications described by Tanagho.

Pressure Transmission Theories

Einhorning proposed, in 1961, that urinary incontinence arose from deficiency of paraurethral support and unequal transmission of abdominal pressures to the urethra and the bladder. He proposed that unequal pressure transmission to the urethra and bladder was a significant contributor to SUI [9]. This theory was supported by subsequent observations by Stevens and Smith [10]. Bump focused on the contribution of urethral pressure to urinary continence and identified that pressure transmission ratios of less than 90% to the proximal urethra had a high sensitivity and positive predictive value for SUI [11].

Urethral Mobility and Sphincteric Theories

Green demonstrated that incontinence was produced when there was a loss of the posterior urethrovesical angle. He divided incontinence into two types according to the angle configuration [12]. Green's theories were further supported using images obtained from chain cystograms.

In some patients who have failed prior incontinence surgery, poor urethral closure function is a frequently associated finding. Some authors have noted that during urethral pressure profilometry, the maximum urethral closure pressure is low and values of <20 cmH_2O are more associated with failure after retropubic procedures [13]. This finding has been termed intrinsic sphincter deficiency (ISD).

ISD is associated with an inability to maintain mucosal coaptation either at rest or in the presence of physical stress. The leak point pressure (LPP) concept was introduced as a simple measure of the degree (or lack thereof) of urethral coaptation. McGuire et al. [5] demonstrated that 76% of those patients with ISD on videourodynamic fluoroscopic visualization had depressed LPPs (<60 cmH_2O). The abdominal LPP (ALPP) has subsequently evolved into one of the primary measures of urethral functional contribution to SUI. The ALPP is defined as the lowest bladder pressure at which leakage occurs during a Valsalva maneuver; however, standardization of measurement has not been universal. Therefore, comparability of this measure across studies is problematic. It has been estimated that up to one-half of patients presenting with incontinence on coughing, sneezing, and other exertional activities actually have a diagnosis of ISD [14].

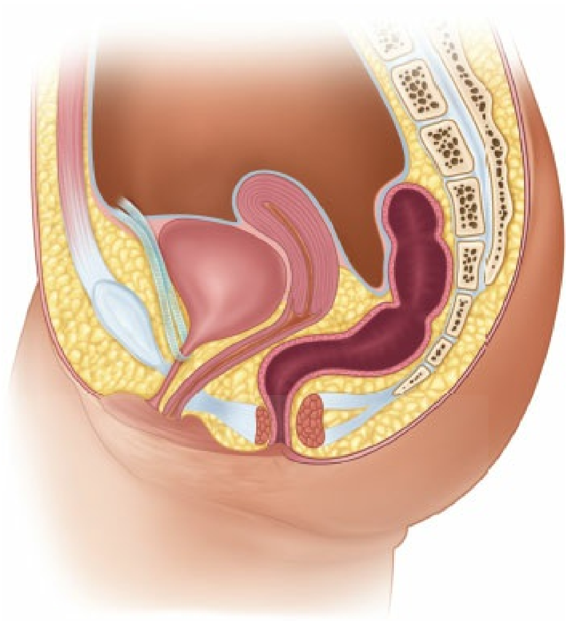

Figure 68.3 Transvaginal tape.

Blaivas demonstrated that genuine SUI caused by anatomical factors or sphincter-related problems such as ISD can be comprehensively diagnosed with videourodynamic studies [15]. He described a classification using videourodynamics, which included anatomical, due to hypermobility of the urethrovesical angle (type 1) or rotational descent of the bladder base (type 2) or due to ISD (type 3). Further classification resulted in the recognition of type IIa incontinence, which was associated with the bladder neck being closed at rest and above the inferior margin of the symphysis pubis. With increased abdominal pressure, the bladder neck and proximal urethra opened and descended more than 2 cm with resultant incontinence. In type IIb, the bladder neck and proximal urethra are displaced more than 2 cm at rest, and the proximal urethra opens with stress and incontinence occurs.

Since midurethral slings have proved to be effective in stress incontinence of either type, this distinction has become less critical, at least between type I and II. With this in mind, a proposal for a new surgical classification simplifies surgical procedures into those that aim to augment urethral closure and those that support or stabilize the bladder neck or urethra [16] (Figure 68.3).

Integral Theory

The description of the “integral theory” substantively impacted the understanding of the continence mechanism and has led to the introduction of the new surgical procedures such as midurethral tapes [17].

This theory holds that pelvic organ prolapse and urinary incontinence are caused by connective tissue laxity in the vagina and supporting pelvic myofascial structures. The vagina has been described as resembling a hammock. Contraction of the pubococcygeus during an increase in intra-abdominal pressure pulls the anterior vaginal wall forward and closes off the urethra. If this system of support is disrupted by laxity in the connective tissues, incontinence ensues. Support of the midurethra is proposed to be the main contributor to continence. Damage to the pubourethral ligaments supporting the urethra, deficient support of the anterior vaginal wall to the midurethra, and weakened function of the pubococcygeal muscles are the described as contributing to SUI [18]. The pubourethral ligaments, inserting at the midurethra, were identified in the early 1960s [19], but their role in functional urethral support was not appreciated until the description of the integral theory.

In 1994, DeLancey proposed the hammock theory. The basis of this theory is that continence depends on the transmission of pressure to the bladder neck and urethra against the rigid support of the pubocervical fascia and anterior vaginal wall. The hammock theory focuses more on causation of SUI than the integral theory [20].

Most recently, a further explained concept has evolved, which is known as the trampoline theory proposed by Daneshgari et al. This theory tries to encompass all previous theories and the multifactorial baseline for incontinence. The trampoline analogy attempts to consolidate the different anatomic and functional elements into a unified concept. Dysfunction of one element of this syncytium may not cause trampoline dysfunction. However, if several elements fail to work properly, functional disorder and urinary incontinence result [21].

SURGICAL PROCEDURES

Details about procedures are not within the scope of this chapter, and extended descriptions of each one of the techniques are described elsewhere in this text. Figure 68.4 shows the timeline for the development of incontinence theories and related procedures.

Urethral Injection Therapy

Urethral coaptation has a contributory effect to urinary continence. The submucosal vascular layer gives a cushion effect that closes the urethral lumen during resting and straining. The mechanism of action of bulking agents is to increase urethral resistance. The use of bulking agents has been described since 1938. Murless et al. used a sclerosing agent to generate scarring and contracture of the vaginal wall in order to improve continence [22].

Another proposed mechanism for bulking effect is that cephalad elongation of the urethra at the bladder neck after bulking results in increased abdominal pressure transmission in the first quarter of the urethra and associated increases in ALPP [23,24].

Agents that have been used for bulking include autologous fat, carbon beads (Durasphere®), calcium hydroxylapatite (Coaptite®), ethylene vinyl alcohol copolymer (Uryx®), glutaraldehyde cross-linked bovine collagen (Contigen®), hyaluronic acid with dextranomer (Zuidex®), porcine dermal implant (Permacol®), polytetrafluoroethylene (Polytef®), and silicon particles (Macroplastique®).

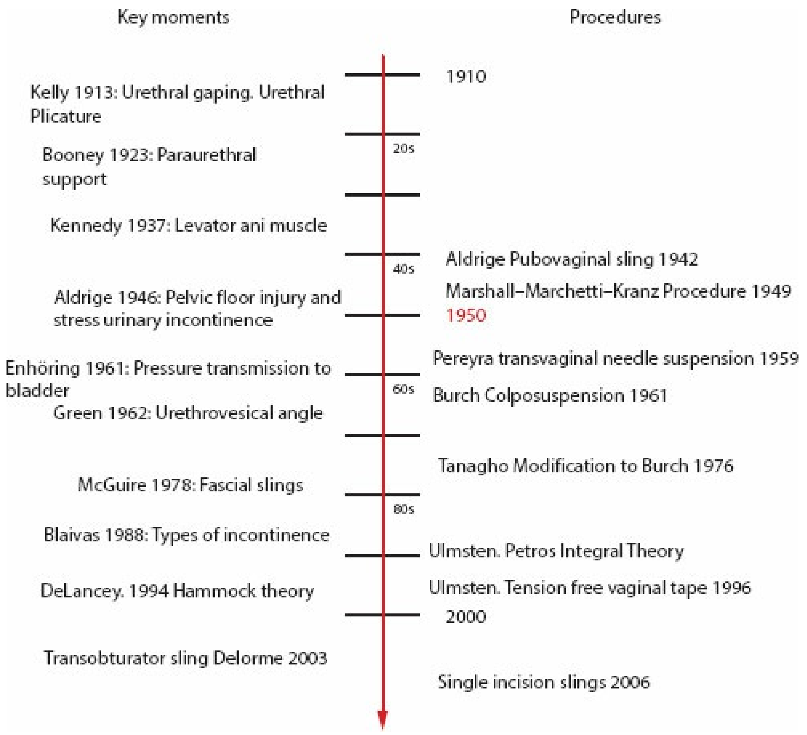
Key moments
Procedures
1910
Kelly 1913: Urethral gaping. Urethral Plicature
20s
Booney 1923: Paraurethral support
Kennedy 1937: Levator ani muscle
Aldrige Pubovaginal sling 1942
40s
Marshall–Marchetti–Kranz Procedure 1949
Aldrige 1946: Pelvic floor injury and stress urinary incontinence
1950
Pereyra transvaginal needle suspension 1959
Enhöring 1961: Pressure transmission to bladder
60s
Burch Colposuspension 1961
Green 1962: Urethrovesical angle
Tanagho Modification to Burch 1976
McGuire 1978: Fascial slings
80s
Blaivas 1988: Types of incontinence
Ulmsten. Petros Integral Theory
DeLancey. 1994 Hammock theory
Ulmsten. Tension free vaginal tape 1996
2000
Transobturator sling Delorme 2003
Single incision slings 2006

Figure 68.4 Timeline of incontinence theories and surgical procedures.

Why urethral injection works is still completely not understood, but based on the knowledge about urethral opening pressure and coaptation of urethral lumen, the use of bulking agents has been proposed as a therapy to correct SUI. It has been identified that urethral opening pressure at rest after bulking agent injection is unchanged but the opening pressure during stress or Valsalva increases, and this might be the reason why symptomatic improvement occurs. Also, the injection of an agent may increase the sarcomere length of the muscle fibers of the urethral sphincter, creating more power of contraction [25]. The most recent Cochrane review has shown that literature about this technique shows diverse results [26] (Figure 68.5).

Retropubic Suspension

Based upon Einhorning's concepts about pelvic support, pressure transmission forces, and hypermobility, retropubic surgical techniques were developed. The common step among all described procedures is the lifting and fixation of the urethra and bladder neck to the pubic bone or ligaments. The most commonly performed procedures are the MMK and the Burch colposuspension. The MMK was first described in 1949 in a man with urinary incontinence after a perineal prostate resection [27]. The original description for female indications included the placement of vaginal and periurethral sutures. These two were anchored to the periosteum of the symphysis pubis. Reports have shown an 82% success rate. The Burch procedure was first described in 1961 as a modification of the MMK, and it involved the approximation of the periurethral fascia to the Cooper's (iliopectineal) ligament by using three pairs of sutures [28]. The procedure underwent a modification by Tanagho that involved an additional approximation of the anterior vaginal wall to the lateral pelvic walls because overcorrection at the bladder neck did not improve success rates and carried a higher risk of voiding dysfunction [29]. The initial success rate was 100%. The 9-year results showed a 93% success rate but an 8% rate of enterocele. Recently, these procedures have been performed laparoscopically with some early encouraging results, but long-term studies have failed to demonstrate complete success [30–33].

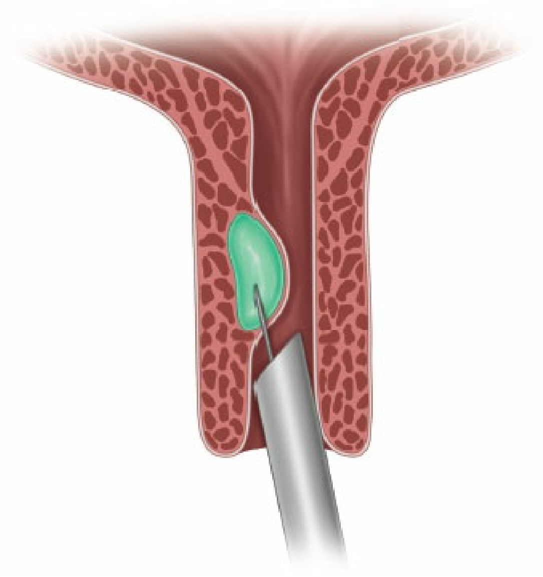

Figure 68.5 Bulking.

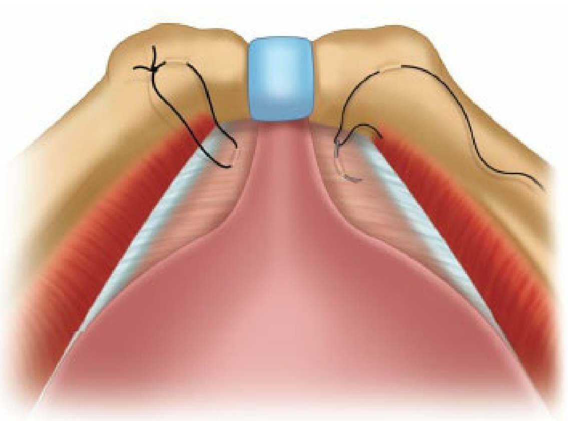

Figure 68.6 Retropubic.

The exact mechanism by which the Burch procedure achieves success is still unknown [34]. Burch originally thought that continence was achieved by the stabilization of the bladder neck and urethra, and MRI studies have shown that descensus of the levator ani muscle and bladder neck is much less in patients with successful results as compared to patients who have failed procedures [35]. With regard to the MMK procedure, how it achieves continence is also unknown. Some propose that Burch colposuspension might show better results because the lateral sutures help to elevate better the levator ani as compared to the more medial sutures of the MMK. For more than 40 years, the Burch colposuspension remained an efficacious and durable procedure in the surgical management of SUI (Figure 68.6).

Transvaginal Suspension

The search for less invasive procedures led to the development of the transvaginal procedures. In 1959, Pereyra described the transvaginal needle suspension. The aim of the procedure was to achieve continence using the same supportive periurethral tissue as the MMK or the Burch colposuspension [36]. Suture fixation stabilized pubocervial fascia to the anterior rectus muscle. A modification proposed by Stamey included the use of an endoscope to verify the correct position of the sutures and synthetic bolters in the vaginal suture to prevent pull-through [37]. Later, Gittes and Loughlin described a similar procedure using blind passage of the ligature carrier without incision of the vagina [38]. Although it is also unknown how the transvaginal procedures exactly work, it is thought that the mechanism is similar to that of the retropubic suspensions. Long-term results of transvaginal suspensions compared to the retropubic procedures are somewhat poor, and the evidence does not support the use of these techniques [39].

Raz in 1981 described his modification to the Pereyra operation. The goal of the procedure was to include the endopelvic fascia for urethral support. The Gittes procedure described in 1987 applied the same technique as Raz however with no vaginal dissection [40].

Pubovaginal Slings

The concept of holding the urethra with a strip of tissue was described more than century ago. Aldridge in 1942 popularized this technique [41]. Some earlier descriptions involved pyramidalis muscle and gracilis muscle. The mechanism of action of the sling procedures runs from passive compression to a dynamic component in which the abdominal musculature plays an important role by pulling upward the sling, giving more resistance to the urethra and bladder neck. McGuire in 1978 used a rectus fascia graft to create an elevation of the bladder neck and give some degree of urethral obstruction during Valsalva maneuvers [42].

The pubovaginal sling procedure consists of a retropubic and transvaginal approach. It does not matter whether the graft is from rectus fascia or fascia lata; the indicated size of the graft tends to be approximately 8 * 2 cm. The area from where the graft will be harvested changes slightly the preparation and patient’s position during surgery. In general, the position is the classic lithotomy position. Once the graft is ready, it is inserted in a “U-shape” way using Stamey needles surrounding the bladder neck with the graft and fixing to the abdominal wall. The common factor among all procedures is that a piece of fascia, graft, or synthetic material is used as a sling that surrounds the urethra in order to increase the support and extrinsic compression at the bladder neck. It is thought that when a Valsalva maneuver occurs, the tension of the sling prevents bladder neck to descend, and urethral wall is fixed and coapts closing the lumen more effectively [41]. The spread of its use was supported by the efficacy in cases with type III incontinence [42] (Figure 68.7).

Tension-Free Vaginal Tapes

This is the latest kind of procedures that have gained the position as the first line of treatment for SUI control given the nature of minimally invasiveness and good long-term results. It was first described by Ulmsten et al. [17]. The initial cure rate was 84% in the first 2 years after surgery. The original description included an incision at the anterior vaginal wall with a submucosal paraurethral dissection immediately behind the symphysis pubis. Then, a polypropylene mesh was introduced on each side of the urethra with a cephalic direction using two pairs of specially designed needles. At the anterior abdominal wall, the needles perforated it and the mesh was then left in place and incisions were closed [43].

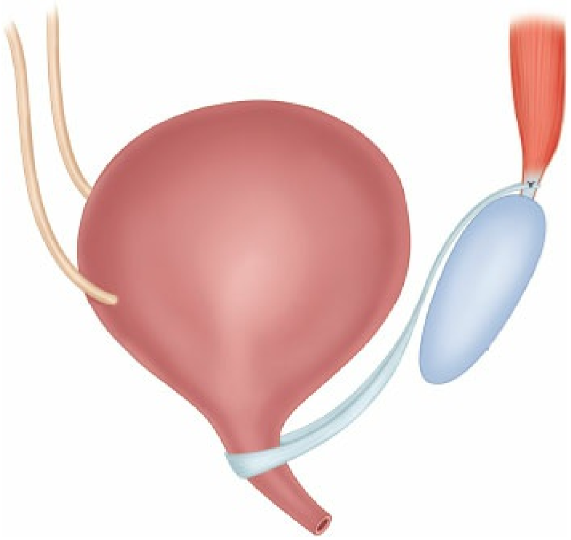

Figure 68.7 Pubovaginal sling.

Several techniques have been described since then, but in general there are two main ones: the transvaginal tape (TVT) and the transobturator tape (TOT) [44]. The difference between these procedures is the direction of vectors. The TVT has a more U-shape kind of vector as oppose to the TOT, which has a more lateral distribution.

All procedures share the same mechanism of action. It is thought that continence is achieved by the support given by the tape, which is focused at the point where the closure transmission forces occur in the midurethra. Since the anterior urethral wall is fixed anteriorly by the pubourethral ligaments and the posterior urethral wall lacks support, real-time imaging has shown that the urethral segment proximal to where the tape is located presents no motion of the posterior urethral wall. This creates a narrowing of the urethral lumen during stress. Surprisingly, the benefit that bladder neck mobility is reduced makes no improvement in continence control [45]. Recent randomized controlled trials have demonstrated equivalence among retropubic and transobturator tension-free slings [46].

CONCLUSIONS

Urinary continence is a complex process, and understanding of this process has evolved over time. The abundance of surgical procedures to correct incontinence, and modifications, thereof, reflects deficiencies in understanding of the pathophysiology of this condition. Currently, urinary continence is considered to be the result of a complex process with contributions from bladder neck, urethral, vascular, neural, and myofascial components. Unfortunately, a comprehensive understanding of the contributions of all of these elements has yet to have evolved. Optimized urethral function (coaptation and vascular flow) with integrity of urethral support and bladder neck smooth muscular function all summate to the continent condition. As of yet, no single procedure addresses all of these components comprehensively, hence the lack of any single procedure providing universal continence to all women undergoing that intervention.

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69 Peri- and Postoperative Care

Sushma Srikrishna and Linda Cardozo

INTRODUCTION

Surgical intervention remains the definitive treatment for the majority of women with pelvic floor dysfunction. Although surgical technique is a major factor influencing outcome, other factors such as appropriate patient selection, preoperative investigation and preparation, and postoperative care are also important considerations.

Urinary incontinence and urogenital prolapse are distressing conditions with a significant deleterious impact on quality of life [1,2], but are rarely, if ever, life threatening. Therefore, surgery for these conditions is elective and allows sufficient time for adequate preparation and case selection, which in turn should improve surgical outcome.

Although urogynecological procedures are very rarely associated with surgical mortality, every attempt must be made to minimize intra- and postoperative morbidity.

PREOPERATIVE CONSIDERATIONS

Procedure Selection and Discussion of Alternative Therapies

In the clinical setting, outcome assessment and the definition of "cure" remain poorly defined [3]. Generally, while measures of objective "cure" tend to be favored in the research setting and in the reporting of clinical trials, in everyday clinical practice, more subjective measures of outcome are preferred [4]. The use of patient-reported goals has been described as the fourth dimension in assessing pelvic floor dysfunction [5]. There is also an evidence to suggest that the use of a more individualized qualitative approach may help to tailor patient care and enable clinicians to focus on those specific and often very personal symptoms, which bother patients most. This may ultimately improve patient satisfaction and overall outcome [6]. More recently, global indices that ask a patient to rate the response of her condition to intervention (such as surgery in pelvic organ prolapse) have been used in clinical and research settings. These are much more simple and easy to use, interpret, and ultimately compare across units offering interventions in the management of urogenital dysfunction [7,8].

It is vital that before proceeding to a surgical procedure, a woman should feel that she has had the opportunity to take part in the decision process as this may have a profound influence on her emotional, psychological, and sexual well-being. The information on the possible effects of surgery on physical (with particular regard to bowel and bladder function), hormonal, reproductive, and sexual function should be provided. The full range of therapeutic measures available, expectant, medical, and surgical, should be discussed to allow an informed choice. It is also important to give a realistic view of success rates of individual procedures as well as any possible complications and their likelihood and possible sequelae. This ensures that the woman has realistic expectations regarding her surgery and a clear idea of potential complications, which goes a long way to reducing medicolegal problems.

Use of Alternative Therapies

Surgical intervention should not be undertaken without a comprehensive discussion on available alternative forms of therapy. These options may be particularly relevant for those women unsuitable or unwilling to undergo surgery.

Pelvic floor muscle training (PFMT), with or without electrical stimulation, remains the mainstay of conservative management of urodynamic stress incontinence. The recent National Institute for Clinical Excellence (NICE) guidelines recommend a trial of supervised PFMT of at least 3 months duration as first-line treatment for women with stress or mixed urinary incontinence [9].

Many studies have shown excellent results, although it is clear that supervised PFMT by a dedicated physiotherapist achieves far better results than vague instructions to perform pelvic floor exercises. A recent Cochrane review supports the recommendation that PFMT be included in first-line conservative management programs for women with stress, urge, or mixed urinary incontinence [10], although similar robust evidence is not available to elucidate the role of PFMT in pelvic organ prolapse [11]. A Cochrane review into conservative management of prolapse found some benefit specifically for PFMT as compared to no intervention. The authors concluded that more randomized controlled trials (RCTs) are still needed to look at the different regimens of PFMT, the cost in relation to benefit, and the long-term effects [12]. More recently, a large multicentered RCT establishing the effectiveness of one-to-one individualized PFMT for reducing prolapse symptoms concluded that while there is no doubt that PFMT is effective in the short term, long-term benefits still need to be investigated [13].

As physiotherapy is associated with good success rates and is not associated with significant adverse outcomes, it is recommended that surgical intervention is undertaken only after adequate course of physiotherapy.

Duloxetine, a balanced serotonin and noradrenaline reuptake inhibitors, is the only medical treatment available for stress incontinence. It enhances urethral sphincter activity via a centrally mediated pathway [14]. The evidence reported to date suggests that duloxetine is significantly better than placebo [15], offers an alternative to surgery, and may be complementary to the use of PFMT in the initial management of women with stress incontinence [16]; however, its use is limited by significant side effects such as nausea in a proportion of women [15].

A number of mechanical devices may also be considered in the conservative management of pelvic floor dysfunction. These may be useful in the short term, while women undergo physiotherapy or are on the waiting list for surgery, in those who are unwilling or unfit for surgery and during pregnancy.

Information Leaflets

Research has shown that at any given time, only 10% of verbal information during a consultation is remembered by the patient afterward. This can be substantially increased by the use of written information given to patients during a consultation [17]. Patient information leaflets can be particularly useful if they have been written locally to reflect practice in a particular unit. Written information leaflets can also be reread at leisure by women, allowing them time to consider treatment options and think of any questions that may be addressed at subsequent consultations. In addition, documentation of the use of such leaflets may be particularly useful in medicolegal disputes. Various urogynecology societies such as the British Society of Urogynaecology and the International Urogynecological Association have produced written patient information leaflets on most surgical procedures, which can be easily downloaded and serve as a useful resource.

Preoperative Nurse Assessment

Preoperative counseling by suitably experienced and trained nursing staff may be particularly beneficial. This allows a more comprehensive discussion of any anxieties than is possible on a traditional preoperative ward round. Nursing staff are also appropriately placed to give information about pre- and postoperative care, catheter regimens, drains, dressings, and ward routine. Ideally, the nurse should be one of the team providing care on the ward.

Deferral of Surgery

As most urogynecological surgery is elective, there should be no need for a procedure to be performed under conditions of undue stress. If it is felt that a patient is unsure about the need for surgery or further investigation or counseling is required, then surgery should be deferred. Finally, the surgeon has the ultimate sanction, and if it is felt that an intervention is inappropriate or not in a patient’s best interest, then (after appropriate explanation) it may be wise to refer back to the general practitioner to suggest a further opinion or investigations.

Physical Fitness for Surgery

Weight Loss

There has been extensive research on the association between obesity and increased perioperative morbidity and mortality. Obesity is associated with increased anesthetic complications such as difficult intravenous access, induction, and intubation as well as technical difficulties during surgery. In addition, there is an increase in most postoperative complications such as wound infection, hematoma formation, thromboembolism, and respiratory infection [18]. Therefore, in ideal circumstances, every attempt should be made to encourage obese patients to lose weight preoperatively, including referral to dietician and use of appetite suppressants.

Intercurrent Illness

Before undergoing any surgical procedure, it is essential that a woman is as fit, physically, as possible. The elective nature of most urogynecological procedures allows surgery to be deferred if any intercurrent illness has impaired a woman's general health.

Smoking

In addition to its deleterious effects on health, smoking increases the risk of postoperative problems, such as thromboembolism and postoperative respiratory infections. Also, chronic cough is a factor in the development or recurrence of urogenital prolapse. Most hospitals now offer smoking cessation advice and specialist clinics. Therefore, any patient who is willing to consider giving up smoking should ideally be referred.

Anemia

Anemia increases the risk of postoperative wound infection and delays full recovery. Depending on the level of anemia, the associated symptoms, and the time prior to surgery, this may be corrected by simple oral iron replacement (ferrous sulfate 200 mg daily), antifibrinolytic therapy (tranexamic acid 1 g qds), use of gonadotropin-releasing hormone (GnRH) to suppress menstruation prior to surgery, or preoperative blood transfusion. In addition, GnRH analogues have the advantage of shrinking fibroids, thereby facilitating vaginal hysterectomy or reducing blood loss at abdominal hysterectomy.

Concomitant Medication

The general advice to most patients on regular medication is to continue with these according to their normal routine. The two exceptions to this rule are hormonal or anticoagulant therapy, which may need to be modified prior to surgery.

Complementary or Alternative Medication

The World Health Organization estimates that 80% of the world population uses herbal medicine [19], with an increasing popularity in the use of alternative and complementary therapies. However, it is important to ask specifically for the use of such medications as these are also associated with significant side effects following indiscriminative usage. For example, ginseng may elevate the blood pressure and its excessive use may lead to ginseng abuse syndrome, manifested by diarrhea, skin lesions, CNS stimulation, and interference with homeostasis. Ginseng also potentiates the antiplatelet effect of Coumadin, aspirin, and NSAIDs and taking these drugs with ginseng may pose surgical risks. *Ginkgo biloba*, another traditional herb used in Chinese medicine, is known to decrease platelet aggregation with the anticoagulant warfarin that can interfere with homeostasis. *Ginkgo biloba* will also react with narcotic analgesics causing hypotension [20]. Dong quai (*Angelica sinensis*), used in China for pain and trauma or "female problems," can also interfere with warfarin in high doses. It may potentiate skin cancer or raise blood glucose levels. This is especially dangerous in patients who are diabetic, have heart problems, or are taking anticoagulants. Another popular herb known as licorice root (*Glycyrrhiza glabra*) and its Chinese counterpart (*Glycyrrhiza uralensis*) contain salts of glycyrrhizic acid. This glycoside can intensify platelet aggregation thereby decreasing the Coumadin function [21]. The potential risks associated with the use of alternative medications are listed in Table 69.1 [22].

Hormonal Therapy

Combined oral contraceptive (COC) pills and hormone replacement therapy (HRT) have been implicated as risk factors for postoperative thromboembolism. However, a recent review of literature suggests that the risk of thromboembolism induced by COC or HRT is very small. The increased risk should be compared with the occurrence of undesired pregnancy after discontinuation of COC or the occurrence of climacteric symptoms after discontinuation of HRT. In most cases, these two treatments can be maintained with the use of antithrombotic prophylaxis [23].

Atrophic changes in the vaginal skin can cause difficulty during vaginal reconstructive surgery and compromise postoperative wound healing. Preoperative treatment with topical estrogen for 6 weeks is worthwhile and carries little risk.

Anticoagulants

Most hospitals have local guidelines for the perioperative management of patients on warfarin. Our local guidelines at King's College Hospital are shown in Box 69.1.

Recent evidence, however, weighs heavily toward the continuation of low-dose aspirin (less than 325 mg/day) unless there is a significant bleeding risk associated with the operation [24]. Clopidogrel binds irreversibly to the platelet receptor P2Y12 thereby inhibiting platelet response to both exogenous and endogenous adenosine diphosphate. It is the second most commonly used antiplatelet agent, typically employed both as a substitute for aspirin or as an additional therapy for patients with unstable angina or after coronary stent implantation. If administered for primary prevention in place of aspirin, it can be discontinued 7 days before operation to allow active platelets to be present in the circulation [24].

In the last decade, several novel oral anticoagulants (NOACs) have been assessed in the setting of major orthopedic surgery. These novel agents, dabigatran, rivaroxaban, and apixaban, which have been approved by the European Medicines Agency for the prevention of venous thromboembolism (VTE) after elective hip or knee replacement surgery, have a more predictable anticoagulant effect and a wide therapeutic window, which allow oral administration in fixed dose regimens without the need for routine laboratory monitoring. Moreover, their half-life, shorter than that of the vitamin K antagonists (VKAs) and similar to that of low-molecular-weight heparin (LMWH), represents an additional advantage [25]. At least 1 in 10 Americans receiving outpatient anticoagulant therapy requires interruption of anticoagulation for an invasive procedure annually, and management of these new agents in the perioperative setting is made challenging by difficulty measuring anticoagulant effect and the lack of effective reversal. Surgical planning must account for individual patient risks for bleeding and thrombosis, the type of procedure, and expected drug clearance. Based upon these considerations, a perioperative plan encompassing timing of target specific oral anticoagulant (TSOAC) cessation and resumption, as well as bridging therapy, if needed, can be developed. Perioperative strategies remain largely predicated on extrapolations from pharmacokinetics and expert opinion, though a growing body of literature is providing greater guidance in this important area [26].

For nonemergency surgery, patients should be evaluated by an anesthetist as early as possible to assess an optimal appointment for surgery and bridging strategy. Management of emergency procedures for patients on NOACs requires an interdisciplinary approach. The individual risk for uncontrolled bleeding versus the urgency for surgery needs to be evaluated on an individual basis. The determination of drug serum levels enables a rough estimation of anticoagulant activity. Emergency procedures in coagulopathy due to active bleeding are treated with the unspecific administration of blood products and coagulation factor concentrates [27].

Preoperative Investigations

Preoperative investigations should be tailored to an individual woman's general health and any existing medical problems. The majority of preoperative investigations can be performed on an outpatient basis with the results available for review prior to admission. This allows time for any form of therapy, further investigation, or referral to be made prior to surgery.

Routine preoperative investigations include hematological and biochemical investigations, urinalysis, electrocardiography (ECG), and imaging.

Hematological Investigations

Every woman should have a full blood screen performed to include a hemoglobin count, hematocrit count, white blood cell count and differential, and hemoglobinopathy screen (where appropriate). In addition, the blood should be typed and serum retained for cross matching prior to any surgical procedures that involves a risk of transfusion.

Biochemical Investigations

In healthy women, with no known or suspected underlying medical disorders, these tests may be limited to blood urea and serum creatinine electrolyte levels.

Blood Glucose Control in the Perioperative Period

Uncontrolled blood glucose is associated with a higher incidence of surgical site infections, greater utilization of resources, and increased mortality. Preoperative screening for diabetes in elective surgical patients is not routinely performed. A recent observational cohort study to assess glycosylated hemoglobin screening for elective surgical patients showed that 23% considered very high risk for diabetes and 4% had a provisional diagnosis of diabetes. Many elective surgical patients are therefore at risk for unrecognized postoperative hyperglycemia and associated adverse outcomes. Random blood sugar testing has limited value and HbA1c may be a more appropriate test for the preoperative assessment of diabetic patients [28]. A recent report from the Surgical Care and Outcomes Assessment Program has shown that perioperative hyperglycemia is associated with adverse outcomes in general surgery patients with and without diabetes. However, patients with hyperglycemia who received insulin were at no greater risk than those with normal blood glucose [29].

Table 69.1 Potential Risks of Herbal Medication

Herbal names	**Botanic names**	**Medical uses**	**Potential risks**
Aloe (other names: hsiang-dan, lu-hui)	*Aloe barbadensis/capensis/vera*	Depresses the action potential generation and conduction at neuromuscular junction processes and analgesic and anti-inflammatory effects; increases the collagen content of granulation; tissue contributed to wound healing, sometimes used to treat AIDS, diabetes, asthma, stomach ulcers, immune weakness, evacuation relief, anal fissures after rectoanal surgery, fungal diseases, constipation, colic, and worm infestations	Loss of electrolytes, potassium, and this hypokalemic effect enhanced in conjunction with thiazide diuretics, loop diuretics, licorice, and corticosteroids (increase the action of cardiac glycosides and antiarrhythmic drugs).
Huang-Qi (other names: superior Chinese astragalus)	*Astragalus* species	Used for respiratory infections, immune depression, cancer, heart failure, viral infections, liver disease, and kidney disease; hyperthyroidism, hypertension, insomnia, diabetes, genital herpes, AIDS, and the side effects of chemotherapy	Bleeding when used with other anticoagulant, antiplatelet, or antithrombotic agents. It is incompatible with opiates.
Chinese rhubarb, da-huang	*Rheum palmatum*	Constipation, appetite stimulant, painful teething, delirium, edema, and diarrhea	Electrolyte loss (especially potassium leading to hyperaldosteronisms and enhanced effects of radioactive drugs). Long-term use causes arrhythmias, nephropathies, and bond loss.
Dandelion (other names: lion's tooth, endive)	*Taraxacam offinae/laevigatum*	Dyspeptic conditions, UTIs, liver and gallbladder dysfunctions, loss of appetite, fluid retention, constipation, rheumatism, and diabetes	Not to be used with diuretics, antihypertensive agents and oral hypoglycemic, and mammal- and lactating-related problems.
Ephedra, ma huang (other names: natural ecstasy,	*Ephedra sinica*	Used as CNS stimulant for appetite suppressant, a nasal decongestant, bronchial asthma, joint symptoms, inability to perspire, edema, and pain in the bones	May alter effects of MAO inhibitors, ephedrine, B-blockers, phenothiazines, and Sudafed. Higher dosages result in blood pressure and cardiac rhythm disorders; it has an additive effect

fen-phen)			with caffeine and decongestants and heart rhythm disturbances when used with halothane.
Garlic (other names: da-suan)	*Allium sativum*	For elevated lipid levels, age-related vascular change and arteriosclerosis, inflammatory respiratory conditions, gastrointestinal ailments, diabetes, constipation, and joint pain	Decrease in hematocrit values and plasma viscosity; concomitant use with Coumadin antiplatelet drugs such as aspirin and dipyridamole could increase the effect of bleeding. Risk of bleeding increased with ginkgo or high-dose vitamin E and may increase serum insulin levels.
Ginkgo, *Ginkgo biloba* (other names: xGinkgo)		For organic brain dysfunction intermittent claudicating, vertigo and tinnitus, improving concentration, asthma, hypertonic, erectile dysfunction, and angina pectoris	Spontaneous bleeding due to potent inhibitory effect on platelet-activating factor; care when used with aspirin and other anticoagulant hypertension with thiazide diuretics.
Ginseng (other names: Chinese Red Panax)	*Panax ginseng*/*quinquefolius*	For fatigue and debility, concentration, loss of appetite, cachexia, anxiety, impotence and sterility, neuralgia, and insomnia	Hypoglycemic effects, hypotension resulting with prolonged high-dose ginseng with caffeine, adverse effects with oral hypoglycemic and MAO inhibitors, concomitant use with aspirin, NSAIDs, heparin, and warfarin should be avoided.
Green tea (other names: Chinese matsu-cha)	*Camellia sinensis*	$$$	Vitamin K in green tea interferes with Coumadin, decreases the absorption of alkaline drugs.
Licorice	*Glycyrrhiza glabra*	For cough/bronchitis and gastritis, also used for appendicitis, constipation, increase milk production, micturition, gastric ulcers, headache, sore throat, spleen disorders, dehydration, and chronic fatigue syndrome	Hypokalemia, hypernatremia, edema, hypertension, and cardiac complaints. Additive effect with furosemide and thiazide diuretics. Hypokalemic effects potentiate digitalis toxicity. Severe ventricular tachycardia of the torsade de pointes type resulted with the concomitant use of antiarrhythmic agents and may prolong the half-life of cortical increasing its effectiveness and its side effects.
Papaya	*Carica papaya*	For gastrointestinal digestive complaints, athletic injuries, and herniated vertebral disks	Fibrinolytic effect, tendency to bleed due to interaction with warfarin and increased INR levels.
Prickly ash (other names: toothache tree, stanberry)	*Zanthoxylum americanum*	For toothache, intestinal gas, to promote circulation, and rheumatism	Promote bleeding when used with aspirin or other blood thinners.
Turmeric (other names: jiang huang)	*Curcuma longa*	Dyspeptic complaints and loss of appetite, also cancer, gallstones, intestinal gas osteoarthritis, and rheumatoid arthritis	Alter the action of Coumadin, NSAIDs, and immune system suppressants.
Wild yam (other names:	*Dioscorea villosa*	For rheumatic conditions, gall bladder colic, dysmenorrheal, and cramps	Decrease the anti-inflammatory effect of indomethacin, additive effect with estrogen.

China root)

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Box 69.1

Low risk	Atrial fibrillation	Stop warfarin 4 days prior to procedure.	Prophylactic dose of enoxaparin.
	Mitral valve disease Cardiomyopathy	If immobilized, use prophylactic enoxaparin, 40	Restart warfarin post-op if hemostasis is secure. Stop enoxaparin when international normalised ratio (INR) > 2.0.
High risk	Venous or arterial thromboembolism	Stop warfarin 4 days prior to procedure.	Restart intravenous heparin 6 hours post-op if hemostasis is secure (do not give loading dose); check aPTT after 12 hours or subcutaneous enoxaparin treatment dose.
	Mechanical valve replacement	Initiate intravenous heparin or enoxaparin treatment dose when INR < 2.0.	Restart warfarin when appropriate.
		Stop intravenous heparin 3 hours pre-op. If on enoxaparin, withhold dose on day of operation/procedure.	Stop enoxaparin/heparin when INR > 2.0.

Perioperative hyperglycemia has also been associated with increased surgical site infections [SSIs] that can cause significant morbidity and mortality and are potentially preventable. Previous recommendations have been to treat glucose levels above 200 mg/dL. However, a recent Cochrane review found insufficient data to support the routine adoption of strict blood glucose control and insufficient evidence to support strict glycemic control versus conventional management around the time of operation to prevent surgical site infections [30].

Urinalysis

Simple ward urinalysis may be used to exclude a urinary tract infection (UTI) in symptomatic women. The urine should be tested for beta-human chorionic gonadotropin in all women of reproductive age to rule out any possibility of pregnancy.

Electrocardiography

ECG traces are not required for most fit women undergoing surgery but may be required if there is a history of hypertension or cardiac disease. Most anesthetic departments now have guidelines for preoperative ECG recording.

Imaging

The roles of plain and contrast radiology, computed tomography, ultrasonography, and magnetic resonance imaging are discussed in the relevant sections of this book.

All women undergoing surgery for uterovaginal prolapse should have transvaginal ultrasound scan of their pelvis to rule out concomitant pelvic pathology. A recent study has shown that associated gynecological pathology may be found in nearly half of the patients on transvaginal ultrasound scan (TVS), leading to a change in planned management in 2.9% of cases [31]. An intravenous urogram should be performed if an anatomic abnormality suggests that the course of the ureters may be aberrant, if malignancy is suspected or in major prolapse where ureteric obstruction is a possibility.

Pulmonary Assessment

Postoperative pulmonary complications play an important role in the risk for patients undergoing noncardiothoracic surgery. Postoperative pulmonary complications are as prevalent as cardiac complications and contribute similarly to morbidity, mortality, and length of stay. Pulmonary complications may even be more likely than cardiac complications to predict long-term mortality after surgery. The American College of Physicians have published a guideline to provide guidance to clinicians on clinical and laboratory predictors of perioperative pulmonary risk before noncardiothoracic surgery and to evaluate strategies to reduce the perioperative pulmonary risk and focuses on atelectasis, pneumonia, and respiratory failure [32]. This shows that patient-related risk factors, such as chronic obstructive pulmonary disease, age older than 60 years, ASA class of II or higher, functional dependence, and congestive heart failure, increase the risk for postoperative pulmonary complications. In addition, patients undergoing such procedures as prolonged surgery, abdominal surgery, thoracic surgery, neurosurgery, head and neck surgery, vascular surgery, aortic aneurysm repair, and emergency surgery are at higher risk for postoperative pulmonary complications. General anesthesia and serum albumin levels below 35 g/L are also a strong marker of increased risk. Good evidence exists to support risk-reduction strategies, including incentive spirometry and deep breathing exercises, and fair evidence exists to support selective nasogastric tube decompression after abdominal surgery. Fair evidence also suggests that short-acting neuroaxial blockade reduces postoperative pulmonary complications compared with long-acting neuroaxial blockade.

Therefore, routine preoperative chest radiography is now rarely required except in women with cardiac or pulmonary disease. A recent review of literature found that 23.1% of preoperative chest radiographs were abnormal but only 3% had findings clinically important enough to influence management [33]. Most anesthetic departments have guidelines for preoperative chest radiography.

Anesthetic Preassessment

Preoperative assessment by the anesthetist is essential to ensure the safe and smooth running of the operating list. In otherwise fit and healthy women, this is often carried out the evening before surgery, or in the case of day surgery, on the day of surgery, with the notes and results of investigations available. Where major medical problems exist or if there have been previous anesthetic problems such as difficult intubation, anesthetic consultation may be carried out prior to admission. This allows enough time for further investigations and therapy to be instituted prior to surgery.

Informed Consent

Treatment and care should take into account the women's individual needs and preferences. Women should have the opportunity to make informed decisions about their care and treatment. If women do not have the capacity to make decisions, health-care professionals should follow the Department of Health guidelines "Reference guide to consent for examination or treatment" (2001) (available from www.dh.gov.uk). From April 2007, health-care professionals need to follow a code of practice accompanying the Mental Capacity Act.

The treatment, care, and information women are given about it should be culturally appropriate. It should also be accessible to women who have additional needs, such as physical, sensory, or learning disabilities, and to women who do not speak or read English.

Carers and relatives should also be provided with the information and support they need.

Consent is difficult to define succinctly but requires three elements: volition, capacity, and knowledge.

Volition

Volition is based on the principles of self-determination and a respect for individual integrity. This requires that a woman is able to make a decision regarding consent without undue pressure from a third party, either a relative or a member of the medical staff. Legally, a spouse or relative cannot give or withhold consent on a woman's behalf, although it is considered good practice to involve the spouse, particularly where the treatment proposed will affect fertility.

Capacity

Capacity to consent requires that a woman has sufficient intellect to appreciate information discussed prior to giving consent and the mental capacity to appreciate the risks and the consequences of the operation proposed. This is a particularly difficult area when dealing with women whose mental capacity is limited as a result of either intellectual handicap or psychiatric illness. In these situations, it is important to seek additional professional opinion and to seek legal clarification where time allows. The situation when dealing with minors (in the United Kingdom, under 16 years of age) is another delicate area. In general, a parent and the child would be involved in giving informed consent.

However, in the United Kingdom, there is the concept of “Gillick” competency, where a medical practitioner must make a clinical judgment as to whether a minor has sufficient maturity to give informed consent. Although this has clarified the situation in the United Kingdom, it is important that practitioners are aware of the law regarding minors in their own country or state.

Knowledge

A woman should not only have sufficient information concerning the diagnosis and prognosis but also be given sufficient information about alternative treatments and also any reasonably foreseeable adverse effects of the proposed treatment. In general, the information given should conform to that given by a responsible body of medical opinion. Those risks that are commonly associated with a procedure should certainly be discussed; more uncommon complications need not be. It is left to the medical practitioner to decide on an individual patient’s ability or wish to discuss these issues. Usually, any complications occurring more than 1% of the time should be discussed. The need to discuss complications also varies with their potential severity and implications for future health. This means that it is essential to discuss the possibility of a complication that may be relatively remote but which would have a major impact on a woman’s life.

It is essential that the possibility of oophorectomy (for either as a technical necessity or an unforeseen indication) is discussed and documented. The risks of surgical complications such as bladder trauma requiring catheterization and wound infection should also be discussed, as appropriate.

The final decision regarding a woman’s capacity to give consent and her ability to understand the information given is left to the professional judgment of the surgeon.

Most practitioners will use a standard consent form and record any particular information on this. However, the concept of informed consent embraces more than just a signature and so it is important that good records are kept of any discussion and information given prior to informed consent. Finally, consent should only be taken by a medical practitioner capable of performing the procedure.

Last-Minute Preparation

Bowel Preparation

The aim of bowel preparation is twofold: first, to remove bulky intraluminal contents and improve both surgical field visualization and handling of the bowel, and, second, to decrease peritoneal and wound contamination by the intraluminal content in case of inadvertent bowel trauma. However, data to support these aims are conflicting. There is only a single randomized study in the literature addressing bowel preparation before benign gynecological surgery, which suggests no evidence to support its routine use [34].

In our practice at King’s College Hospital, women undergoing pelvic reconstructive surgery, such as colposuspension or vaginal repair, receive a sachet of sodium picosulfate the afternoon before surgery to ensure an empty rectum and a stool softener such as lactulose in the postoperative period to prevent discomfort and straining associated with constipation. Complex surgery such as sacrocolpopexy requires complete access to the sacral promontory or mobilization of the rectum. In these cases, thorough bowel preparation with two sachets of sodium picosulfate the day before surgery ensures an empty rectum.

Thromboprophylaxis

Thromboembolism accounts for around 20% of perioperative hysterectomy deaths [35]. As prophylaxis has been shown to be effective in reducing the risk of thromboembolism, women undergoing gynecologic surgery should be assessed for clinical risk factors and overall risk of thromboembolism and should receive prophylaxis according to the degree of risk [36].

Risk factors may be associated with the disease or surgical procedure (infection, polycythemia, heart failure) or with the patient (age over 37 years, obesity, previous deep vein thrombosis, congenital or acquired thrombophilia, etc.)

Assessment of these risk factors allows patient categorization into low-, medium-, or high-risk categories. The NICE guidelines on reducing the risk of VTE in surgical patients advice the following:

- Patients should be assessed to identify their risk factors for developing VTE (see Box 69.2).

- Health-care professionals should give patients verbal and written information, before surgery, about the risks of VTE and the effectiveness of prophylaxis.
- Inpatients having surgery should be offered thigh-length graduated compression/antiembolism stockings from the time of admission to the hospital unless contraindicated (for example, in patients with established peripheral arterial disease or diabetic neuropathy). If thigh-length stockings are inappropriate for a particular patient for reasons of compliance or fit, knee-length stockings may be used as a suitable alternative.
- The stocking compression profile should be equivalent to the Sigel profile, and approximately 18 mmHg at the ankle, 14 mmHg at the midcalf, and 8 mmHg at the upper thigh.
- Patients using graduated compression/antiembolism stockings should be shown how to wear them correctly by health-care professionals trained in the use of that product. Stocking use should be monitored and assistance provided if they are not being worn correctly.
- Intermittent pneumatic compression or foot impulse devices may be used as alternatives or in addition to graduated compression/antiembolism stockings while surgical patients are in hospital.
- In addition to mechanical prophylaxis, patients at increased risk of VTE because they have individual risk factors (see Box 69.2) should be offered LMWH. Fondaparinux, within its licensed indications, may be used as an alternative to LMWH.

Box 69.2 Patient-Related Risk Factors for Venous Thromboembolism

- Active cancer or cancer treatment
- Active heart or respiratory failure
- Acute medical illness
- Age over 60 years
- Antiphospholipid syndrome
- Behcet’s disease
- Central venous catheter in situ
- Continuous travel of more than 3 hours approximately 4 weeks before or after surgery
- Immobility (for example, paralysis or limb in plaster)
- Inflammatory bowel disease (for example, Crohn’s disease or ulcerative colitis)
- Myeloproliferative diseases
- Nephrotic syndrome
- Obesity (body mass index ≥ 30 kg/m^2)
- Paraproteinemia

- Regional anesthesia reduces the risk of VTE compared with general anesthesia. Its suitability for an individual patient and procedure should be considered, along with the patient’s preferences, in addition to any other planned method of thromboprophylaxis.
- Health-care professionals should encourage patients to mobilize as soon as possible after surgery.

The Royal College of Obstetricians and Gynaecologists (RCOG) has also issued guidelines on the use of thromboprophylaxis in gynecologic surgery [37]. Patients deemed at low risk require attention to hydration and early mobilization only. Those at moderate risk should receive specific prophylaxis with either LMWH (doses varying depending on the heparin used, for example, enoxaparin and tinzaparin) or intermittent pneumatic leg compression. Patients deemed to be at high risk should be given heparin as the aforementioned and in addition be fitted with graduated compression stockings. In patients who are at high risk, a hematologist should also be actively involved in the preoperative thromboprophylactic management.

Prophylactic Antibiotics

Prophylactic antibiotics have been clearly shown to reduce the risk of postoperative wound infection. A reduction in infectious morbidity has been shown with the use of broad spectrum antibiotic prophylaxis in both abdominal and vaginal hysterectomy [38]. Adverse reactions to prophylactic antibiotic regimens are reported rarely, with an incidence of less than 1%. The cost of antibiotic cover is outweighed by the considerable economic savings, most notably the reduction in inpatient stay. The clinical and economic evidence clearly demonstrates the effectiveness of routine preoperative antibiotic prophylaxis. The choice of antibiotic depends upon local guidelines. As the pattern of microbial resistance varies, the most appropriate combination of agents should be selected after consultation with the local microbial service.

However, to reduce bacterial resistance, short courses should be used with routine *first-line* agents. Newer agents should be reserved for the treatment of established antibiotic resistant infections. As the aim of chemoprophylaxis is the prevention rather than the treatment of established infection, regimens used should aim to achieve a high tissue concentration of the chosen antibiotics at the time of surgery when inoculation of the wound occurs. However, as this would mean the administration of intravenous antibiotics some hours prior to surgery, a more practical compromise is to give the first dose at the time of induction of anesthesia, with a further two doses in the first 24 hours postoperatively. It is our practice at King’s to routinely use gentamicin as prophylaxis in any surgery involving urethral instrumentation. In addition, prior to mesh augmentation surgery such as sacrocolpopexy, it is our practice to presoak the mesh in gentamicin solution prior to its use.

MRSA Screening

Over the last 25 years, MRSA has become endemic in many acute hospitals in the United Kingdom.

If a patient does develop an infection, however, different antibiotics have to be used, such as vancomycin, which may not be as effective, has more side effects, and is more expensive than conventional therapy. For these reasons, every effort should be made to prevent the spread of MRSA. The guidance issued in 2008 has also placed a requirement on Trusts to introduce routine MRSA screening for all elective admissions by March 2009. Sufficient time must be allowed between screening and admission, to enable completion of MRSA clearance and rescreening (3 weeks allows time for repeat screening and retreatment, if required). Samples must be taken from the following sites:

1. Nose
2. Throat
3. Groin or perineum
4. Any wounds or open lesions
5. Any line sites

The purpose of the topical eradication protocol is to try to eliminate MRSA skin carriage, reducing the risk of subsequent wound infection and transmission to other patients.

The basic regimens are the following:

1. Chlorhexidine gluconate 4% (Hibiscrub or Hydrex) for body and hand washing daily for 5 days. Alternatively, triclosan 2% (Aquasept) may be used in the event of a patient allergy.
2. Mupirocin 2% nasal ointment (Bactroban Nasal) applied to the inside of the nostrils, using a gloved finger, three times daily for 5 days. Press the nostrils together for a few seconds to thoroughly spread the ointment over the insides of both nostrils.

When MRSA is isolated in an inpatient for the first time, the ward will be contacted by either a microbiology doctor or an infection control nurse. The patient must be isolated in a side room. Gloves and plastic aprons must be worn by all staff for any patient contact. The hands must be decontaminated prior to donning gloves and disposable plastic apron. After contact with patients or patient environment, the gloves and apron must be removed while in the room and disposed of in the clinical waste bin, and the hands must be decontaminated before leaving the room or immediately upon exit.

POSTOPERATIVE CONSIDERATIONS

Immediate Postoperative Care

Normal clinical monitoring of postoperative patients with pulse and blood pressure recording is adequate for most gynecologic patients. In high-risk cases, the hourly urine output is a sensitive measure of peripheral circulation.

Analgesia

Postoperative respiratory complications associated with wound pain may delay recovery [39]. Effective postoperative analgesia can facilitate recovery and reduce morbidity in surgical patients by blunting autonomic, somatic, and endocrine reflexes [40]. Postoperative pain is mediated via nociceptive, inflammatory, and neuropathic mechanisms and varies between individuals and different operative procedures. Multimodal postoperative analgesia addresses both different pain modalities and types of surgery [41]. Multimodal analgesia may also be opioid sparing and reduce opioid-related side effects, thereby facilitating patient recovery and ambulation [42]. Most hospitals usually have a local protocol for postoperative analgesia, which is initiated by the anesthetist. This can then be tailored according to the needs of the individual patient. Postoperative pain management following major abdominal surgery may require the use of patient-controlled analgesia (PCA) or epidural analgesia. A retrospective cohort study showed postoperative pain management was excellent in both groups, although problems related to the delivery of pain control such as prolonged catheterization, increased risk of UTIs, and epidural catheter leaks were more common in the epidural group [43].

Vaginal Pack and Indwelling Catheter Care

Indwelling urinary catheter and vaginal pack has been the standard practice after pelvic floor dysfunction surgery. The catheter is used to allow bladder emptying when natural voiding is difficult or impossible due to the presence of vaginal pack, pain, or soft tissue swelling. The vaginal pack is expected to prevent slight bleeding. The duration of catheterization and vaginal packing has been reduced over the years, but there is no consensus on how to minimize complications, and practice varies.

A recent RCT conducted in our department has shown that there is no evidence to suggest that packing increases pain scores or postoperative morbidity. A trend toward increased hematoma and significant complications was seen in the no-pack group. As vaginal packing does no harm and may be of some benefit, it may be argued that packing should be recommended as routine clinical practice [44].

In a Cochrane study on short-term urinary policies following urogenital surgery in adults, no randomized studies were found comparing the use of urinary catheter versus no urinary catheter in patients following prolapse operations. Seven trials also including other urogenital surgery suggest fewer UTI when the catheter was removed earlier, but no clear pattern in respect of recatheterization [45].

Whether or not to use a particular policy concerning when to remove the urinary catheter and vaginal pack is usually a trade-off between the risks of morbidity (especially infection) and risks of recatheterization. In our practice, both the vaginal pack and indwelling catheter are usually removed in the morning, on the first day after surgery.

Anticipation of Postoperative Voiding Problems

Voiding difficulties may occur acutely following any pelvic surgery and after continence procedures in particular. Acute over distension of the bladder leads to damage of the detrusor syncytium with ischemic damage to the postsynaptic parasympathetic fibers. This may result in insidious deterioration of detrusor function and the onset of voiding dysfunction [46]. Factors that may increase the risk of acute postoperative retention include older patients, long operation time, and high doses of opiate analgesia and PCA, together with large amounts of intravenous fluids [47]. In suspected cases of acute urinary retention, an indwelling urethral catheter should be inserted immediately, although some authors prefer intermittent catheterization [48].

In women judged to be at high risk of retention, suprapubic catheterization may be a preferable option. This can be performed easily at the time of surgery and avoids the need for repeated urethral catheterization. Following removal of a catheter, close monitoring of fluid balance should be continued to prevent recurrent retention.

As voiding difficulties are more common following continence procedures, it is important that women are counseled adequately. The need for suprapubic catheterization, which may occasionally be prolonged as well as the occasional need for clean intermittent self-catheterization (CISC), should be carefully explained preoperatively.

When voiding difficulty is predicted by urodynamic studies, it may be worth teaching CISC prior to surgery. Even though perhaps only a minority of these women will need to self-catheterize, from the psychological standpoint, short-term voiding problems are much better dealt with when they have been anticipated. In other cases, sending patients home with a catheter (urethral or suprapubic) on free drainage for a week or two, followed then by a trial without catheter, is usually a successful strategy.

It is our policy to give patients going home with urethral catheter prophylactic antibiotics to preempt a UTI. A Cochrane review into antibiotic policies for short-term catheter bladder drainage in adults (up to and including 14 days) has also shown that there is evidence that antibiotic prophylaxis compared to giving antibiotics when clinically indicated reduced the rate of symptomatic UTI in female patients with abdominal surgery and a urethral catheter for 24 hours. The evidence indicated that receiving antibiotics during the first three postoperative days or from postoperative day two until catheter removal reduced the rate of bacteriuria and other signs of infection such as pyuria and gram-negative isolates in the patient's urine [49].

Hemorrhage

Intraoperative Hemorrhage

Significant hemorrhage is very rare following urogynecological surgery. In the event of massive hemorrhage, it is important to monitor the coagulation status of the patient repeatedly during resuscitation to diagnose the onset of a consumptive coagulopathy. If an abnormality develops, expert advice from a hematologist should be sought. In cases of massive intraoperative bleeding complicated by coagulopathy, it may be very difficult to achieve hemostasis. In such situations, the use of pelvic packs for 48 hours may be the only option, although this necessitates a second laparotomy to remove the packs. Occasionally, embolization of actively bleeding blood vessels using interventional radiology techniques may be an effective alternative to surgery.

Postoperative Hemorrhage

The management of hemorrhage in the immediate postoperative period may be approached in several ways. In broad terms, bleeding may be classified as either localized or generalized.

If localized, the bleeding is usually related to the operative site and/or the wound. Occasionally, the bleeding may be at a point removed from both these areas, for example, gastrointestinal hemorrhage from a stress-related gastric erosion. Bleeding from the wound site is usually indicative of a mechanical problem or a local sepsis. Generalized bleeding may reflect a coagulation disorder and may be manifested by the oozing of fresh and unclotted blood from wound edges and with bleeding from sites of cannula insertion.

Most cases of reactionary (and primary) hemorrhage are from a poorly ligated vessel or one that has been missed and are not secondary to any coagulation disorder. The bleeding point may go unnoticed during the operation if there is any hypotension and makes itself known only when the patient's circulating volume and blood pressure have been restored to normal. The bleeding in secondary hemorrhage is due to erosion of a vessel from spreading infection. Secondary hemorrhage is most often seen when a heavily contaminated wound is closed primarily and can usually be prevented by adopting the principle of delayed wound closure.

The approach to management will depend on the overall condition of the patient and the assessment of the type of bleed. A stable patient with a localized blood-soaked dressing will be managed differently from a hypotensive patient with 2 L of fresh blood in an abdominal drain, who in turn will be managed differently from a patient with a low platelet count and fresh blood oozing from all raw areas.

In the first case, the tendency might be to apply another dressing in an attempt to achieve control by pressure. A more positive approach is to remove the dressing and inspect the wound. In most instances, a single bleeding point can be identified and controlled. In the next case, the patient has a major bleed and this is probably from a bleeding vessel within the operative site. Return to the operating room and formal re-exploration must be seriously considered. In the third case, the prime problem is one of an anticoagulation defect requiring urgent correction.

The diagnosis of postoperative hemorrhage is a clinical one, based on the knowledge of the surgical procedure, the postoperative progress, and an assessment of the patient's vital signs. The blood loss may not always be visible and could be concealed at the operative site or within the digestive tract. The treatment of postoperative hemorrhage depends on the severity of the bleed and the underlying cause. Hypovolemia and circulatory failure will demand urgent fluid replacement and consideration of the likely cause and site of bleeding. Careful consideration must be given to control of localized hemorrhage and whether reoperation is warranted. Decision regarding re-exploration may be difficult and the advice and help of the most experienced person should be sought. As a general rule, the sooner after the surgery the bleeding presents, the more likely that re-exploration will identify a single obvious bleeding vessel, whereas delayed bleeding is usually due to infection.

Infection

It is uncommon for women undergoing routine urogynecological procedures to develop infections in the immediate postoperative period, if they have been given prophylactic antibiotics as outlined previously. A recent large study looking at morbidity outcomes in nearly 80 thousand hysterectomies done for benign indications showed that the odds of postprocedural infections (excluding UTI) were generally lower for women who had vaginal hysterectomies. The odds of UTIs were higher in women undergoing hysterectomy for leiomyoma, genital prolapse, and pelvic inflammatory disease [50]. Early detection and vigorous treatment in accordance with hospital protocols is vital in the management of any postoperative infection.

Bowels

Routine procedures such as hysterectomy done for benign indications are not associated with significant alteration in bowel function in the postoperative period. In a recent prospective cohort study, neither abdominal nor vaginal hysterectomy has been associated with constipation, aggravation of constipation, or rectal emptying difficulties 3 years after surgery [51]. In our practice, we routinely advise a mild suppository on the second postoperative day to ensure normal bowel function prior to discharge. All patients with a history of constipation are advised on regular laxatives to ensure regular bowel movements. We would recommend the use of Senokot or Movicol rather than Fybogel or Lactulose.

Removal of Suture and Pelvic Drains

Most urogynecological surgery is performed vaginally using absorbable sutures. In the minority of women who undergo abdominal surgery, removal of skin sutures is usually arranged on the fourth to sixth postoperative day if nonabsorbable sutures have been used. Pelvic drains may be used in conjunction with surgery; the general rule is to remove these when they are no longer draining significant amounts of fluid, most commonly the morning after the procedure.

Mobilization

Early postoperative mobilization is beneficial in the prevention of VTE [52] as well as postoperative ileus [53].

Follow-Up

It is our routine practice to arrange follow-up appointments for all patients at 6 weeks postoperatively as well as to arrange postoperative urodynamic assessment at the 6 months postoperative visit for all patients who have undergone continence surgery.

CONCLUSION

Adequate preparation for surgery has an important role in ensuring an optimal outcome and reducing morbidity. The elective nature of most urogynecologic surgery allows time to ensure that all women are well prepared, both psychologically and physically, before undergoing the chosen operation.

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70 Traditional Surgery and Other Historical Procedures for Stress Incontinence

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INTRODUCTION

The surgical management of stress incontinence has traditionally been based on basic principles with slight modifications accompanied by the occasional advancement by a handful of individuals, leading to dramatic changes in practice.

Our concept of what is historical or obsolete can change rapidly. In part, this reflects the emergence of new and compelling clinical or economic evidence [1,2], but there is no doubt that fashion also plays its part. Surgeons are easily seduced by new technology, and a woman's perception of whether a procedure is newer or older affects the choices she makes [3]. The regulation of new techniques, in most countries, is almost absent, and so the commercial pressure on manufacturers to exploit the market is irresistible. Innovative techniques that facilitate rapid turnover and minimal hospital time are embraced by healthcare providers long before anything is known about the long-term outcomes or risks.

These have been powerful influences and so, once popular operations such as autologous fascial slings, biological grafts, needle suspensions, and anterior colporrhaphy (AC), as well as lesser known operations, find themselves relegated to the historical section of this book. This is in line with the current guidelines from the National Institute for Health and Clinical Excellence (NICE) [2], the International Consultation on Incontinence (ICI) [4], and the American Urological Association (AUA) [5]. However, recent concerns by the Food and Drug Administration (FDA) regarding mesh have presented surgeons with a unique challenge as patients may approach surgeries involving mesh with trepidation, suggesting that these "historical" procedures may become relevant yet again. Thus, a careful review of these techniques remains a valid study, partly as it provides a backdrop and illustration of the changing thought processes that have emerged over the years, but also as a yardstick against which newer techniques can be compared.

AIM OF SURGERY

The aim of any operation for stress incontinence is to achieve balance between continence and voiding as simply and as durably as possible without serious operative complication such as the creation of obstruction or urgency.

It has always been understood that by simply obstructing the urethra, one could render a woman continent. Early slings addressed the problem in this way with an acceptance that obstruction could result in urinary retention.

A long-held belief about the etiology of stress incontinence declared that it was necessary to lift the urethrovesical junction and hence proximal urethra into an intra-abdominal position, in order that during moments of increased pressure, that pressure could be equally conveyed to the bladder and urethra with no resultant leakage. This was the basis of retropubic suspensions such as the Marshall–Marchetti–Krantz (MMK) and Burch colposuspension as well as subsequent needle suspensions.

Blaivas popularized a classification of stress incontinence in which the cause was seen as either anatomical, due to hypermobility of the urethrovesical angle (type 1) or rotational descent of the bladder base (type 2), or alternatively due to intrinsic sphincter deficiency (ISD) (type 3) [6]. Diagnosis along these lines made urodynamics—even video urodynamics essential. It followed then that where hypermobility was identified that procedures to elevate the bladder neck were used, and where ISD was shown, an obstructing procedure would be chosen. The current prevalent view—based on DeLancey's theories [7]—holds that there is a passive component of compression against a "backboard" created by the normal supporting structures of the urethra and bladder base, together with an active sphincteric component, which provide continence. However, since midurethral slings have proved effective in stress incontinence of either type, this distinction has become less critical, at least at the time of primary surgery.

INDIVIDUAL CHOICES

The need to treat each patient individually is obvious. There are many factors that, intuitively, one feels must have an impact on surgery and its outcomes. However, the evidence to support the contributory significance of these “confounding variables” is generally poor or absent. The subject has been extensively reviewed as part of the work of the ICI working group on surgery for women with incontinence [8].

Age, parity, estrogenization, and body mass index are all factors that might alter tissue quality and laxity. Previous surgery will usually have produced scarring with resultant tethering or fixity, possibly have interfered with normal sensory innervation, and possibly have altered sphincter function and pressure transmission in some way. The coexistence of varying degrees of hypermobility and descent of the vagina, the bladder base, and its fascial supports, and how much this bothers the patient, will influence the choice of surgery. While there is no evidence that coexistent medical conditions affect results of stress incontinence surgery specifically, surgeons tend to think that coughing and straining at stool are likely to adversely affect mechanical repairs and that comorbidities that are known to affect healing, such as diabetes, will also have a negative impact.

The psychological profile, expectations, and motivation of women will differ greatly, and this may significantly alter perceptions of outcome, even when the degree of urinary control experienced by two individuals is the same.

All of these issues require good-quality research studies to establish their importance. How much we should take them into account when choosing operations or interpreting what we read is unclear, while the ideal operation would work just as effectively regardless of these factors.

INTERPRETING THE LITERATURE

The randomized controlled trial (RCT) in surgery remains something of a rarity. Two reviews in the 1990s found that the total number of women in the world who had ever been recruited into a randomized trial for stress incontinence surgery was less than 600 in only seven studies [9,10]. By 2006, there were 53 RCTs and over 5000 women had been treated in this context [2]. However, the quality of that evidence remained poor, and there is probably only one adequately powered study to pass the demanding test set by CONSORT [11] in the field of stress incontinence research [12]. Even in recent years few RCTs have been devoted to these procedures, many of which are now considered obsolete.

There are other problems with the literature. The lack of consistency of outcome measures makes comparison of evidence dangerous. Many authors refer to subjective and objective cure rates, but these terms are rarely defined. There are degrees of objectivity, and it is debatable whether a quality-of-life questionnaire is truly objective unless the context in which it is applied is both independent and carefully controlled [13]. Some papers report complications and others do not. In some cases, outcomes have been recorded by “chart review” and in others by independent assessors using validated tools.

Most innovators are constantly changing their surgical practice in search of refinements, which make procedures easier, quicker, cheaper, less morbid, or more effective. Thus, it is rare for the original technique described to remain constant over the years that the surgeon performs it, and one must question the extent to which, when operations are lumped together into a series, the procedure was truly the same for every woman. Surgeons remain reluctant to report poor outcomes, and publication bias always favors the positive message.

One critical issue is how nonattenders and dropouts are reported. Most studies ignore them and offer their results as a proportion of patients who were available for follow-up. However, this makes unsafe assumptions about nonattenders, which may not be justified. The UK tension-free vaginal tape (TVT) versus Burch colposuspension trial [1] illustrated this point very clearly—in the same study, success could vary from less than 30% to over 90% depending on the outcome definition and which population was analyzed. We have observed the same phenomenon in the trial of two lengths of autologous fascial sling [14].

An interesting debate is emerging about the relative value of RCTs on the one hand and large national or international registries on the other. The RCT asserts a rigor to the collection and reporting of data, but sanitizes recruitment and disallows the kind of individual decision making and modification of approach that occurs with patients in normal practice. This results in poor external validity. The large-scale registry, on the other hand, can include all women and all surgeons [15].

For the purpose of this review, evidence has been presented as the original author intended. In most cases, this is a “per protocol” analysis in which dropouts are disregarded. A few studies report outcomes as “intention to treat,” and this is often what accounts for apparently poorer results. What matters most to women who are about to undergo surgery is what happens in the hands of their surgeon, and for this reason, surgeons should audit their own outcomes rigorously and compare their performance with others by participating in larger registries.

ANTERIOR COLPORRHAPHY

The operation (AC) aims to restore a normal anatomical position of the anterior vaginal wall by means of plication sutures to the endopelvic fascial layers between the bladder base and vaginal skin. These structures, under normal conditions, provide support to the bladder base, urethra, and entire sphincter mechanism. The thinking behind this was to restore the urethrovesical junction to an elevated position above the urogenital diaphragm and to provide a restored backboard against which the urethra could be compressed during coughing, straining, etc. The obvious flaw in this proposal is that success will depend on the integrity of intrinsically weak and damaged tissues. Ultimate failure therefore seems inevitable unless the scar tissue, which replaces the weakened fascia, will have greater strength than normal fascia. Many authors have added a sling to colporrhaphy to support the urethra—this makes interpretation of the evidence from these studies difficult to interpret [16].

The operation begins with infiltration of the anterior vaginal wall to perform hydrodissection of the vesicovaginal plane. A longitudinal incision is made from the urethral meatus to the vaginal apex and held apart using Allis forceps.

Lateral dissection of this avascular plane continues laterally sufficiently to expose the hernial defect in the endopelvic fascia, and, in women with significant prolapse, this may be extended as far laterally as the pubic ramus to fully expose the bladder base and urethra. The next step is to place “buttressing sutures” to the fascia on either side of the urethrovesical angle or bladder neck and one or two additional similar sutures to the paraurethral tissues—these sutures are tied in the midline, creating a shelf or hammock upon which the bladder neck and urethra will then be supported. Any additional prolapsing of the bladder base, or cystocele, is then reduced by means of additional plicating sutures or alternatively by means of a purse-string suture—in effect a reduction of the hernia with consequent cranial distortion of the bladder neck. The judgment in this procedure is in providing enough support to the previously prolapsed structures while avoiding overtightening and consequent vaginal narrowing. Excess vaginal epithelium is then sometimes trimmed away though not all surgeons would do this because of the attendant risk that removal of the epithelium could cause a stenosing ring in the midvagina. All such narrowing can be a cause of postoperative dyspareunia.

In execution, if not in intent, this procedure was in effect a hernia repair. While this made some sense if the underlying defect constituted a central defect of the paravaginal fascia, many anterior wall defects result not so much from central attenuation of this layer but from loss of attachment laterally to the arcus tendineus fascia pelvis (ATFP). In these patients, it is possible for the central layer of vesicovaginal fascia to remain intact. The failure to make this distinction may lie behind some of the poor reported results for AC.

There is arguably still a place for anterior repair for the treatment of pure anterior wall prolapse or where stress incontinence is only a minor part of this problem. It can also be used in conjunction with another procedure such as a sling simply to control the cystocele element when both coexist.

A great deal of the literature on AC relates to its use in the repair of prolapse, and relatively few studies address the question of how it performs as a stress incontinence operation. This review focuses only on the latter (Table 70.1). Seven RCTs were identified, four of which compared AC to Burch colposuspension [17–20] and one which compared it to a four-corner Raz suspension [21]. A total of 180 women have been treated by AC in an RCT compared to 195 Burch. Objective cure ranges from 69% at 12 months to 37% at 5 years compared to 87% and 82% for Burch. Deterioration with time does seem to be a problem [18,21]. Two other studies listed compare AC to the newer transvaginal mesh procedures, though this is predominantly covered in another chapter. Both of these studies showed superior results at 12- and 24-month follow-up when compared to AC alone [22,23].

Seven separate cohort studies with follow-up in excess of 5 years were found, which reported comparisons with Burch [24–26] and MMK [27–30]. In these studies, the subjective cures for AC ranged from just 21% to 50%.

It does seem that the long-term outcomes for AC as a treatment for stress incontinence are poor, by any standards.

PARAVAGINAL REPAIR (PVR)

In women in whom there is anterior wall descent but maintenance of normal rugosity of the vaginal epithelium, there is usually an underlying defect of the paravaginal fascia. That is to say that the normal attachment of the endopelvic fascia to the ATFP has become disrupted, and very often in these women, the layer of the fascia in between the bladder base and vaginal epithelium remains intact. It is logical in such women to attempt PVR. The operation can be performed either transvaginally, retropubically, or laparoscopically. The latter two approaches will be described in other sections of this book. Paravaginal defect repair is more commonly reported in association with other techniques such as sling or Burch, so it is difficult to establish how much effect this procedure has on the control of stress incontinence.

When repaired through a vaginal approach, the operation commences as for an AC, but the dissection of the vesicovaginal plane continues laterally to the pubic rami and into the space behind the pubic ramus. In a normal woman, the thick layer of the endopelvic fascia will prevent further progress at this point, but when this layer has failed, dissection will continue into the retropubic space without difficulty.

Laterally, along the surface of obturator internus muscle runs the ATFP from the pubic symphysis anteriorly to the ischial spine laterally and can usually be easily palpated. A series of plicating sutures are then applied, which incorporate three bites each—the lateral structure of ATFP or obturator fascia, the medial structure of endopelvic fascia as it lies under the bladder base or paraurethral tissues, and thirdly the vaginal muscularis itself. A row of sutures is placed on each side and then carefully tied so that accurate tissue apposition is achieved without distorting the positions of the bladder neck or vaginal vault. As the sutures are tied, the anterior wall descent should be seen to reduce itself back toward a normal anatomical position. When performed from a retropubic approach, the same three layers of tissue are exposed and approximated using sutures placed from above. It has to be said that exposure is much easier through the retropubic or laparoscopic approach than through the vagina.

Scotti et al. [31] did a cadaver study in which he identified the strongest attachment points for this procedure—namely, the ischial periosteum and the obturator membrane—using these fixation points as the basis for plication of the more medial structures. His series of 36 women with stress incontinence achieved a 94% subjective cure rate at a median follow-up of 39 months.

The PVR would be a rare procedure to correct isolated stress urinary incontinence (SUI) and would only be potentially beneficial in the setting of preoperative hypermobility with an obvious lateral vaginal defect. One of the difficulties with interpreting any literature on this subject is the uncertainty about whether case selection followed these principles.

Once again, PVR has been reported more commonly in association with other suspensory procedures, and it is impossible from these studies to ascertain what contribution has been made by the PVR alone.

Only one RCT exists for PVR as a stress incontinence operation compared to Burch [32]. However, the length of follow-up was not reported, and “objective cure” was said to be 61% compared to 100% for Burch; thus, little confidence can be placed in this study.

In three case series, the subjective cure rate at a minimum of 12 months ranges from 43% to 94% [31,33,34]. In conclusion, there is insufficient evidence to support the widespread use of PVR alone for stress incontinence control. For urogenital prolapse, see further Section 8.

Table 70.1 Evidence Table for AC and PVR

	Outcome measures													
Author	Year	Study type	Evidence level	Intervention	Comparator[a]	No. of patients	FU mos	Objective cure	Objectively improved	Subjective cure %	Subjectively improved %	De novo DO or OAB	CISC/ prolonged retention	Prolapse (any)
AC														
Colombo et al. [20]	2000	RCT	1+	Ant colporrhaphy		34	m167	42		52				
					Burch	*37*	*m167*	*74*		*86*				
Kammerer-Doak et al. [19]	1999	RCT	1+	Mod Ant Colporr		16	12	40		19				
					Burch	*19*	*12*	*83*		*95*				
Bergman et al. [46]	1989	RCT	1−	Ant repair		99	12	69						
					Burch	*101*	*12*	*87*						
Bergman and Elia [18]	1995	RCT	1−	Ant repair		35	60	37				2.8		
					Burch	*38*	*60*	*82*				*2.8*		
Di Palumbo [21]	2003	RCT	1+	AC		52	>9	73.1						
					Raz 4 corner	*28*	*>9*	*85.7*						
Tamussino et al. [24]	1999	Cohort	2−	AC		107	60			61		10		
Cosiski Marana et al. [25]	1996	Cohort	2−	AC		57	m60			21				
Van Geelen et al. [26]	1988	Cohort	2−	AC		56	>60	31	31	31	31			3.6
Luna et al. [27]	1999	Cohort	2−	AC		77	m135.6			55				
Demirci et al. [28]	2002	Cohort	2−	AC		67	120			38				
Park and Miller [29]	1988	Cohort	2−	AC		336	>60	58						
Riggs [30]	1986	Cohort	2−	Mod Pereyra + AC		252	<204			50	50			
Altman et al. [22]	2011	RCT	1	TVM	AC	389	12	60.870		78.470				33
Tamanani et al. [23]	2014	RCT	1	TVM	AC	92	24	95.270	74.270	47.6				
PVR														
Colombo et al. [32]	1996	RCT	2	Abdo paravaginal defect repair		18		61		72		0	11	
					Burch	*18*		*100*		*100*		*6*	*17*	
Bruce et al. [33]	1999	CS	3	PVR		25		m17		72	84			20
Mallipeddi et al. [34]	2001	CS	3	PVR		21	>12			43				37
Scotti et al. [31]	1998	CS	3	PVR		40	m39			94				

Abbreviations: DO, detrusor overactivity; OAB, overactive bladder; CISC, clean intermittent self-catheterization; AC, anteri colporrhaphy; PVR, paravaginal repair; RCT, randomized controlled trial; CS, case series; mos, months; TVM, transvaginal mesh.

[a] Italics refer to comparator procedures only.

NEEDLE SUSPENSIONS

In the late 1950s, the most common operations performed for stress incontinence were the MMK and the AC. Pereyra felt that failure was less likely to occur if the suspensory sutures could be supported by the abdominal fascia rather than the periosteum of the pubic bone [35]. In this way, he believed that contraction of the rectus muscle would provide dynamic support of the bladder neck. He designed a special angulated trocar and cannula through which stainless steel wires could be inserted from a suprapubic stab incision to emerge lateral to the bladder neck about an inch apart (Figure 70.1). These wires in turn were tied over the rectus sheath to provide elevation of the bladder neck. A series of diathermy burns made with a pointed diathermy probe pushed through the vaginal skin lateral to the urethra was used to induce paraurethral scarring so that the wires could elevate fibrous tissue rather than cutting through. In his first 31 cases. there were apparently just three failures.

As is usual with all innovative procedures, other surgeons (including himself) immediately adapted and modified his ideas. However, it was not until the late 1970s and early 1980s that needle suspensions became highly popular. The essence of Pereyra's procedure—placement of nonabsorbable sutures through the retropubic space by means of a long needle/suture carrier, fixation at one end to paraurethral tissues, and at the other end fixation to the rectus fascia (RF)—was the basis of every subsequent modification of the technique.

Two major modifications led to the popularization of these techniques.

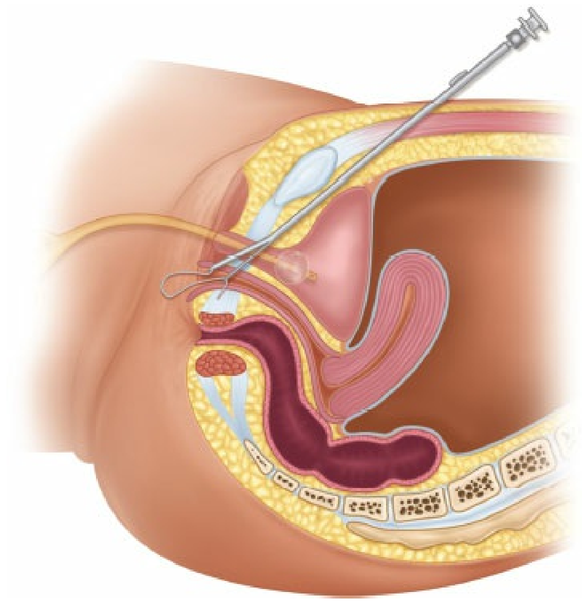

Figure 70.1 Pereyra operation. Illustration showing the angled trocar and needle used by Pereyra to load a stainless steel suture with a measured thickness of paraurethral tissue in between to facilitate elevation.

Stamey

In 1973, Tom Stamey described the use of the cystoscope to standardize the procedure [36]. The cystoscope was used both to check suture placement and also to adjust the tension so that appropriate closure of the bladder neck could be achieved.

Stamey's operation is performed in the lithotomy position using a weighted vaginal speculum. Having emptied the bladder with catheter placement and identified, by palpation, the position of the bladder neck, a T incision is made on the anterior vaginal wall to expose the urethrovesical angle. Many other surgeons, of course, adapted this, and incisions of all shapes have been used to expose the area

(Figure 70.2).

With minimal dissection of the vaginal wall away from the pubocervical fascia, a small pocket is created in the paraurethral tissues adjacent to and approx. 1 cm lateral to the bladder neck. Through two small suprapubic stab incisions, a single pronged needle (either straight or bent at 30°) is introduced, puncturing the rectus sheath and then downward through the retropubic space to emerge onto the tip of the surgeon's finger in the previously created pocket. The needle is threaded with a nonabsorbable suture and withdrawn. A 1 cm length of Dacron arterial graft is threaded onto the suture. A second needle passage is then made, about 1 cm from the first toward the same pocket and the remaining end of the suture pulled cephalad to emerge through the stab incision. On pulling up the sutures, the Dacron cuff settles into the pocket and pulls up the bladder neck on that side. This procedure is repeated on the other side.

At this point, the cystoscope is passed, and by pulling upward on the sutures, the surgeon can confirm that they are positioned correctly at the level of the bladder neck, that they are not passing through the bladder, and the correct amount of tension for tying the suture over the rectus sheath can be selected by observing the point at which the proximal urethral mucosa begins to oppose. Initial voiding difficulty was the norm, so the routine was to place a suprapubic catheter postoperatively and undertake an initial trial of voiding after say 48 hours.

This operation was devised at a time when the prevailing thinking was still that one should achieve elevation of the bladder neck, and this implied that tension need be applied.

All subsequent minimally invasive procedures for incontinence have applied this principle of midoperative cystoscopy until the advent of the obturator tape in recent years.

Stamey's original series reported a cure rate of 93% in 203 patients [37]. Modifications were inevitable and are difficult to identify in the literature—one notable exception is the use of silicone tubing rather than Dacron, to reduce the infection risk [38], inflammatory changes, and stones forming around the nylon threads. Cervigny [39] and Mundy [40] advocated the passage of needles from below to reduce risk of bladder injury. Golomb et al. [41] designed the double pronged ligature carrier to separate the passage of the two needles (Table 70.2).

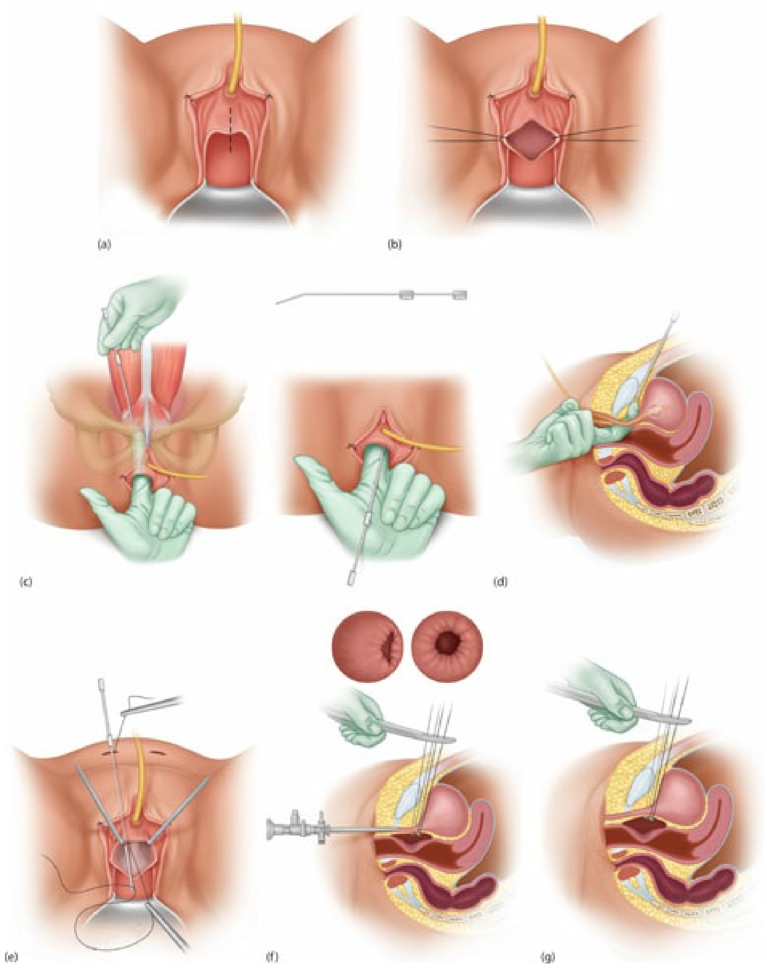

Figure 70.2 Stamey operation: (a) longitudinal vaginal incision, (b) exposure of the bladder neck and paraurethral fascia from below, indicating the points at which the Stamey needles should perforate the paraurethral fascia, (c) the needle can be passed downward to the vaginal incision or, applied to the index finger, from vagina to rectus sheath. This facilitates passage of the nylon suspensory sutures, (d) needle being passed downward onto the tip of surgeon's finger lying alongside bladder neck, (e) positioning of the Dacron cuff, which will support the paraurethral tissues, (f) the bladder neck is checked endoscopically to ensure that sutures do not pass through the bladder and the effect of suture tension on bladder neck closure can be checked, (g) final positioning of the bladder neck after elevation of sutures.

Table 70.2 Needle Suspension Evidence Table

	Outcome measures													
Author	Year	Study type	Evidence level	Intervention	Comparator[a]	No. of patients	FU mos	Objective cure	Subjective cure %	Total subjectively improved %	De novo DO or OAB	Pain any	CISC/ prolonged retention	Prolapse (any)
RCTs														
Mundy [40]	1983	RCT	1−	Stamey		25	>12		76					
					Burch	*26*	*>12*		*88*					
Palma [47]	1988	RCT	2	Stamey		40	>12	96			10	5		
					MMK	*30*	*>12*	*86*			0	0		
Hilton [48]	1989	RCT	1+	Stamey		20	m24	80	70		10			
					Porcine dermis	*20*	*m24*	*90*	*90*		*20*			
Bergman et al. [17]	1989	RCT	1−	Pereyra (M)		34	60		50					*n* = 2
					Burch	*38*	*60*		*16*					*n = 1*
					Ant repair	*35*	*60*		*54*					*n* = 3
Bergman et al. [46]	1989	RCT	1−	Pereyra (M)		98	*12*	*70*						
					Burch	*101*	*12*	*87*						
					Ant repair	*99*	*12*	*69*						
Athanassopoulos and Barbalias [44]	1996	RCT	1−	Stamey		24	>8	71		83			12.5	
					Burch	*27*	*>8*	*74*		89			*7*	
Gilja et al. [45]	1998	RCT	1+	Raz(M)		46	m36	80.4	84.8		6.8			
					Burch	*56*	*m36*	*89.3*	*92.9*		6.8			
Valpas et al [50]	2014	RCT	1	TVT	lap Burch	121	60	94	90	64				
Causlin et al. [51]	2013	RCT	1	TVM	AC+ Burch	68	48	100	70				0	
Cohort studies														
Spencer et al. [53]	1987	Cohort	2−	Stamey		41	m68		44	16		10		
Wang [52]	1996	Cohort	2−	Stamey		209	>24	20	10		12	4		
Christensen et al. [57]	1997	Cohort	2−	Stamey		83	m84		32	39			2	
Case series														
Kelly et al. [64]	1991	CS	3	Pereyra (M)		114	m42		51	76	30	26	16	

Trockman [65]	1995	CS	3	Pereyra (M)	125	m118		20	71				
Masson and Govier [66]	2000	CS	3	Pereyra (M)	135	m50		14	79				
Raz et al. [61]	1992	CS	3	Raz	206			83	90	14	5	2.4	5
Korman et al. [62]	1994	CS	3	Raz	106	m25	47	72	89	17	22	4	8
Gilja [63]	2000	CS	3	Raz (M)	71	>60	69						
Dmochowski et al. [68]	1997	CS	3	Raz 4 corner	47	m37		53	83				
Mustafa and Wadie [69]	2006	CS	3	Raz "in situ"	14	>11		86			14		
Huland and Bucher [55]	1984	CS	3	Stamey	66	m48	71	85		5	8		
Hilton and Mayne [38]	1991	CS	3	Stamey	100	m27	60			0	6		
O'Sulllivan [59]	1995	CS	3	Stamey	66	m43		34	62		7	3	
Gofrit et al. [60]	1998	CS	3	Stamey	63	m90		70		13		10	
Kuczyk et al. [58]	1998	CS	3	Stamey	85	m61		34	52		9	2	
Takahashi et al. [54]	2002	CS	3	Stamey	86	m38		90			17	17	
Elkabir and Mee [67]	1998	CS	3	Gittes	52	m53		23	50		10		

Note: Excluding case series with <50 patients except for odd operations.

Abbreviations:DO, detrusor overactivity; OAB, overactive bladder; CISC, clean intermittent self-catheterization; RCT, randomized controlled trial; CS, case series; MMK, Marshall–Marchetti–Krantz; mos, months; TVT, transvaginal tape; TVM, transvaginal mesh.

[a] Italics refer to comparator procedures only.

Raz

In 1981, Shlomo Raz described his personal take on the Pereyra operation, which was slightly different to Stamey [42]. His underlying principle was to use the nonabsorbable suture to grasp and bind together the component layers of the endopelvic fascia and to use this to provide support. In essence, his operation was a PVR because it reconstituted the same disrupted fascial layers as that operation (Figure 70.3).

After preparing the patient in a similar way to a Stamey or Pereyra procedure, an inverted U incision is made over the urethra to expose the underlying urethrovesical angle or bladder neck. Dissection then continues—more extensively than with Stamey—to open the endopelvic fascia on either side of the bladder neck. This is achieved by passing the tips of scissors behind the pubic bone, about 2 cm lateral to the urethra, and while keeping the tips in close proximity to the back of the bone, passing them in the direction of the ipsilateral shoulder and then rotating more caudally to pass through the retropubic space to emerge onto the back of the rectus sheath, which is then penetrated. A finger can then be inserted into the defect, though some surgeons prefer to do this using a long handled instrument to minimize tissue disruption.

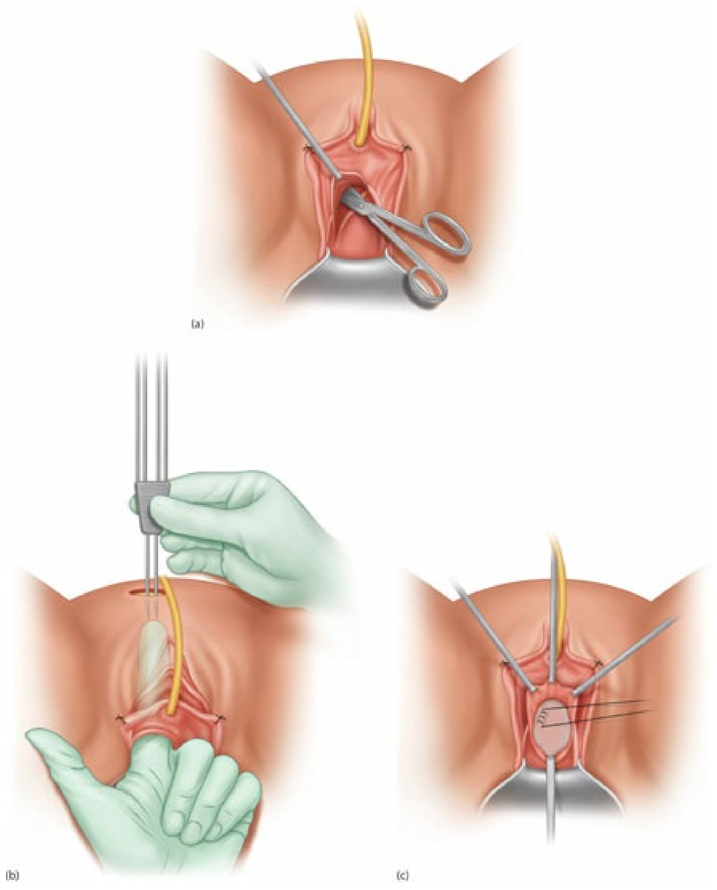

Figure 70.3 Raz cystourethropexy: (a) a lateral dissection of the paraurethral fascia, (b) a finger penetrating the retropubic space from the vaginal incision, and (c) a helical suture is incorporating endopelvic fascia, pubocervical fascia, and subdermal layer of vaginal wall.

The long handled needle is again used from above—passing downward through the retropubic space to reach the examining finger in the paraurethral defect and to pick up a nonabsorbable suture, which is pulled through to the suprapubic stab incision. However, before the second end is pulled through, three helical bites are taken with an attached needle to include three structures: the detached urethropelvic ligament/endopelvic fascia medially, the pubocervical fascia, and the subdermal layers of the vaginal wall. Once this suture is pulled together, the defect in the endopelvic fascia automatically closes and the tissues become elevated alongside the bladder neck.

Endoscopy was not described by Raz, but of course, many who subsequently performed this operation adopted Stamey’s recommendation of cystoscopy along with Raz technique of tissue plication rather than graft insertion.

In his first description of the new technique, he reported 96 of 100 patients cured of SUI [42].

Gittes

Whether the Gittes operation [43] represents a significant modification of these two highly popular operations is unclear—certainly, it never achieved the same degree of popularity. Gittes essentially dispensed with the need for any vaginal dissection by applying the same technique as Raz in terms of needle passage, but with passage of the helical sutures directly through the vaginal wall. His hypothesis was that the paraurethral dissection suggested by Raz was unnecessary—indeed it created a defect that might or might not have already been present only to immediately repair it again. By placing the sutures directly into the vaginal skin, he was securing the same layers, but they would cut through the vaginal skin and become buried in the paraurethral tissues where they would provide support. It is not clear whether the lack of dissection was an advantage or disadvantage in providing tissue of adequate strength to hold the sutures in place (Figure 70.4).

The outcomes from reviewed studies are shown in Table 70.3. Seven RCTs were identified for needle suspensions, making comparisons of needle suspension with the Burch colposuspension [17,40,44–46], anterior repair [17,46], MMK [47], and porcine dermis sling [48]. The evidence suggests that outcomes are inferior to retropubic suspensions (except for one study with poor methodology [47] in which there were more failures for MMK at 12 months) and equivalent to the results of the anterior repair/colporrhaphy. The Cochrane Review [49] on needle suspensions drew this conclusion after commenting that the quality of the studies was poor. More recently, there have been studies comparing transvaginal mesh placement to laparoscopic Burch colposuspension as well as to a combined AC and Burch combination repair showing that the transvaginal mesh repairs in both studies were superior, with sustainable results at long-term follow-up [50,51].

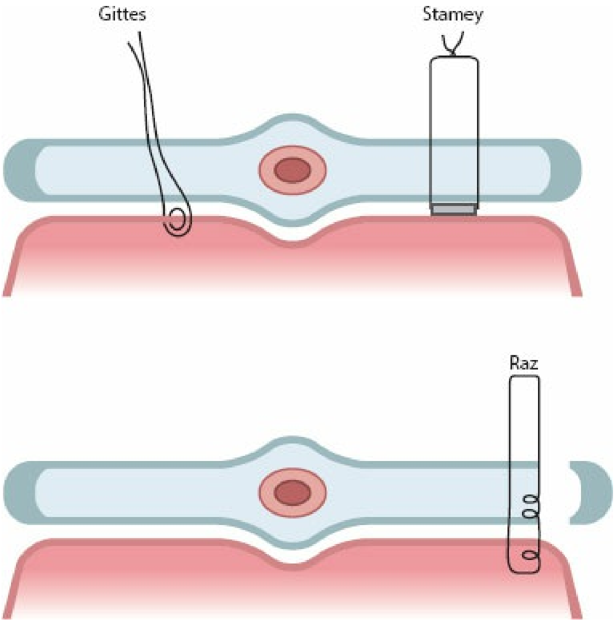

Figure 70.4 Schematic diagram to illustrate the different suture positions of (a) a Gittes suspension (vaginal wall only), (b) Stamey operation (Dacron cuff placed in paraurethral “pocket”), and (c) the Raz cystourethropexy (a 3-0 bite helical suture including pubocervical fascia, endopelvic fascia, and subdermal layer of vaginal wall).

Table 70.3 Evidence Table for Autologous Fascial Slings

Author	Year	Study type	Evidence level	Intervention	Comparator[a]	No. of patients	FU mos	Outcome measures Objective cure	Objectively improved	Subjective cure %	Subjectively improved %	De novo DO or OAB	Pain any	CISC/ prolonged retention	Prolapse (any)
RCTs															
Kaplan et al. [90]	1996	RCT	2	RF		43	m21			95		14		2	
					VW	*36*	*m21*			*97*		*8*		*0*	
Barbalias et al. [92]	1997	RCT	2	RF		*32*	*>30*				*66*				
					Gore-tex	16	*>30*				*87*				
Demirci and Yucel [93]	2001	RCT	2	RF		*17*	*>12*				100				
					Burch	17	*>12*				94				
Viseshsindh et al. [91]	2003	RCT	2	RF		*15*	*m7*			*93*		*13*			
					VW	*11*	*m7*			*100*		*9*			
Guerrero et al. [14]	2007	RCT	1+	RF		81	>60	29		62		*7*		2	
					short "sling on a string"	*84*	*>60*	*44*		*57*		*2*		*2*	
Albo et al. [12]	2007	RCT	1+	RF		326	>24		66			3		14	
					Burch	*329*	*>24*		*49*			*3*		*2*	
Krauschu [12]	2011	RCT	1	AFL	Buch	655	24	17				14			
Case series and Cohort studies															
Flynn and Yap [106]	2002	Cohort	2−	RF		71	>24			77	13			4	1
Rodriques [108]	2004	Cohort	2−	RF		128	m70			73	13	5		11	
Howden et al. [105]	2006	Cohort	2	RF		153	m85			72					
Giri et al. [107]	2006	Cohort	3	RF		46	>36	57	80						
Jeon et al. [104]	2008	Cohort	2	RF		87	m36			83		16		18	
Onur et al. [120]	2008	Cohort	3	RF		25	m18		68				8	8	

Muller et al. [101]	1993	CS	3	RF	108	m60			67				2
Zaragoza [103]	1996	CS	3	RF	60	m25			95		12	5	
Chaikin et al. [94]	1998	CS	3	RF	251	m37.2	73	92	73	92	3	0.4	2
Cross et al. [96]	1998	CS	3	RF	134	m22	93				19	0.7	4
Hassouna and Ghoniem [98]	1999	CS	3	RF	78	m41			81	86	21	25	0
Morgan et al. [100]	2000	CS	3	RF	235	m52			88	92	30		2
Groutz et al. [97]	2001	CS	3	RF	67	m34			67	97	10		
Hawkins et al. [99]	2002	CS	3	RF	198	m72			41	72	29	11	9
Chou et al. [95]	2003	CS	3	RF	98	m36			93		2		1
Reichelt et al. [102]	2004	CS	3	RF	86	m39	26		61	65			
AFL													
Wright et al. [126]	1998	Cohort	2–	AFL	33	m16			94				
Brown and Govier [127]	2000	Cohort	2–	AFL	46 (30)	m44			73	27		11	7
Almeida et al. [128]	2004	Cohort	2–	AFL	30	m33			70	20			

Abbreviations:DO, detrusor overactivity; OAB, overactive bladder; CISC, clean intermittent self-catheterization; RF, rectus fascia; FL, *autologous* fascia lata; RCT, randomized controlled trial; CS, case series; mos, months; VW, vaginal wall sling.

[a] Italics refer to comparator procedures only.

Ten case series or cohort studies for Stamey are reviewed with follow-up ranging from 12 to 90 months [38,48,52–60]. Outcomes are reported with widely differing measures, some objective and other subjective, ranging from 20% objective cure at 2 years to 90% subjective cure at a mean of 38 months. For the series reporting the Raz operation, the range is from 89% subjective cure at 12 months to 47% objective cure at 25 months [61–63]. The subjective cure rates from both the original and modified Pereyra [64–66] and the Gittes operation [67] do seem particularly disappointing. There are little data on the Raz four corner or in situ sling technique [68,69], and it is impossible to say how it compares to other procedures.

The general conclusion about needle suspensions is that the long-term results were disappointing. Those studies that presented outcomes at differing time points [17,46,63] appear to show a greater progressive deterioration with time than for Burch, but this difference does not reach statistical significance, since the event (failure) itself is uncommon. However, if one plots the length of follow-up, in case series, against subjective cure rates, no correlation can be seen. This is most probably because of differing definitions of cure. Urinary retention occurred between 2% and 17%, while de novo urgency was reported in up to 30% of individuals. Postoperative pain has been reported in up to 70% of women, but figures for long-term pain are sparse. Progressive prolapse tends not to have been reported in these series.

BONE ANCHORING

Leach was the first to describe the use of bone anchoring to provide support for the sutures of a needle suspension [70]. He was conscious of the tendency for nonabsorbable sutures used in needle suspensions to cut through tissues and result in failed support and or pain and felt that securing them to the rigid structure of the pubic bone would be more reliable. Benderev [71] in 1992 reported their use in 53 women with no initial complications and few failures.

The concept of being able to sell a bone anchoring device was appealing to the device manufactures, and two devices in particular were introduced. The Vesica system involved a screw, derived from orthopedic surgery, with electric driver that could be driven into the pubic bone through a small suprapubic incision [72]. A Gittes type of suspension was then applied in which the suprapubic needle passage penetrated the vaginal skin several times lateral to the bladder neck to create a Z-shaped configuration.

The other system (in tac) introduced at the same time involved a C-shaped drill device, which, when inserted into the vagina like an upside-down speculum, would drive a screw into the back of the pubic arch [73,74].

As with most new procedures, the initial results were encouraging and devices were enthusiastically employed in many women. However, in 2004 Goldberg reported osteomyelitis of the pubic bone, a serious complication potentially leading to a lifetime of pain and disability, in 3 of 290 women undergoing bone-anchored sling placement [75], after which other similar reports followed. Screw dislodgement also occurred at an unacceptable level [76], and other poor results were reported [77–79]. In 2003, NICE finally recommended that these techniques should be abandoned [80].

FOUR-CORNER VAGINAL PATCH

Raz, in his continued personal quest to find the fail proof operation for stress incontinence, developed a further modification of his earlier operation with the “in situ” vaginal wall sling in 1989 to obviate the need for implanting artificial mesh or indeed for transplanting autologous material from one place to another [81]. In concept, this was really a combination of needle suspension technique and autologous fascial sling.

With the patient in lithotomy position, a four-sided patch was incised in the vaginal wall based at the level of the bladder neck with the narrower edge over the distal urethra (Figure 70.5). Through the lateral margins of this incision, dissection was extended laterally and caudally and into the retropubic space as for a standard Raz procedure, but not underneath the patch. The patch was to be used as the autologous fascia with which to elevate the whole urethra. Four individual sutures were then inserted into the corners of this patch and passed upward through the endopelvic fascial defect by means of a needle carrier and then tied over the rectus sheath in the same manner as previously. Vaginal wall has the potential advantage that it is likely to be more flexible than harvested fascia and hence less likely to cause obstruction.

Initial results again were encouraging—93% of the first 160 women achieved continence at medium-term follow-up [82]. The operation never caught on—presumably because of its perceived difficulty and the concurrent emergence of simple and effective midurethral slings.

SLINGS

Well over 100 years ago, the principle of placing a strip of autologous tissue beneath the urethra to provide an obstructive effect was established. It is never quite clear in retrospect who made the first contribution since one relies entirely on what others have written on the subject. However, undoubtedly the person who popularized the concept of placing RF around the urethra was Aldridge in 1942 [83]. Previous descriptions of surgery had included the use of pyramidalis muscle tendon transplanted to elevate the urethra [84] and the addition of RF and bladder neck plication [85] to this technique. Modifications of this technique were practiced in some centers until fairly recently [86]. The gracilis muscle was also used as early as 1907 [87], and these tendon and muscle, innervated or otherwise, have repeatedly been used over the years to wrap both the urethra and the anorectum, but suffer from the extent of dissection and mobilization required, the bulk of tissue requiring accommodation in the new site, and overall poor results.

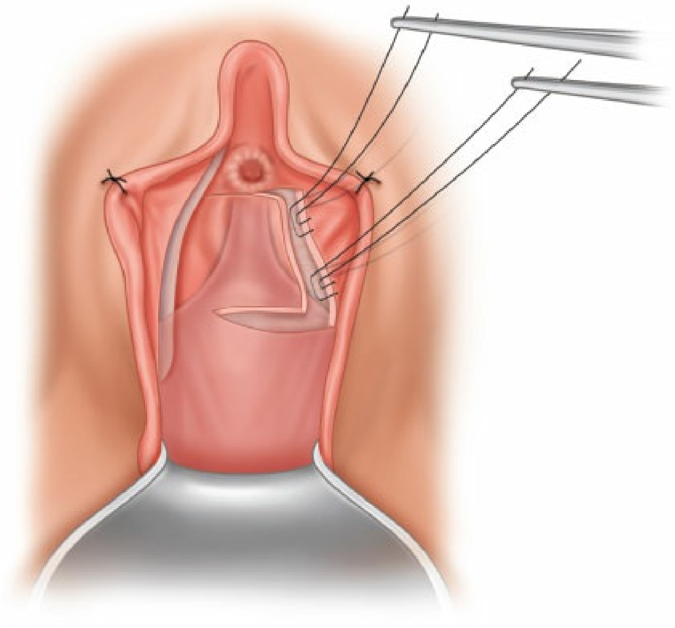

Figure 70.5 Four-corner “in situ” vaginal wall sling. A placard shaped incision is made with its base at the bladder neck and narrow edge distally to expose the paraurethral fascia. Four separate helical sutures are used to gather up the endopelvic fascia, pubocervical fascia, and the subdermal layer of the vaginal wall.

The mechanism of action of sling procedures has always been a subject of debate and uncertainty. Early wrappings with denervated muscle of one kind or another may have simply provided additional passive resistance, but subsequent designs in which slings were passed around the suburethra, at whatever level, and fixed above to an immovable structure, may have offered either passive occlusion during straining or possibly a dynamic component as well. The concept of a dynamic effect is that abdominal straining involves rectus muscle contraction, which will pull upward on the attached sling, thereby elevating the bladder neck for the duration of the contraction.

All slings therefore have the potential to obstruct the urethra or simply to provide passive occlusion during moments of stress. It is a feature of all biological materials, whatever their provenance, to have the potential to shrink/contract by up to 30% of their initial length. Shrinkage of this degree will obviously further elevate the bladder neck or urethra and risk causing voiding difficulty. The tendency may be more marked with some tissues than others, but this has not really been established. Every sling material should have more or less the same effect to begin with, but the specific material used evidently matters in terms of its capacity for shrinkage, infection, erosion, and subsequent stretching or failure, while the amount of tension applied to the sling and its positioning will possibly adversely affect filling and voiding function. Whether slings are inserted from top-down or bottom-up appears to make little difference though there is evidence that the more extensive the vaginal dissection required, the more likely it is that innervation will be disturbed [87].

Aldridge described an operation in which, following a transverse suprapubic incision, two strips of RF were mobilized in the line of the external oblique fibers, detached at their lateral extremities, and left attached to the RF close to the midline. Thus, strips of fascia were created at least 10 cm in length on each side (Figure 70.6). A midline suburethral vaginal incision was then made to expose the pubocervical fascia and dissection continued cranially toward the retropubic space. A midline colporrhaphy was first performed to provide bulking of tissue under the urethra, and the ends of the rectus strips were then passed downward through the retropubic space on each side to emerge into the vaginal incision on either side of the urethra. Here, they were then sewn together under the urethra to provide elevation and support of the urethra.

Of course, in the finest surgical tradition, the procedure has been much modified, a neat idea being that used by Warrell in which dissection of the medial component of the rectus strip was angled downward to create additional length, thereby also reducing the need for lateral dissection (Figure 70.6). Lateral dissection in the original procedure was complicated by the thinness of external oblique fascia beyond the lateral border of the rectus sheath and the risk of lateral angle pain postoperatively.

Leaving the sling attached at one end obviated any need for fixation except under the urethra, but this created difficulties in establishing the correct amount of tension; in addition, there were times when sometimes the sling would not reach the vagina.

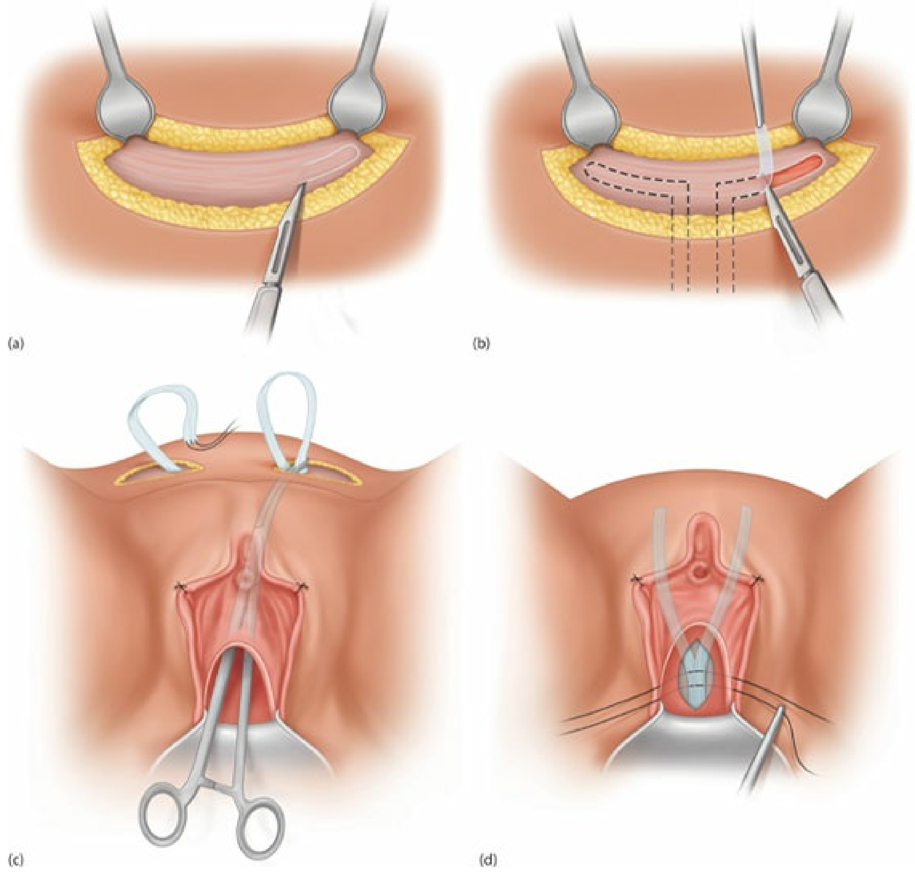

Figure 70.6 The Aldridge sling: (a) four separate fascial strips are mobilized with a medial attachment, (b) Warrell's modification provides extra length, (c) the lateral ends are tunneled down into the paraurethral space by attachment to a long-handled forcep, (d) the lateral ends are sutured together under the proximal urethra—the number and position of sutures will determine the degree of elevation and tension.

In 1978, McGuire reported the use of a free graft of RF, which facilitated adjustment of tension, though it is clear that his intention was to create a significant elevation of the bladder neck [88]. During his dissection of the vaginal end, he deliberately opened the bladder in order to prevent damage to it, a surprising suggestion coming several years after Stamey popularized peroperative endoscopy, in part, for the same reason. Blaivas also reported the use of a free graft [89], and, between them, these two surgeons radically influenced surgical practice throughout the United States over the next 20 years. The reasons for this were the growing awareness of poor long-term outcomes from needle suspensions and that a fascial sling would be effective in women with either hypermobility or intrinsic sphincter weakness or both. It became known that slings with less tension remained effective but with diminished likelihood of postoperative voiding dysfunction, which remained a problem for retropubic suspensions.

Full-Length Autologous Rectus Fascial Sling: Technique

The procedure described is that used throughout the 1990s; inevitably, modifications took place with the adoption of ideas from others and the growing realization that tension should be minimal and the midurethral rather than bladder neck support was the objective (Figure 70.7).

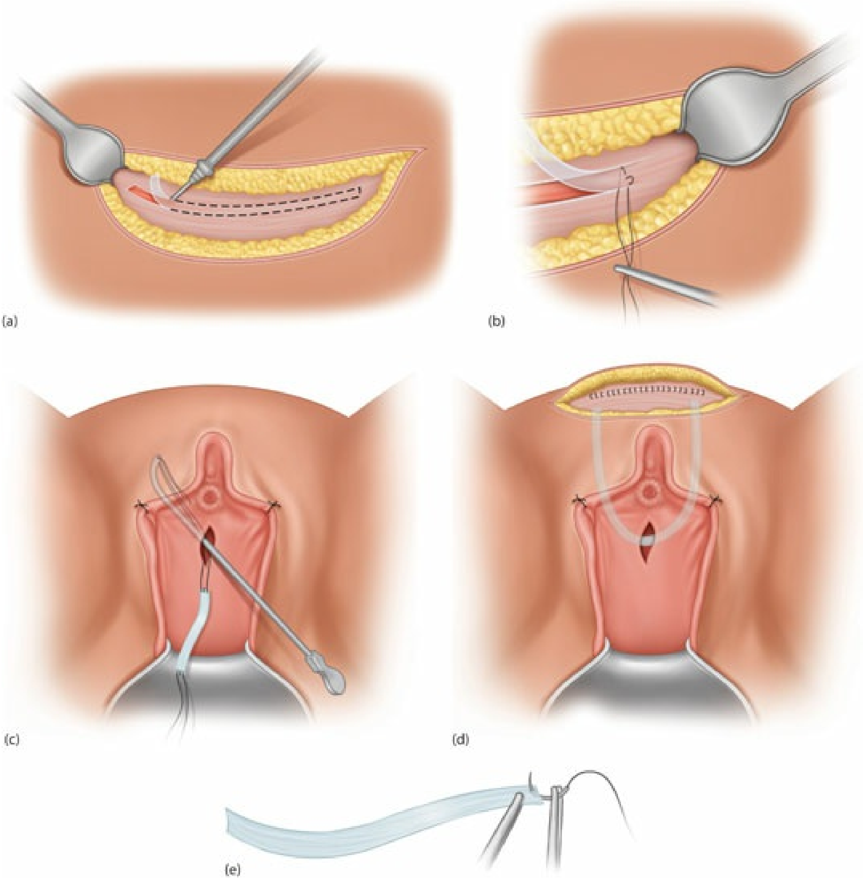

Figure 70.7 Free rectus fascia pubovaginal sling: (a) a free graft is fashioned from the rectus sheath. (b) Before dividing, a suture is placed through the lateral ends of the mobilized sling, (c) a modified Clutton sound is used to pass the suture with sling attached upward through the space of Retzius, (d) the ends of the fascial sling are sutured to the rectus sheath with minimal tension, (e) alternatively, a short length of fascia is used and mounted on nylon sutures to minimize the dissection of the rectus—"sling on a string."

The patient is placed in lithotomy position with the legs flexed to <90°. A degree of Trendelenburg tilt in the operating table provides a good view of the anterior vaginal wall and helps to autoretract any abdominal fat apron. Particularly, fatty labia may be temporarily gently sutured laterally to provide a good vaginal view. The bladder is catheterized, following which the anterior vaginal wall infiltrated with 1:200,000 epinephrine in saline solution. This may then be left for a few minutes while the abdominal dissection takes place (Table 70.4).

A transverse suprapubic incision is made down to the RF, and two parallel transverse incisions commenced in the rectus about 2 cm apart—these are extended laterally with scissors in the line of the fibers of rectus and external oblique—that is, angling upward. This dissection can easily provide 20–25 cm of fascia. Laterally, the fascia divides into two layers. Before dividing the fascial strip laterally, a transfixion suture of 2-0 nonabsorbable material is used to bind the tissues together. The fascia is then divided obliquely rather than at 90° so that the initial repair stitches will not cause too much tethering in the lateral angles—the probable cause of postoperative lateral angle pain. The fascial strip, which has been separated, is stripped of any attached fat and then wrapped in a saline-soaked swab for later use. The fascial defect is first undermined for a few centimeters with scissors and then repaired with multiple 2-0 nonabsorbable sutures applied at right angles to the cut edge of the fascia, thus ensuring proper alignment of the repair. The use of multiple small sutures spreads tension effectively and minimizes the risk of tearing, which will occur with larger, less frequent stitches.

Table 70.4 Evidence Table for Donor Materials

	Outcome measures														
Author	Year	Study type	Evidence level	Intervention	Comparator[a]	No. of patients	FU mos	Objective cure	Objectively improved	Subjective cure %	Subjectively improved %	De novo DO or OAB	Pain any	CISC/ prolonged retention	Prolapse (any)
Allograft fascia lata															
Basok et al. [115]	2008	RCT	1	FD FL		67	12	52	79			22		12	
					IVS	*72*	*12*	*47*	*70*			*6.9*		*11*	
Wright et al. [126]	1998	Cohort	2−	FL		59	m9.6			98					
Brown and Govier [127]	2000	Cohort	2−	FL		104	m12			74	19		1	2	
Flynn and Yap [106]	2002	Cohort	2−	FL		63	>24			71	13			1.5	
Almeida et al. [165]	2004	Cohort	2−	FL		30	m33			40	28				
Simsiman [129]	2006	Cohort	2	FL		80	m25	64		45					
Howden et al. [105]	2006	Cohort	2	FD FL		150	m42			57					
Onur et al. [120]	2008	Cohort	3	FD FL		24	m13		75				12	20	
Amundsen et al. [118]	2000	CS	3	FD FL		91	m19			63	84	15		1	2
Fitzgerald et al. [117]	2004	CS	3	FD FL		27	m12	59						4	
Huang et al. [119]	2001	CS	3	SD FL		18	m9.6			72	83				
Onur and Singla [130]	2005	CS	3	SD FL		25	m12	68	80	76		12		28 months 9 days	
Elliott Boone [116]	2000	CS	3	SD FL		26	m15			77	92	8			
Richter et al. [121]	2003	CS	3	FL		102	m35				75		28		
Soergel et al. [122]	2001	CS	2−	FL		12	m6	17	33	91					
Walsh et al. [123]	2002	CS	3	FL		31	m13.5			94	85			3	
Owens and Winters [125]	2004	CS	3	Duraderm		25	m6			68	92			12 > 2 weeks	
Nazemi et al. [124]	2008	CS	3	FL bone anchored		238	>24	71							

Porcine dermis															
Hilton [48]	1989	RCT	1+	Z		20	m24	90		90		20			
					Stamey	*20*	*m24*	*80*		*70*		*10*			
Arunkalaivanan and Barrington [133]	2003	RCT	2	P		74	>12			89				7	
					TVT	*68*	*>12*			*85*				*3*	
Guerrero et al. [14]	2007	RCT	1	P		50	>12	20	56					0	
					TVT	*72*	*>12*	*53*	*89*					*0*	
					RF	*79*	*>12*	*41*	*76*					*0*	
Jarvis and Fowlie [134]	1985	CS	3	Z		50	m21	78				4		2	
Kinn et al. [135]	1994	CS	3	Z		47	m20			68		4.2		2.1	
Giri [107]	2006	Cohort	3	P		48	>36	31	54						
Morgan [138]	2007	Cohort	3	P		30	>12	8				30		13	10
Simsiman [129]	2005	Cohort	2	P		83	m17	54		47					
Giri et al. [137]	2005	CS	3	P		40	m6	75	90			5	5		
Iosif [136]	1987	CS	3	P		53	>18			89				0	
Bovine pericardium															
Pelosi et al. [166]	2002	CS	3	BP		22	m20			95					
Lyophilized human dura mater															
Enzelberger et al. [132]	1996	RCT	1+	LD		36	m37	92				13		13	
					Burch	*36*	*m37*	*86*				*5*		*3*	
Rottenberg et al. [131]	1985	CS	3	LD		36	m6	89							
Porcine intestinal submucosa															
Jones et al. [139]	2005	CS	3	SIS		34	m24			79	88	3			
Rutner et al. [76]	2003	CS	3	SIS		152	m28				93	2			

Abbreviations:BP, bovine pericardium; DO, detrusor overactivity; OAB, overactive bladder; CISC, clean intermittent self-catheterization; RCT, randomized controlled trial; CS, case series; FL, fascia lata; FD, freeze dried; IVS, intravaginal slingplasty; SD, solvent dehydrated; P, Pelvicol; Z, Xenoderm; LD, lyophilized dura mater; SIS, subintestinal submucosa; RF, rectus fascia; TVT, tension-free vaginal tape; mos, months.

[a] Italics refer to comparator procedures only.

Attention is then returned to the vagina, and a 2-cm midline incision is made over the midurethra. The edge of the incision is lifted with strong toothed forceps and dissection commenced with Metzenbaum scissors, angled with the concave curve facing the surgeon, to create a tunnel toward the pubic arch. On making contact with the pubic arch, the scissors are turned so that they point toward the ipsilateral shoulder and gently advanced behind the pubic arch by a spreading motion in order to penetrate the endopelvic fascia and enter the retropubic space. The same dissection is then carried out on the other side. Despite the use of epinephrine infiltration, there are numerous tenuous veins applied to the endopelvic fascia, which can easily be ruptured by this dissection, and, consequently, at this point, bleeding can appear to be copious. This will almost always settle as the operation proceeds.

The sling can now be inserted into the tunnels on either side of the urethra. This can be done by using a long-handled Roberts forceps either passed upward with the sling attached using the previously applied sutures. The sound is then passed into the previously created tunnel on either side of the urethra and upward through the retropubic space to push through the back of the RF and emerge into the suprapubic wound a couple of centimeters caudal to the previous repair. The sling is then adjusted so that it lies comfortably under the midurethra and can be fixed into place using four 4-0 absorbable sutures to avoid curling or displacement of the sling. The free ends of the sling protruding through the RF can then be sutured into place using a nonabsorbable suture. For many years, this was done in such a way as to cause the urethral end of the sling to just begin to move cranially. An instrument can be placed between the sling, and the urethra as the slack is taken up or a cystoscope can be placed within the urethra at this point to ensure correct tensioning. Cystoscopy is also usually performed to ensure that no bladder injury has occurred and also to check the position of the sling in relation to the urethra. For this procedure, on account of the necessarily extensive suprapubic dissection, a suprapubic catheter would typically be placed and delay a trail of voiding for at least 48 hours; however, this has often been abandoned in recent years.

Fascia Lata

A disadvantage with RF is its varying thickness and length, and to overcome this problem, the use of host fascia lata was described. In this operation, the patient is first placed in a full lateral position and a line drawn on the skin between the greater trochanter and the lateral condyle of the femur (the external markings of tensor fascia lata). A series of two or three small transverse incisions are made over this line and dissected down onto the muscular fascia. Using these small incisions for access, two parallel longitudinal incisions are made into the fascia lata, 1.5–2 cm apart and extended with dissecting scissors (Figure 70.8). By performing the same technique in two or three sites, a length of up to 20 of fascia can be mobilized and separated from its ends. The resultant defect does not widen (as is the case with the RF defect) and so does not need to be closed. However, pain and hematoma can still occur so a small suction drain should be placed.

The patient is then placed in the standard lithotomy position, and the sling is inserted around the urethra through a combination of suburethral and suprapubic incisions and fixed either to itself over the rectus sheath or alternatively to the rectus sheath itself (Figure 70.7).

The way in which autologous sling surgery is performed has matured gradually over the years, and it is a little contrived to suggest that all slings done before a certain date should be consigned to history. Nevertheless, for this chapter only, those slings that could be identified to be full-length fascial strips are reviewed—shorter supported slings are left out. However, the precise positioning and varying degrees of tension are impossible to classify by review, and so the evidence presented is a somewhat selective view of the evidence.

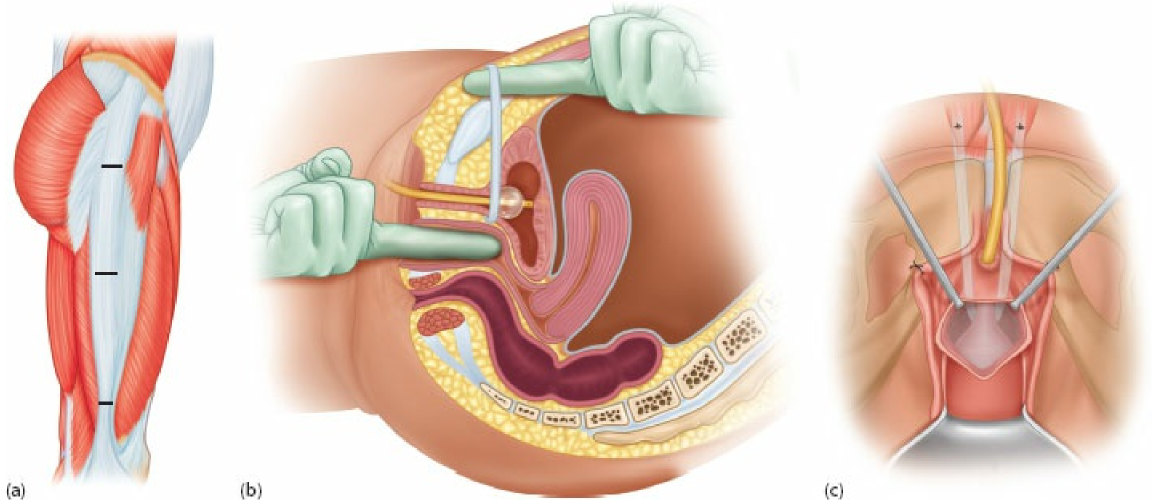

Figure 70.8 Fascia lata sling. (a) Diagram showing the skin markings and incisions required to mobilize a strip of fascia lata from the lateral thigh. (b and c) Original technique described by Govier for placing a fascia lata sling around the urethra and sutured to itself over the rectus sheath.

Some very small RCTs in which the quality of study was considered to be very poor have been left out. Six RCTs comparing rectus fascia to other interventions are reviewed involving 514 women (326 in one trial) [12,14,90–93]. A further 16 studies are reviewed, which present either a case series [94–103] or one arm of a cohort study [104–108] of women receiving autologous RF, involving over 1800 women in total. The single large-scale RCT [12] shows that the efficacy of RF is superior to Burch colposuspension though the risk of adverse events is higher. Guerrero et al. [14] showed that the efficacy and risk of shorter suspended slings equate to full-length slings, and this evidence reflects the changing use of rectus fascial slings in which the use of full lengths has become unusual and shorter lengths the norm.

Rates of urinary retention range from 0% to 18%. Postoperative pain (of any type) ranges from 0% to 25% and de novo urgency from 2% to 30%, the median value being 15% in those studies that reported this outcome.

A Cochrane Review in 2005 of traditional sling surgery [109] failed to draw any conclusions about the relative efficacy or risk of various sling procedures. Complications of autologous sling have included hemorrhage, wound infection, and bladder perforation. Long-term complications include de novo urgency, voiding difficulty, lower abdominal pain, incisional hernia, and erosion. However, a well-funded study reported by Albo establishes the relative efficacy and risk of RF sling and Burch with confidence [12]. Additionally, according to recent AUA guidelines, the estimated cured/dry rates for an autologous sling (rectus fascia or fascia lata) ranged between 90% at 12–23 months and 82% at 48 months or longer [5]. This is supported by the recent Stress Incontinence Surgical Treatment Efficacy Trial was performed, which was a multicenter RCT of 655 women randomized to autologous sling versus Burch. The study showed a higher success rate in the treatment of stress incontinence with the autologous fascial sling (47% vs. 38%, $p = 0.01$) but also a higher complication profile when compared to the traditional Burch repair [12].

Donor Materials

The major disadvantage of all autologous grafts used for sling surgery is that they require significant dissection, and this brings with it potential for morbidity—especially bleeding and pain.

Consequently, the use of donor materials to perform a similar procedure has been extensively explored over the last 15 years. By using preprepared strips of donor tissue, a sling procedure becomes minimally invasive with the need only for a small suburethral incision and one or two small suprapubic incisions. The possibility of local anesthetic procedures carried out in a day case setting, with the commensurately low use of hospital resources, is highly attractive to patients and health commissioners alike, even if the cost of the material used is relatively high.

Knowledge of how biological grafts behave in humans with the passage of time is scant though many animal studies have been done to explore this question. It is known that autologous fascia will become rapidly infiltrated by neovascularization and fibroblasts. Whether the grafted tissue remains intact or is completely replaced by new fibrosis however is not clear. Woodruff et al. biopsied 24 explanted grafts and found that, while host tissue infiltration was greatest with polypropylene meshes, autologous fascia and porcine dermis degraded, with the latter became encapsulated with no sign of tissue infiltration [110]. Lemer studied the mechanical properties of a variety of implantable materials and showed that solvent-dried fascia lata and dermal allografts were as strong as autologous fascia but that freeze-dried fascia lata was substantially weaker [111].

Although Karram (1990) was first to describe fascia lata in 10 patients [112], Beck was probably the first person to use the technique since he wrote up a 22-year series in 1990, having started in 1965 [113]. Beck reported a 100% success rate for his most recent 148 cases—out of 170—stating that failure occurred in 13 of his first 22 patients. However, only 12 patients of this series were followed for more than 5 years, and whether the women themselves were asked if they felt cured is not clear.

ALLOGRAFTS

Allograft (cadaveric) fascial material can be implanted into humans once all cellular and antigenic material has been removed. This is achieved by freeze-drying, by fresh freezing, or by solvent dehydration techniques. All of these have been used in women with stress incontinence. The risk of disease transmission (e.g., hepatitis B and C, HIV, and variant CJD) has always been a fear, but manufacturers offer strong reassurances that this is theoretically impossible. Selection of donors for allograft material involves rigorous screening for disease [114], and there have been no reported cases as yet.

Once implanted, allograft material goes through a similar process of fibroblast invasion and neovascularization to autologous tissue, but the timing of these steps is unpredictable—hence, there may be a period of relative weakness before step 2 when grafts can give way.

One RCT was found, which compared cadaveric fascia lata to intravaginal slingplasty [115], one of the new generations of minimally invasive techniques. The data are limited to short-term follow-up, and no conclusions can be drawn about relative efficacy.

A further 10 case series [116–125] and seven cohort studies [105,106,120,126–130] including over 1000 women who received cadaveric fascia lata are reviewed. Subjective cure ranged from 40% to 98% and objective cure from 17% to 68%. However, the range of follow-up and outcome measures, as usual, varies so much that it is impossible to draw conclusions about the relative merits of freeze-dried versus solvent-dried preparations or how this procedure compared to other autologous or synthetic grafts. One study [124], which used bone anchors, shows progressive deterioration over time, but it is not clear whether the failure is related to the material or the method of anchoring used. Fewer complications were reported for fascia lata than for other types of autologous fascia but not in the context of randomized trials.

The other main allograft material that has been used is lyophilized dura mater. There are data from a case series [131] and one RCT comparing dura mater to Burch [132]. The limited medium-term results suggest a higher efficacy than Burch but with more urgency and voiding problems.

XENOGRAFT

Xenograft (animal) tissues have also been used and are prepared using similar techniques. After going through a stepwise process of cellular destruction and sterilization, these materials essentially provide a framework of collagen, which lends itself to invasion with fibroblasts and new blood vessels. Whether the tissues become completely replaced by host fibrous tissue or remain intact remains unclear.

Of the available xenografts materials, more has been written about porcine dermis. Xenoderm was a dried preparation requiring preliminary soaking before implantation, while Pelvicol is a prewetted dermal graft that handles much like a piece of autologous fascia. One early RCT with 12-month follow-up promised excellent outcomes from Pelvicol when compared to TVT [133]. Case series presenting early outcomes from Pelvicol implantation [133] promised encouraging efficacy, but longer-term studies have shown unacceptable failure rates.

Two case series [134,135] and one RCT [48] reported the use of Xenoderm. The material was awkward to handle and was withdrawn from the market by the manufacturers in the mid-1990s.

Pelvicol has been reported in two case series [136,137] and in three cohort studies [107,129,138], one reporting high failure rates at medium-term follow-up. The two RCTs involving Pelvicol present totally different outcomes, one with 89% subjective cure at 12 months [133] and the other reporting (Guerrero) only a 20% objective cure at 12 months.

Small intestinal submucosa has also been used for urethral support as well as many other uses. There are no data from RCTs, but two case series focus exclusively on women with stress incontinence [76,139]. There have been conflicting reports on the extent of tissue reaction related to the use of this tissue [140,141].

Synthetics

As aforementioned, the long-term durability of these procedures with graft materials has been questioned, with reports of graft failure and declining success rates over time [5]. As such, the midurethral synthetic sling was developed, replacing the pubovaginal sling as the gold standard for stress incontinence, and thus, polypropylene mesh is worth mentioning here as a graft material though it is discussed at length in another chapter [142].

The AUA SUI guideline panel's meta-analysis estimated cured/dry rates in patients without prolapse treatment ranging from 81% to 84% at all time points, which is comparable to the medium-term results for the Burch suspensions and autologous fascial slings, showing comparable efficacy between midurethral slings and autologous slings in the surgical treatment of stress incontinence [5].

However, in 2008, the FDA issued a statement cautioning against the vaginal placement of mesh for both pelvic organ prolapse and urinary incontinence. In 2011, an updated FDA warning stated that most mesh-related complications were associated with the transvaginal placement of mesh for pelvic organ prolapse, and there were insufficient data to recommend against using mesh for SUI [143]. Nonetheless, patients are not necessarily aware of these differences and should be counseled appropriately prior to any surgical intervention, especially when voicing concerns about mesh placement [144]. As such, patients should be informed that synthetic slings are considered a first-line treatment option for stress incontinence. In fact, the American Urogynecologic Society and Society of Urodynamics, Female Pelvic Medicine, and Urogenital Reconstruction issued a joint statement in 2014 strongly supporting the use of polypropylene mesh for the treatment of SUI, stating that the midurethral sling procedure is safe and effective and remains the standard of care for the treatment of SUI [145].

BULKING AGENTS

Coaptation of the urethral mucosa is thought to be an important contributory mechanism in maintaining continence, the effect being apparently conferred through submucosal vascular cushions. Attempts to improve this coaptation effect through minimally invasive injection techniques have challenged clinicians for over 50 years. The mechanics of urethral bulking seem to be that by increasing the passive resistance of the urethra, leakage is diminished. The ideal injection material should be nonimmunogenic, thus causing no localized inflammatory reaction; stable chemically; nondegradable so that its bulking effect remains; and easy to inject to minimize the difficulties of surgery. Since most of these agents consist of particles suspended in a carrier gel or fluid, it is also important that the particles are large enough not to be absorbed and risk migration, and for as little carrier gel as possible to be absorbed, which results in reduction in efficacy.

The first injection techniques to be tried and reported were by Murless in 1938 [146]. He used sclerosing agent, sodium morrhuate, in 20 women and achieved continence in 17 of them, presumably through the effect of scarring and contracture of the vaginal wall. Quakels in 1955 used paraffin to achieve the same effect, but reports of pulmonary embolism stopped the technique [147].

In 1964, Politano and Harper [148] began using polytetrafluoroethylene (PTFE, Teflon, Polytef) paste for injection into the vesicoureteric junction, and numerous reports followed over the next 30 years of its use in the paraurethral tissues [149–151]. The speed of this procedure and its apparent efficacy, even if this was lower than conventional surgery, appeared to offer a truly minimally invasive alternative to surgery for women who wanted to avoid the risk of morbidity. However, reports of serious complications began to emerge including periurethral abscess [152,153] pulmonary granulomata [154,155], and obstructive uropathy [156], and long-term outcomes were observed to deteriorate from 80% initial response to 27% at 3 years [157] and to 33% at 5 years [158]. As a consequence of these reports, PTFE paste lost its licensing for use as a bulking agent from the FDA, and NICE in 2006 recommended that it should not be used for this purpose.

Gonzales de Garibay, in 1989, reported an alternative bulking agent that utilized autologous fat cells obtained by microliposuction and reinjected into the periurethral tissues [159]. This had the major advantage of being autologous tissue with no immunogenicity problems, cheapness, and ease of use. However, the initial results were disappointing with only 23% of women improved at 12 months [160] and none in another study [161] though Palma achieved 64% cure at 12 months by means of repeated injections [162].

The only RCT carried out in this area, before the advent of newer injectable materials, was by Lee et al. in 2001 [163]. Of the 68 women enrolled, 35 received fat and 33 received saline injections of whom 22% and 20%, respectively, were improved at three months. The lack of convincing efficacy together with further reports of pulmonary embolism, in this case leading to death, have resulted in the use of autologous fat also being officially discouraged both by NICE (2006) [2] and by ICI [4].

Much further research and clinical development has continued into the modern era using a variety of injectable materials. In brief, recently developed injectables such as silicon particles and calcium hydroxylapatite can result in an improvement in incontinence, but patients may not necessarily achieve dryness. According to the 2012 Cochrane Review on injection therapy for urinary incontinence, there is insufficient evidence in the use of bulking agents to guide clinical practice, and this is discussed in detail in another chapter [164].

CONCLUSIONS

This chapter has described some obsolete operations and others that marked a turning point in surgical practice. Nevertheless, understanding these procedures is paramount as our current surgical treatment options are based on these fundamental surgical principles.

The continued use of what some would regard as archaic may be defensible in experienced hands, where the outcomes are well monitored and known to surgeon and patient alike. Historically, objective data in stress incontinence surgery are sparse, but as new advances emerge, researchers understand the importance of RCTs. Thus, scrutiny of surgical technique and materials is becoming commonplace, ultimately providing better patient care, which is the ultimate goal.

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71

Retropubic Urethropexy

Dudley Robinson and Linda Cardozo

INTRODUCTION

The term stress urinary incontinence may be used to describe the symptom or sign of urinary leakage on coughing or exertion but should not be regarded as a diagnosis. A diagnosis of urodynamic stress incontinence can only be made after urodynamic investigation, and this is defined as the involuntary leakage of urine during increased abdominal pressure in the absence of a detrusor contraction [1].

Stress incontinence is the most commonly reported type of urinary incontinence in women. In a large epidemiological study of 27,936 women from Norway [2], overall, 25% of women reported urinary incontinence, of whom 7% considered it to be significant, and the prevalence of incontinence increased with age. When considering the type of incontinence, 50% of women complained of stress, 11% urge, and 36% mixed incontinence. The prevalence of urinary incontinence among nulliparous women ranged from 8% to 32% and increased with age. In general, parity was associated with incontinence, and the first delivery was the most significant. In the age group 20–34 years, the relative risk of stress incontinence was 2.7 (95% CI: 2.0–3.5) for primiparous women and 4.0 (95% CI: 2.5–6.4) for multiparous women. There was a similar association for mixed incontinence although not for urge incontinence [3].

PATHOPHYSIOLOGY

There are various different underlying causes that result in weakness of one or more of the components of the urethral sphincter mechanism (Table 71.1).

The bladder neck and proximal urethra are normally situated in an intra-abdominal position above the pelvic floor and are supported by the pubourethral ligaments. Damage to either the pelvic floor musculature (levator ani) or pubourethral ligaments may result in descent of the proximal urethra such that it is no longer an intra-abdominal organ, and this results in leakage of urine per urethram during stress.

This theory has given rise to the concept of the “hammock hypothesis,” which suggests that the posterior position of the vagina provides a backboard against which increasing intra-abdominal forces compress the urethra [4]. This is supported by the fact that continent women experience an increase in intraurethral closure pressure during coughing [5]. This pressure rise is lost in women with stress incontinence although it may be restored following successful continence surgery [6].

In addition to pelvic floor damage, there is also evidence to suggest that stress incontinence may be caused by primary urethral sphincter weakness or intrinsic sphincter deficiency (ISD). In order to distinguish this type of stress incontinence from that caused by descent and rotation of the bladder neck during straining, the Blaivas Classification has been described based on videocystourethrographic observations [7]. This proposes that type I and type II stress incontinence are caused principally by urethral hypermobility, whereas type III, or ISD, is caused by a primary weakness in the urethral sphincter. Factors associated with ISD are pudendal innervation [8], integrity of the striated urethral sphincter [9], urethral smooth muscle, the urethral mucosa, and submucosal urethral cushions.

More recently, the “midurethral theory” or “integral theory” has been described by Petros and Ulmsten [10]. This concept is based on earlier studies suggesting that the distal and midurethra play an important role in the continence mechanism [11] and that the maximal urethral closure pressure is at the mid-urethral point [12]. This theory proposes that damage to the pubourethral ligaments supporting the urethra, impaired support of the anterior vaginal wall to the mid-urethra, and weakened function of part of the pubococcygeal muscles, that insert adjacent to the urethra, are responsible for causing stress incontinence.

RETROPUBIC URETHROPEXY

History

In 1923, Victor Bonney observed that “incontinence depends in some way upon a sudden and abnormal displacement of the urethra and urethrovesical junction immediately behind the symphysis” [13]. This association of urethral hypermobility and stress urinary incontinence was also noted by Watson in 1924 [14] although it was not until 1949 that the first retropubic procedure for stress incontinence was described by Marshall et al. [15]. This early example of cooperation between two urologists and a gynecologist described “the correction of stress incontinence by simple vesicourethral suspension” in a series of 50 patients including 12 men with postprostatectomy stress incontinence. They reported an initial 82% success and 7% improvement rate, and the procedure became popular in the management of women with stress urinary incontinence.

In 1961, John Burch described his modification of the Marshall–Marchetti–Krantz procedure when he encountered difficulty in suture placement. Rather than placing the sutures in the periosteum of the pubic symphysis, he described the attachment of the anterolateral vagina to the pectineal ligament using three sutures on each side [16]. He initially reported a series of 53 patients with 100% success rate and subsequently published a 9-year series of results in 1968 with a 93% success rate and an 8% incidence of enterocele [17].

Over the last 50 years, the Burch colposuspension has remained an efficacious and durable procedure in the surgical management of stress urinary incontinence and has undergone several modifications. In 1976, Tanagho recommended avoiding dissection of the midline neurovascular supply to the urethra to reduce the risk of causing ISD [18] and also observed that overcorrection at the level of the bladder neck did not improve success rates but led to a higher incidence of voiding difficulties [19]. This observation led to the widely adopted technique of providing support to the bladder neck without overelevation.

Table 71.1 Causes of Urodynamic Stress Incontinence

- Urethral hypermobility
  - Urogenital prolapse
- Pelvic floor damage or denervation
  - Parturition
  - Pelvic surgery
  - Menopause
- Urethral scarring
  - Vaginal (urethral) surgery
  - Incontinence surgery
  - Urethral dilatation or urethrotomy
  - Recurrent urinary tract infections
  - Radiotherapy
- Raised intra-abdominal pressure
  - Pregnancy
  - Chronic cough (bronchitis)
  - Abdominal/pelvic mass
  - Fecal impaction
  - Ascites
  - Obesity

With the increasing trend to minimal access techniques, the laparoscopic colposuspension was first reported in 1991 [20]. Although many authors have reported excellent short-term subjective results from laparoscopic colposuspension [21], early studies showed inferior results to the open procedure [22,23].

More recently, the description of the “integral theory” has revolutionized the concept behind the traditional approach to retropubic surgery and has led to the introduction of the mid-urethral tapes using a retropubic [24,25] and transobturator approach [26]. While these procedures have largely replaced retropubic urethropexies in clinical practice, the colposuspension still has an important role in the management of women with stress urinary incontinence.

Marshall–Marchetti–Krantz

Operative Technique

The patient is placed in the modified lithotomy position and a Foley catheter inserted. A low transverse suprapubic incision is made and the retropubic space entered. The bladder neck and proximal urethra are then mobilized from the vagina with the assistance of the index and middle fingers of the surgeon's left hand placed within the vagina. Between one and three sutures are inserted on each side. Each suture should include the paraurethral tissue, lateral wall of the urethra, and the vaginal wall. The sutures are then fixed to the periosteum of the superior pubic ramus or the perichondrium of the symphysis pubis. Further sutures may then be placed between the anterior surface of the bladder and rectus abdominis to provide additional elevation and support (Figure 71.1). At the end of the procedure, a Redivac drain should be placed in the retropubic space and a suprapubic catheter used for postoperative urinary drainage. When the urinary residuals are less than 100 mL, the catheter may be removed.

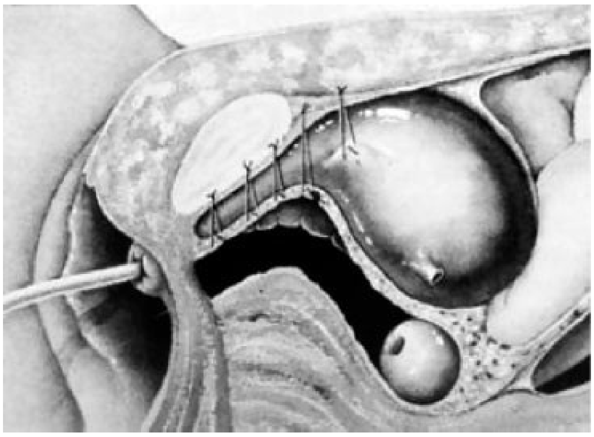

Figure 71.1 Marshall–Marchetti–Krantz.

Results

Overall, there have been 58 published papers between 1951 and 1998 that have included 3238 patients, although many of these studies were retrospective case series. Overall cure rates were approximately 88% with results of 92% and 84% in primary surgery and redo surgery, respectively [27].

While there has been no formal Cochrane Review of the procedure, there has been a review of comparative trials with colposuspension [28–30]. Although the early results of MMK are not significantly different to colposuspension, both subjective and objective cures were found to be significantly better following colposuspension than after MMK at 1–5 years (RR 0.44; 95% CI: 0.25–0.77) [31].

In addition, two further studies comparing MMK with colposuspension were identified by the National Collaborating Centre for Women's and Children's Health (NCCWCH) in the United Kingdom. While one study showed significantly better objective outcome based on negative stress test in the MMK group (93% vs. 53%; $p = 0.02$) [32], the other showed significantly better subjective outcomes in the colposuspension group at 2-year follow-up (59% vs. 49%; $p = 0.02$) [33]. More recently, a case series comparing MMK with tension-free vaginal tape (TVT) has been published in 228 women with a 10-year follow-up. The short-term success in the MMK was 89%, although this fell to 68.2% at 5 years and only 32% at 10 years. Conversely, the cure rate for TVT was 90.0% initially and 84.3% at 5 years [34].

Data regarding the long-term success of MMK are more limited, although six studies have been reported with a mean cure rate of 58% reported between 4 and 15 years [35–40]. Two of these long-term studies have shown the efficacy rates to reduce over time with reported success rates being 90% and 77% at 1 year, 86% and 57% at 5 years, and 72% and 28% at 10 years [34,36].

Complications

The major complication associated with the MMK procedure is osteitis pubis, which has been reported to occur in 2.5%–7% of cases [41,42]. Patients present with a history of severe suprapubic pain radiating into the groins and perineum, and a bone scan shows increased uptake in the suprapubic region. Long-term antibiotic treatment over several months is generally required, and occasionally, a retropubic abscess may require drainage.

Colposuspension

Operative Technique

The patient is positioned on the operating table in the modified lithotomy position using Lloyd–Davies stirrups. The abdomen and vagina are then prepared as a sterile operating field in order to allow the manipulation of the vaginal fornices and bladder neck by the surgeon. An indwelling Foley catheter is then inserted and the balloon inflated with 6 mL of water to allow the identification of the bladder neck.

A low transverse suprapubic incision approximately 1 cm above the pubic symphysis is made and the rectus fascia incised taking care not to open the peritoneal cavity unless a concomitant intra-abdominal procedure is being performed. A Turner–Warwick self-retaining retractor may then be inserted (Figure 71.2a), and the retropubic space (cave of Retzius) is opened using both sharp and blunt dissections (Figure 71.2b) until the white paravaginal tissue lateral to the bladder neck and urethra is identified (Figure 71.2c). Vaginal manipulation is also used to further assist in the elevation of the lateral vaginal fornices while the bladder is swept medially. Two to four delayed absorbable sutures are inserted into the paravaginal fascia on each side and each tied down onto the vaginal tissue ensuring hemostasis. The first suture is at the level of the bladder neck and 1 cm lateral (Figure 71.2d). The suture is then passed vertically through the ipsilateral iliopectineal ligament, taking care not to pull the bladder neck open, and left untied. Each subsequent suture is then placed 1 cm lateral and 1 cm cephalad (Figure 71.2e) and all left untied before the sutures are placed on the opposite side (Figure 71.2f). Once all the sutures are positioned correctly, each lateral fornix is elevated by an assistant allowing the sutures to be tied easily without tension (Figure 71.2g). After checking for adequate hemostasis, the retropubic space is drained with a Redivac suction drain and the abdomen closed (Figure 71.2h and i). The bladder is left on free drainage using a suprapubic catheter for 48 hours prior to starting a clamping regimen. When the urinary residuals are less than 100 mL, the suprapubic catheter may be removed.

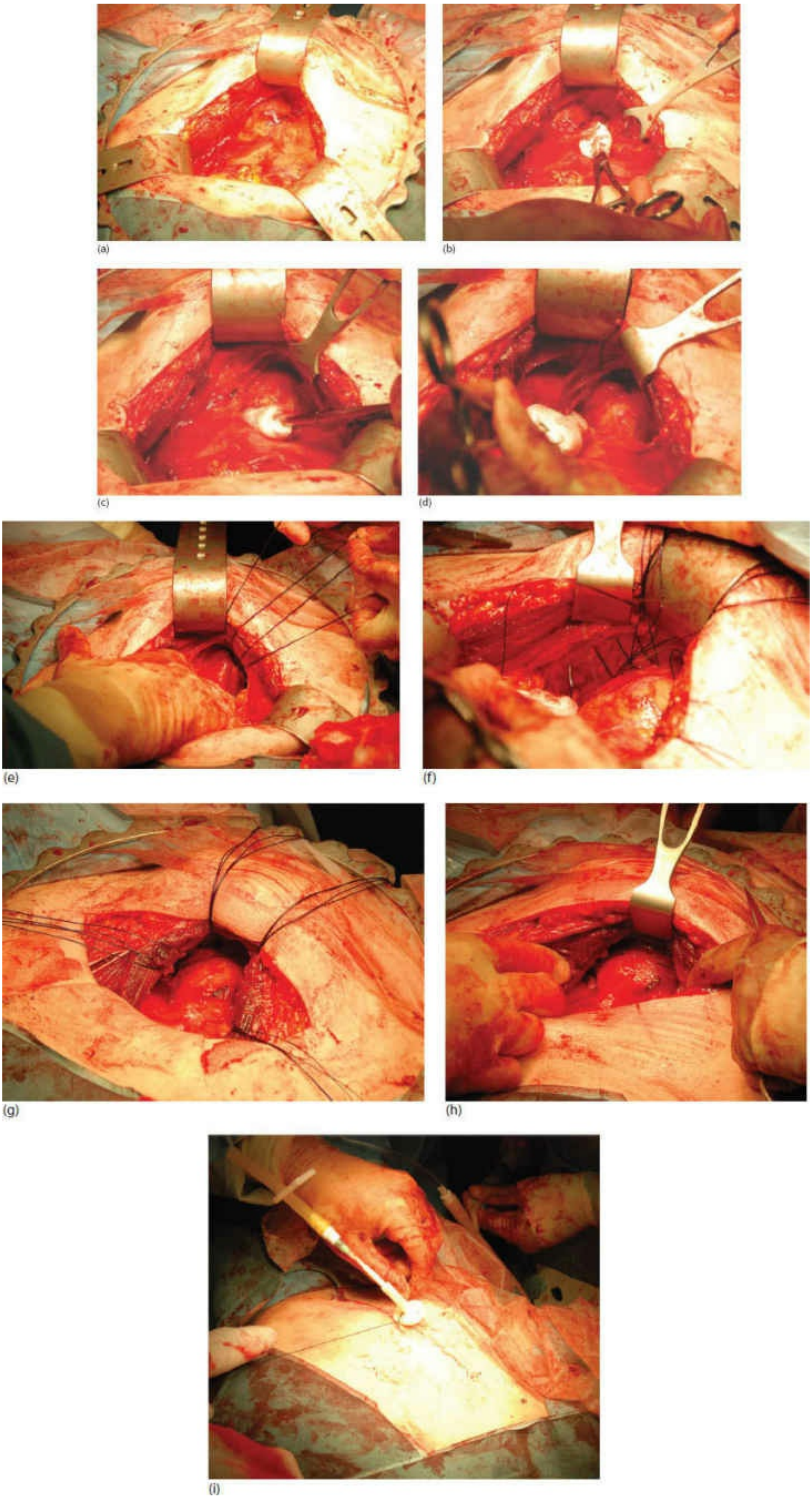
(a)
(b)
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Figure 71.2 (a–d) Operative technique.

Results

The 4th International Consultation on Incontinence (ICI) [27] on 33 published randomized trials of colposuspension in addition to the following:

- Seven trials comparing colposuspension with anterior colporrhaphy
- Four trials comparing colposuspension with Marshall–Marchetti–Krantz
- Nine trials comparing colposuspension with needle suspension
- One trial comparing colposuspension with abdominal paravaginal repair
- Seven trials comparing colposuspension with traditional sling procedures
- Five trials comparing colposuspension with TVT
- One trial comparing colposuspension with transobturator tape (TOT)
- Seven trials comparing open colposuspension with laparoscopic colposuspension

In total, these studies included 4161 women of whom 1900 were randomized to colposuspension. Additionally, there have been two recent meta-analyses performed by the Cochrane group [31] and also by the NCCWCH within the United Kingdom. Since the 4th report from the ICI, a further two additional studies have been published comparing retropubic mid-urethral slings to open colposuspension in the updated 5th report [43].

When considering all studies of colposuspension, objective cure rates varied between 59% and 100% (median 80%) and subjective cure rates between 71% and 100% (median 88%). Based on these results, colposuspension would appear to have comparable objective and subjective outcomes to traditional sling procedures and to both retropubic and transobturator mid-urethral tapes. The evidence would also appear to suggest that outcomes with colposuspension are significantly better than those achieved with anterior colporrhaphy, needle suspension procedures, paravaginal repair, and the Marshall–Marchetti–Krantz procedure.

Outcome: Colposuspension

Historically, there have been many prospective case series and cohort studies assessing the efficacy of colposuspension with some studies providing long-term follow-up data up to 20 years (Table 71.2).

In addition, there have also been three reported meta-analyses. The first of these was reported by Jarvis in 1994 [41] who reviewed 1726 women with a follow-up of at least 1 year and a mean objective success rate of 84.3%. Very similar results were reported from a meta-analysis of 2196 women reported by the American Urological Association in 1997. Overall mean objective cure rates were 84% at 48 months (CI: 79%–88%) with a follow-up to at least 4 years [44]. More recently, the Cochrane group has published a meta-analysis of 39 randomized controlled trials involving 2403 women with a mean follow-up of 1 year. Objective cure rates were found to be 85%–90%, and there was a slow decline in cure rates to 70% over 5 years [31].

Table 71.2 Subjective and Objective Outcome of Colposuspension: Case Series and Cohort Studies

Study	No.	Objective outcome (%)	Subjective outcome (%)	Follow-up (months)
Burch [16]	53	—	100	Unstated
Burch [17]	143	—	93	10–60
Stanton et al. [45]	32	80	—	6–30
Milani et al. [46]	44	79	—	>12
Cardozo and Cutner [47]	100	80	—	6–12
Herbetsson and Iosif [48]	72	90	—	84–144
Feyereisl et al. [49]	87	82	—	60–120
Alcalay et al. [50]	109	90	—	120–240
Langer [51]	127	94	—	120–180

Outcome: Redo Colposuspension

There have been several case series reporting the outcome of colposuspension following failed previous surgery (Table 71.3). While success rates tend to be slightly lower following failed previous continence surgery, continence rates between 65% and 86% are generally reported indicating the efficacy of colposuspension as a secondary procedure.

Outcome: Colposuspension versus Anterior Colporrhaphy

There have been seven trials comparing colposuspension with anterior colporrhaphy (Table 71.4) and one meta-analysis. In general, success rates tend to be lower in the group of patients having anterior colporrhaphy as compared to colposuspension. Consequently, the 4th ICI [27] recommended that anterior colporrhaphy should not be used alone in the management of stress urinary incontinence.

Outcome: Colposuspension versus Marshall–Marchetti–Krantz

There have been four trials comparing colposuspension with the Marshall–Marchetti–Krantz procedure (Table 71.5). While some studies indicate comparable success rates in the short term, the longer-term studies would suggest that efficacy is less good when compared to colposuspension. Consequently, the 4th ICI concluded that there is no evidence to support the use of the Marshall–Marchetti–Krantz procedure over colposuspension [27].

Table 71.3 Objective Outcome of Redo Colposuspension: Case Series

Study	Objective cure (%)	Follow-up (months)
Stanton [52]	65	60
Galloway et al. [53]	63	54
Stanton and Cardozo [54]	77	12
Jarvis [41]	83	>12
Alcalay et al. [50]	61	120–240
Cardozo et al. [55]	78	9
Maher et al. [56]	81	9
Bidmead et al. [57]	86	12
Thakar et al. [58]	65	60–180

Table 71.4 Comparative Studies: Colposuspension (Colpo) versus Anterior Colporrhaphy

Study	Type of study	Success rate (objective/subjective) colpo vs. AC (%)	Follow-up (months)
Bergman et al. [59]	RCT	89 vs. 63	12
Bergman et al. [60]	RCT	87 vs. 69	12
Bergman and Elia [61]	RCT	82 vs. 37	60
Black and Downs [62]	Meta-analysis	85 vs. 50–70	12
Liapis et al. [29]	RCT	88 vs. 57	36
Liapis et al. [30]	RCT	89 vs. 56	60
Kammerer-Doak et al. [63]	RCT	89 vs. 31	12
Colombo et al. [64]	RCT	74 vs. 42	>96

Table 71.5 Comparative Studies: Colposuspension (Colpo) versus Marshall–Marchetti–Krantz

Study	Type of study	Success rate (objective/subjective) colpo vs. MMK (%)	Follow-up (months)
Colombo et al. [36]	RCT	80 vs. 65	12–84
Liapis et al. [29]	RCT	89 vs. 67	60
Quadri et al. [32]	RCT	93 vs. 53	12
McCrery and Thompson	RCT	59 vs. 49	6–60

[33]

Outcome: Colposuspension versus Needle Suspension Procedures

There have been nine trials comparing colposuspension with needle suspension procedures (Table 71.6). The majority of reported studies suggest that needle suspension operations are less effective than colposuspension both in the long and short term, and the 4th ICI has concluded that their use should not be recommended [27].

Outcome: Colposuspension versus Paravaginal Repair

There has been only one randomized controlled trial comparing colposuspension with paravaginal repair in 72 women with a follow-up at 24 months [65]. There was a significantly higher success rate in the colposuspension arm compared to the paravaginal repair arm (100% vs. 61%; $p = 0.004$), and consequently, the trial was discontinued early for ethical reasons. The 4th ICI has concluded that the evidence would suggest that abdominal paravaginal repair is less effective than colposuspension [27].

Outcome: Colposuspension versus Traditional Sling Procedures

Seven trials have compared colposuspension with traditional sling procedures (Table 71.7). The evidence suggests that traditional sling procedures have similar efficacy to colposuspension although it may be associated with a higher incidence of voiding difficulties [27]. While there is considerable evidence to support the use of autologous fascial slings, adverse events may be more common following the use of synthetic sling materials.

Table 71.6 Comparative Studies: Colposuspension (Colpo) versus Needle Bladder Neck Suspension Procedures

Study	Type of study	Success rate (objective/subjective) colpo vs. NBNS (%)	Follow-up (months)
Mundy [66]	Quasi RCT	88 vs. 76	12
Bergman et al. [59]	RCT	89 vs. 65	12
Bergman and Elia [61]	RCT	82 vs. 43	60
Klute et al. [67]	RCT	87 vs. 70	12
German et al. [68]	RCT	86 vs. 53	12–44
Black and Downs [62]	Meta-analysis	85 vs. 50–70	12
Athanassopoulos and Barbalias [69]	Quasi RCT	74 vs. 71	8–27
Leach et al. [44]	Meta-analysis	84 vs. 67	≥48
Gilja et al. [70]	RCT	89 vs. 80	18

Table 71.7 Comparative Studies: Colposuspension (Colpo) versus Traditional Sling Procedures

Study	Type of sling	Type of study	Success rate (obj/subj) colpo vs. Sling (%)	Follow-up (months)
Black and Downs [62]	—	Meta-analysis	83 vs. 74	12
Enzelsberger et al. [71]	Dura	RCT	86 vs. 92	32–48
Leach et al. [44]	—	Meta-analysis	84 vs. 67	≥48
Sand et al. [72]	Gore-Tex	RCT	90 vs. 100	3
Culligan et al. [73]	Gore-Tex	RCT	85 vs. 100	33–116
Demirci and Yucel [74]	Fascia	Quasi RCT	88 vs. 94	12
Bai et al. [75]	Fascia	RCT	88 vs. 93	12
Albo et al. [76]	Fascia	RCT	49 vs. 66	24

Outcome: Colposuspension versus Tension-Free Vaginal Tape

There have been seven reported trials comparing colposuspension with the TVT (Table 71.8). While efficacy rates are similar for both procedures, operation time, hospital stay, and time to resume normal activities were significantly shorter with the TVT [76,79,81]. However, the number of bladder injuries was found to be higher in those women having a TVT when compared to colposuspension [76,79]. Conversely, significantly, more patients were found to have voiding difficulties following colposuspension [76] and subsequently were taught self-catheterization. In addition, significantly more women required surgery for urogenital prolapse following colposuspension [78]. The 4th ICI has suggested, based on the available evidence, that TVT is more effective than colposuspension and equally effective as the more traditional sling procedures [27]. These findings are also supported by the more recently published 5th report [43].

Table 71.8 Comparative Studies: Colposuspension (Colpo) versus Tension-Free Vaginal Tape

Study	**Type of study**	**Success rate (obj/subj) colpo vs. TVT (%)**	**Follow-up (months)**
Ward and Hilton [77]	RCT	57 vs. 66	6
Ward and Hilton [78]	RCT	81 vs. 80	24
Ward and Hilton [79]	RCT	81 vs. 90	60
Liapis et al. [80]	Quasi RCT	84 vs. 86	24
Wang and Chen [81]	RCT	82 vs. 76	12–36
El-Barky et al. [82]	RCT	72 vs. 72	3–6
Bai et al. [75]	RCT	88 vs. 87	12
McCracken et al. [83]	Retrospective	40 vs. 45	60
Tellez Martinez-Fornes et al. [84]	RCT	24 vs. 25	36

Outcome: Colposuspension versus Transobturator Tape

To date, there has been only one randomized controlled trial comparing colposuspension to a TOT procedure [85] in 100 women followed up at 12 and 24 months. Success rates at 12 months were 80% and 86% in the colposuspension and TOT, respectively, and were no different at 24 months (84% and 88%, respectively).

Outcome: Colposuspension versus Laparoscopic Colposuspension

There have been seven reported studies comparing open and laparoscopic colposuspension (Table 71.9). In addition to the published studies, the Cochrane group has also reported a meta-analysis of 22 studies including laparoscopic colposuspension [86]. In comparison to open colposuspension, they found subjective cure rates from 58% to 96% in the open group compared to 62% to 100% in the laparoscopic group at 18-month follow-up. This resulted in a nonsignificant 5% lower relative subjective cure rate for the laparoscopic procedure (RR 0.95; 95% CI: 0.90–1.00). Objective cure rates, using cough test or pad test, were found to be lower in the laparoscopic group when compared to the open colposuspension group (RR 0.91; 95% CI: 0.86–0.96) at 18 months although not at 5 years (RR 1.01; 95% CI: 0.88–1.16). However, when objective cure was assessed using repeat urodynamic studies, there was a significantly higher success rate following the open procedure (RR 0.91; 95% CI: 0.85–0.89).

Table 71.9 Comparative Studies: Colposuspension (Open) versus Laparoscopic Colposuspension (Lap)

Study	**Type of study**	**Success rate (obj/subj) open vs. lap (%)**	**Follow-up (months)**
Su et al. [92]	RCT	96 vs. 80	6
Fatthy et al. [93]	RCT	85 vs. 88	18
Cheon et al. [94]	RCT	86 vs. 85	12
Ankardal et al. [95]	RCT	92 vs. 90	12
Usten et al. [96]	RCT	81 vs. 81	3–24
Kitchener et al. [97]	RCT	70 vs. 80	24
Carey et al. [98]	RCT	80 vs. 69	24

There are only two small trials providing long-term data at 5 years comparing laparoscopic and open colposuspension, one favoring the open procedure [87] and the other the laparoscopic [88].

In light of the available evidence, the 5th ICI concluded that laparoscopic colposuspension has comparable subjective and objective outcomes when compared with open colposuspension in the short to medium term, although longer-term outcomes are unknown. Laparoscopic colposuspension has similar subjective outcome to TVT, although the objective outcome is less good [43].

COMPLICATIONS

Perioperative Complications

Common perioperative complications encountered during colposuspension include hemorrhage and lower urinary tract injury.

While major hemorrhage is rare [55], one series of 151 patients reported blood loss of over 1000 mL in 2% of cases [89] and transfusion rates have been reported to be approximately 5% (CI: 3%–8%) [43].

Bladder and urethral trauma may occur during dissection in the retropubic space, and the reported incidence of bladder injury is 1.2% [90] to 2.0% [55]. In addition, the ureters may be injured or kinked at the level of the most cephalad suture with one series of 60 cases reporting an incidence of 6.7% [91].

Postoperative Complications

Overactive Bladder

“De novo” urgency and urge incontinence may be reported, although whether this really represents new pathology or simply symptoms that were not adequately diagnosed preoperatively remains open to debate. While the exact cause may be multifactorial and partially explained by increased outflow resistance, postoperatively, there is some evidence to suggest that damage to the autonomic innervation may occur following dissection and mobilization of the bladder neck [99].

Overall, the incidence of “de novo” symptoms suggestive of overactive bladder (OAB) has been reported as 11% (CI: 8–16) [43]. These findings support the findings of earlier studies that reported an incidence of detrusor overactivity between 12% and 18.5% [49,96,100,101].

Unfortunately, there are no reliable predictors of outcome with regard to OAB, although there is some evidence to suggest that increased bladder wall thickness may be associated with a higher risk of “de novo” detrusor overactivity postoperatively [102]. Conversely, there is also evidence from some series to suggest that OAB symptoms may improve in 20% [49] to 60% [55] of women following colposuspension.

Voiding Difficulties

Voiding difficulty may occur early or late in the postoperative period. While the former may be caused by overelevation of the bladder neck at the time of the procedure [103], the latter may be related to gradual detrusor muscle compensation secondary to prolonged outflow obstruction. In addition, many women also notice that their urinary stream is slower and may need to change position to empty their bladder completely. Overall, the incidence of voiding difficulties lasting over 1 month is reported as 5% (CI: 3–5) [43], although other series have reported rates as high as 21% [76].

Urogenital Prolapse

While elevation of the anterior vaginal wall during colposuspension is effective in correcting a mild to moderate cystocele, it also results in alteration of the vaginal angle and hence a change in pressure transmission down the vaginal axis. This may exacerbate posterior vaginal wall defects and leads to an increased incidence of posterior vaginal compartment prolapse. In addition, although colposuspension offers effective support of the bladder, neck prolapse of the upper third of the anterior vaginal wall may result in a “high” cystocele.

To date, several large retrospective studies have been performed examining the outcome of colposuspension, which, as well as giving valuable outcome data in terms of cure, also provides information regarding complications. In a retrospective study of 131 women undergoing colposuspension between 1977 and 1986, 35 women (26.7%) required a total of 40 procedures to correct urogenital prolapse [104]. There was no association between age, weight, parity, menopausal status, and prior pelvic surgery, although a large cystocele preoperatively was a significant risk factor.

These findings are supported by a further follow-up study of 186 women in Finland 1 year following colposuspension in which 12% of women were found to have a rectocele or enterocele requiring surgical repair [105].

In a similar 6-month follow-up study of 74 women following colposuspension in Mexico, the site of urogenital prolapse was assessed [106]. The prevalence of urethrocele was 2.7%, cystocele 50.6%, uterine prolapse 21.3%, vault prolapse 9.3%, and enterocele 41.9%. The authors concluded that while posterior vaginal repair was effective in posterior compartment defects, a Moschcowitz procedure was not.

More recently, a 10–15-year follow-up study of 127 women undergoing Burch colposuspension has been reported [50]. The mean length of follow up was 12.4 years, and objective cure rate was 93.7%. While 18.7% of women complained of anatomical defects, the majority of these were not detected until more than 5 years following surgery implying that long-term follow-up should be mandatory. A further study of 220 women with a mean follow-up of 18 months again gives similar results: 18 (8.2%) women complained of cystocele, 32 (14.5%) rectocele, and 35 (15.9%) enterocele [107].

From these studies, it is clear that the incidence of urogenital prolapse, and in particular posterior compartment defects, increases following colposuspension. In view of these findings, it is important to counsel women regarding outcome not only in terms of cure but also in respect to the need for further pelvic floor surgery.

Sexual Dysfunction

By elevating the bladder neck and anterior vaginal wall, a colposuspension may lead to the posterior vaginal being pulled forward and upward leading to a change in the vaginal angle causing dyspareunia [108]. Postoperative sexual dysfunction has been described in 2%–8% of women following continence surgery although there were no significant differences between procedures [43].

ECONOMIC ANALYSIS

Two studies have been reported comparing a cost analysis of colposuspension in comparison to both TVT and laparoscopic colposuspension.

As part of the UK colposuspension study, a cost utility analysis was also performed. At 6-month follow-up, TVT resulted in a mean cost saving of £243 when compared to colposuspension. Differential mean quality-adjusted life year (QALY) per patient (TVT—colposuspension) was 0.01 (95% CI: −0.01–0.03). The probability of TVT being less costly than colposuspension was 100%, while the probability of TVT being more cost-effective was 94.6% if the willingness-to-pay threshold was £30,000 per additional QALY gain [109].

A cost analysis comparing laparoscopic to open colposuspension was also performed alongside the UK laparoscopic colposuspension study [110]. While laparoscopic surgery produced QALY gain, there was an additional cost when compared to open colposuspension. Healthcare resource use over the first 6-month follow-up period translated into costs of £1805 for the laparoscopic group versus £1433 for the open group. At 6 months, QALYs were slightly higher in the laparoscopic group relative to the open group. Therefore, the cost of each extra QALY (incremental cost-effectiveness ratio [ICER]) was £74,000 at 6 months. At 24 months, the laparoscopic arm also had a higher mean QALY score compared to the open group. Consequently, the ICER was effectively reduced to £9300 at 24 months.

CONCLUSIONS

Retropubic urethropexy remains a durable and efficacious surgical treatment for stress urinary incontinence in women. The description of Burch colposuspension in 1961 revolutionized the surgical approach to stress incontinence and rapidly replaced the Marshall–Marchetti–Krantz procedure.

Almost 50 years later, the available evidence demonstrates that open retropubic suspension is an effective treatment for the treatment of stress incontinence in both long- and short-term trials. Comparative studies have demonstrated that colposuspension is superior to anterior colporrhaphy and needle suspension procedures and is comparable to traditional sling procedures and laparoscopic colposuspension. The evidence from individual trials suggests that colposuspension is as effective as both retropubic and transobturator mid-urethral tape procedures, although a more recent meta-analysis has shown that overall cure rates (OR 0.61; 95% CI: 0.46–0.82; $p = 0.00009$) and objective cure rates

(OR 0.38; 95% CI: 0.25–0.57; $p < 0.0001$) are lower for colposuspension when compared to mid-urethral tapes [111]. These findings are also supported by the most recent Cochrane analysis, which has also shown a higher cure rate with mid-urethral slings when compared to colposuspension (RR 0.75; 95% CI: 0.62–0.90) [112].

Colposuspension has also been shown to be a durable and long-lasting procedure. A recent long-term study has reported outcome in 155 458 women over 10 years following surgery for stress urinary incontinence. The 9-year cumulative incidence of repeat surgery after all procedures was 14.5% (95% CI: 13.4–15.5), after sling procedures 13.0% (95% CI: 11.7–14.3), and colposuspension 10.8% (95% CI: 9.3–12.3). Overall, the rate of repeat surgery was 28% higher for sling procedures when compared to colposuspension (adjusted HR 1.28; 95% CI: 1.19–1.37) [113].

In the 5th report of the ICI, colposuspension continues to be recommended as an effective treatment for primary stress incontinence, and, while superseded by the less invasive mid-urethral tapes, it should still be considered for those women who are having a concomitant abdominal procedure [43]. Consequently, colposuspension still has a role in women having concomitant surgery such as abdominal hysterectomy, oophorectomy, and open abdominal sacrocolpopexy. In addition, colposuspension may offer an alternative to a mid-urethral tape procedure following urethral diverticulectomy or repair of a urethra–vaginal fistula, where it may be preferable to avoid the interposition of a synthetic mesh.

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72 Fascial Slings

Aaron Brothers, David James Osborn, Melissa R. Kaufman, W. Stuart Reynolds, and Roger R. Dmochowski

INTRODUCTION

Early in their inception, pubovaginal bladder neck slings (PVSs) were primarily reserved for the treatment of refractory stress urinary incontinence (SUI). However, owing to an improved understanding of SUI pathophysiology and the introduction of several technological advancements, the PVS has become the surgical gold standard for women who suffer from uncomplicated or complicated SUI. The ideal material for the construction of a pubovaginal sling is sterile, biocompatible, noncarcinogenic, and consistent in quality. In the literature, several allograft, xenograft, and synthetic materials meeting these criteria have been studied. Allograft and xenograft materials are not commonly used for pubovaginal slings because of questions about their durability and cost. Most synthetic materials are made out of polypropylene mesh. In addition, while synthetic meshes are certainly durable, they do carry the potential drawbacks of higher rates of graft infection, urinary tract perforation, and vaginal exposure. Outcomes data have shown that synthetic pubovaginal slings are 15 times more likely to perforate into the urethra (0.02%) and are exposed 14 times more often in the vagina (0.007%) compared to autologous slings [1,2]. For these reasons and others, autologous fascial slings remain the material of choice. Their use and outcomes will be the focus of this chapter.

PATHOPHYSIOLOGY OF STRESS URINARY INCONTINENCE

Female continence depends on a complex interaction between urethral and bladder neck support, intrinsic urethral properties, the urethral sphincter mechanism, and the pelvic floor musculature. In 1990, Petros and Ulmsten proposed a unifying concept called the integral theory [3]. This theory stated that the most important factors for preserving continence were adequate function of the pubourethral ligaments, the suburethral vaginal hammock, and the pubococcygeus muscle. The authors postulated that injury to any of these three components from surgery, parturition, aging, or hormonal deprivation could lead to impaired midurethral function and subsequently urinary incontinence. Dynamic ultrasound studies have shown that stress maneuvers can cause the posterior wall of the urethra to slide away from the anterior urethral wall and allow for opening of the bladder neck and proximal urethra (funneling), resulting in the loss of urine [4]. The goal of a PVS is to provide adequate urethral coaptation (without causing obstruction, ischemia, and erosion from unnecessary tension) and to increase urethral responsiveness to abdominal pressure such that leakage is avoided during stress maneuvers.

PUBOVAGINAL SLING OPERATIVE PROCEDURE

Preoperative Considerations

A comprehensive history and a physical examination including a focused neurourologic exam and pelvic exam should be performed on all patients to properly characterize the nature of their incontinence and to identify all aspects of pelvic support. While not all elements of vaginal prolapse require repair, consideration must be given to addressing prolapse at or distal to the hymenal ring, or symptomatic prolapse of a lesser degree. Doing so may minimize the possibility of postoperative SUI, urinary retention, or worsening prolapse in the future. An in-office cough stress test should also be performed on all patients and confirming the diagnosis in this manner is helpful. According to the AUA Guideline for the surgical management of SUI, additional testing should also include a postvoid residual (PVR) measurement and a urinalysis [5]. Some clinicians may also find quantitative measurement of urethral hypermobility and a voiding diary helpful. A cystoscopy or upper tract imaging for women is not part of the routine assessment of SUI. In addition, urodynamics are not required for the evaluation of primary SUI; however, they may be helpful in cases of mixed urinary incontinence, concomitant pelvic prolapse, incomplete emptying, neurogenic dysfunction, prior surgical failures, and when the diagnosis of SUI is in doubt.

A preoperative bowel preparation is not needed unless a concomitant hysterectomy, vaginal vault suspension, or posterior compartment surgery is planned. Preemptive perioperative clean intermittent catheterization (CIC) training may decrease trips to the emergency room and the need for indwelling catheters postoperatively.

As with any surgical intervention, a thorough discussion of the risks, benefits, and alternative therapies needs to be undertaken. Intraoperative risks include bleeding (with potential for transfusion); injury to the bladder, urethra, or bowel; and hematoma formation. Postoperative risks include transient or permanent voiding dysfunction (possibly requiring urethrolysis or sling incision), worsening or de novo storage or emptying symptoms, urinary tract infections (UTIs), or even sling exposure in the case of synthetic slings. For autologous slings, harvest site complications include seroma formation, wound infection, and incisional hernia formation. As with all surgical procedures, preoperative discussion should also include mention of the rare but serious risks of cardiovascular, pulmonary, and thromboembolic events. In the authors' opinion, sequential compression devices should be placed on the bilateral lower extremities prior to the induction of anesthesia. According to the AUA Best Practice Policy Statement for the Prevention of Deep Venous Thrombosis in Patients Undergoing Urologic Surgery, consideration for the use of low-dose unfractionated heparin or low-molecular-weight heparin should be based on individual patient and procedural risk factors [6].

Patient Positioning and Preparation

PVS surgery can be performed under spinal or general anesthesia. Prior to the start of the procedure, patients should receive a single dose of one of the following: a first- or second-generation cephalosporin, aztreonam (in cases of renal insufficiency), an aminoglycoside plus metronidazole, or clindamycin [7]. The patient is then positioned in a slightly exaggerated dorsal lithotomy position. The abdomen just above the umbilicus and the vagina are prepped with povidone-iodine or chlorhexidine gluconate solutions. The thigh is also widely prepped if autologous fascia lata (FL) is to be used. After draping, a weighted speculum is placed in the vagina and an 18 F Foley catheter is inserted into the urethra and placed to continuous gravity drainage.

Fascial Harvest

A Pfannenstiel incision is made approximately 2 cm above the pubic symphysis, providing excellent exposure and cosmesis. In women with a history of prior pelvic surgery, a preexisting skin incision can also be used. Electrocautery is used to carry the incision down to the rectus fascia (RF). A strip of RF measuring approximately 1.5 by 7 cm is then excised at least 2 cm from the pubic symphysis to help ensure a tension-free fascial closure. This is illustrated in Figure 72.1. The graft is then soaked in a 0.9% normal saline solution and the overlying fat and perifascial tissue is cleaned off. A No. 1 polydioxanone (PDS) or 1–0 polypropylene suture is secured to each end of the graft and left long. The fascial defect is closed with continuous or interrupted #1 PDS. The skin and Scarpa's layer are left open for passage of sling sutures later in the procedure.

In cases where FL is being harvested, an initial 3 cm longitudinal incision is made above the patella over the iliotibial band. This dissection is carried down to the level of the FL, where two parallel, longitudinal incisions are made, approximately 2 cm apart. The graft is then bluntly separated from the underlying muscle and transected as far distally as possible. This free end is then secured with a No. 1 PDS suture as described for the RF graft. This distal FL is then completely freed from any adipose tissue and muscle fibers before a Crawford fascial stripper is used to extend the fascial incision proximally up to 20 cm. The proximal flap is transected and another No. 1 PDS is secured to the free end. The flap is then stored in 0.9% normal saline until needed. Immediate compression should be applied to the thigh to constrict perforating vessels. Once hemostasis is ensured, the thigh wound is closed in three layers without closing the FL. A compressive wrap is then placed for 8 hours postoperatively and early ambulation is encouraged [8].

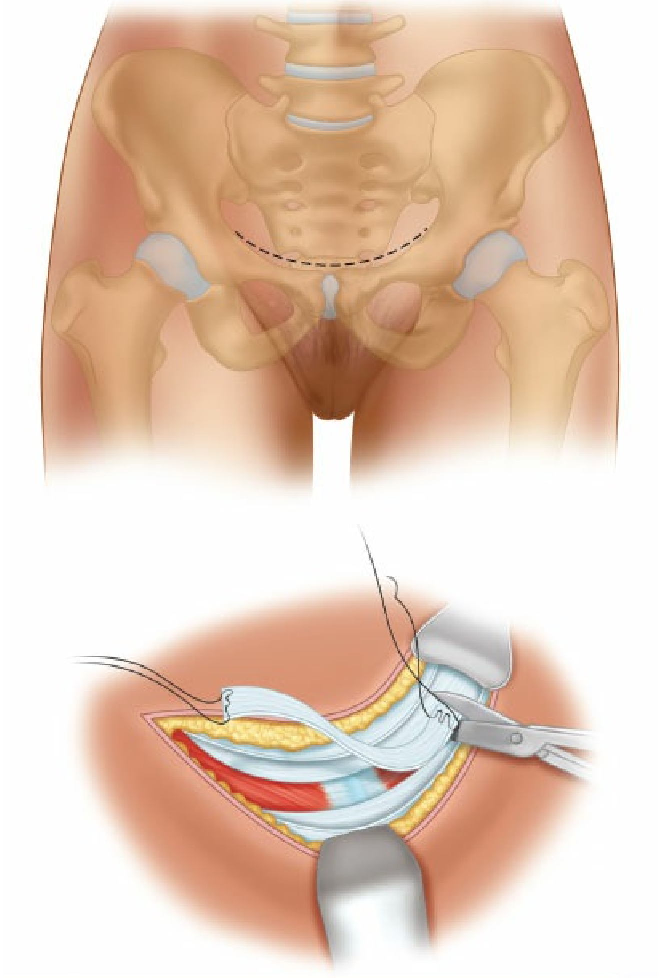

Figure 72.1 The rectus fascia graft is harvested and attached to 2-0 polypropylene sutures. The rent in the rectus fascia is closed while the skin and Scarpa's fascia are left open. (Reproduced from Blaivas JG and Chaikin D, Pubovaginal fascial sling for the treatment of all types of stress urinary incontinence: surgical treatment and long-term outcome, in Cardozo L and Staskin D, eds., *Textbook of Female Urology and Urogynecology*, Informa, London, U.K., 2006. With permission.)

Vaginal Dissection

If no concomitant surgery is planned, an inverted U-shaped incision is made in the vaginal epithelium after injection of 0.9% sterile normal saline with the apex of the U based at the mid-urethra and the widely spaced legs of the U extending just proximal to the bladder neck. Alternatively, a vertical midline incision can be made if concomitant anterior or apical compartment surgery is planned. The vaginal mucosa is then dissected sharply off the underlying surface of the pubocervical and periurethral fascia, with lateral dissection proceeding up to the inferior edge of the pubic symphysis. The vaginal flaps are retracted with help of a vaginal ring retractor.

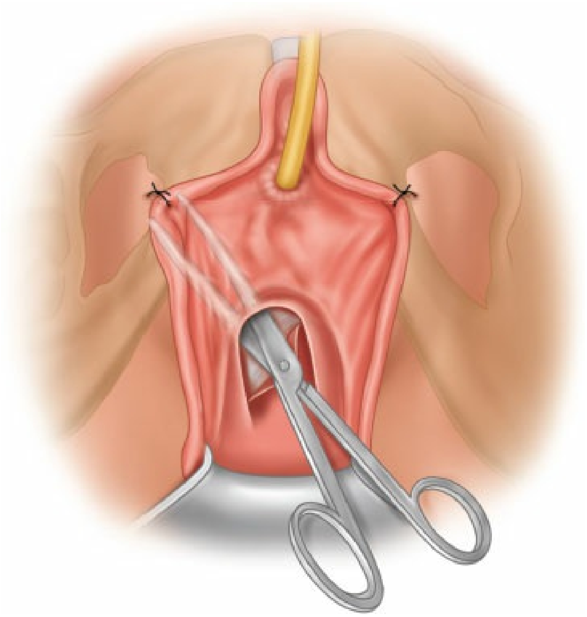

Figure 72.2 After incising the vaginal mucosa in a midline or inverted-U incision, the endopelvic fascia is perforated with Metzenbaum scissors aimed at the ipsilateral shoulder. The retropubic space is entered. (Reproduced from Blaivas JG and Chaikin D, Pubovaginal fascial sling for the treatment of all types of stress urinary incontinence: surgical treatment and long-term outcome, in Cardozo L and Staskin D, eds., *Textbook of Female Urology and Urogynecology*, Informa, London, U.K., 2006. With permission.)

To prevent inadvertent bladder injury, bladder drainage is ensured prior to perforation of the endopelvic fascia with Metzenbaum scissors. The space of Retzius is then entered. The scissors should be aimed at the ipsilateral shoulder and remain just inferior to the pubic symphysis. This is illustrated in Figure 72.2. Once the endopelvic fascia is perforated, periurethral adhesions in the retropubic space are released manually with an index finger (Figure 72.3). With this dissection, the infrapubic and retropubic dissection planes are now connected. During this step, it is important to ensure that the retropubic space is fully opened. The posterior surface of the pubic symphysis should be easily palpable with very little intervening tissue.

Sling Placement and Fixation

If not already done, bladder drainage is again ensured. A finger in the retropubic space is then used to carefully guide Stamey needles from the abdominal incision into the vaginal incision on either side of the urethra (Figure 72.4). The needles should pass directly behind the pubic symphysis. Cystoscopy with a 70° lens is then performed to diagnose inadvertent bladder perforation. Indigo carmine is given intravenously to document ureteral integrity via efflux of blue urine bilaterally. If bladder perforation is identified, the needle can be repositioned until it is outside the bladder and the surgery can proceed.

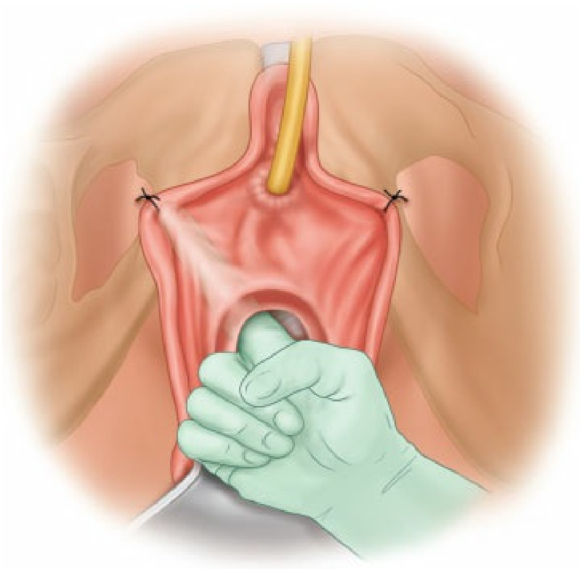

Figure 72.3 Once the endopelvic fascia is perforated sharply, manual dissection with the index finger is performed to release any adhesions and develop the retropubic space. (Reproduced from Blaivas JG and Chaikin D, Pubovaginal fascial sling for the treatment of all types of stress urinary incontinence: surgical treatment and long-term outcome, in Cardozo L and Staskin D, eds., *Textbook of Female Urology and Urogynecology*, Informa, London, U.K., 2006. With permission.)

The graft sutures are then passed into the Stamey needle eyelets and brought out through the abdominal incision and tagged with clamps. The midportion of the sling is positioned over the bladder neck and the distal aspect is sutured to the periurethral tissue with two simple 4-0 polyglactin 910 sutures. The vaginal incision is then closed with running 2-0 polyglactin 910 sutures.

Adjusting Sling Tension and Abdominal Wound Closure

Sling tension is then set from the abdominal incision. The sling PDS sutures are tied above the RF to their contralateral partner while cystoscopy with a 30° lens is performed to visualize adequate coaptation of the proximal urethra. Typically, the sling is tensioned with a two-fingerbreadth width distance between the RF and the PDS knot (Figure 72.5). Before tying a 3rd knot, a cystoscope sheath is passed into the bladder to ensure that there is no *hitch*. If significant resistance is encountered, the two knots can be undone and the tension adjusted until the sheath passes without a hitch.

Once the sling is correctly tensioned, Scarpa’s fascia is reapproximated with an interrupted 3-0 absorbable suture. The skin is closed with a subcuticular 4-0 absorbable suture and the vagina is carefully packed with gauze impregnated with conjugated estrogen cream (or saline or povidone-iodine-soaked gauze in premenopausal women). The urethral catheter is left to gravity drainage.

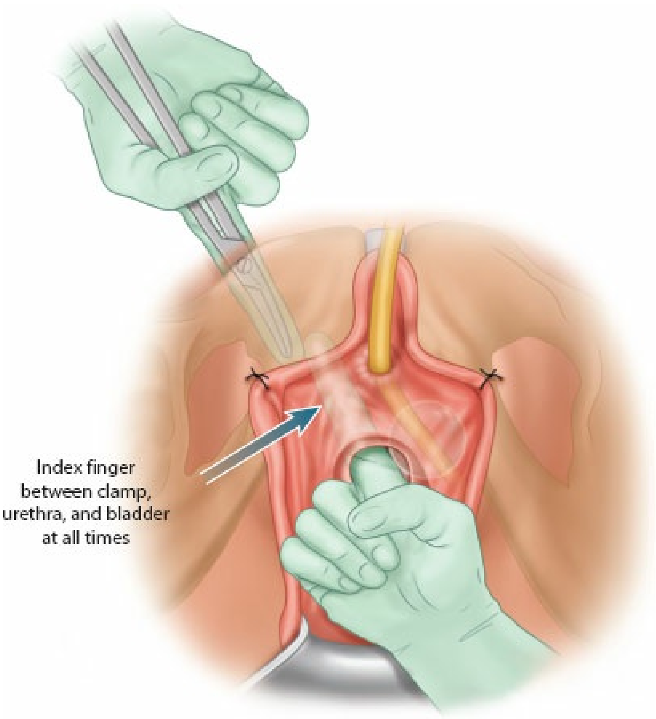

Figure 72.4 A tonsil-tip clamp or double-headed needle is passed from the abdominal incision, through the rectus fascia, and into the vaginal incision on either side of the urethra. Care is taken to stay just behind the posterior aspect of the pubic symphysis. The index finger of the nonpassing hand guides the clamp from below. (Reproduced from Blaivas JG and Chaikin D, Pubovaginal fascial sling for the treatment of all types of stress urinary incontinence: surgical treatment and long-term outcome, in Cardozo L and Staskin D, eds., *Textbook of Female Urology and Urogynecology*, Informa, London, U.K., 2006. With permission.)

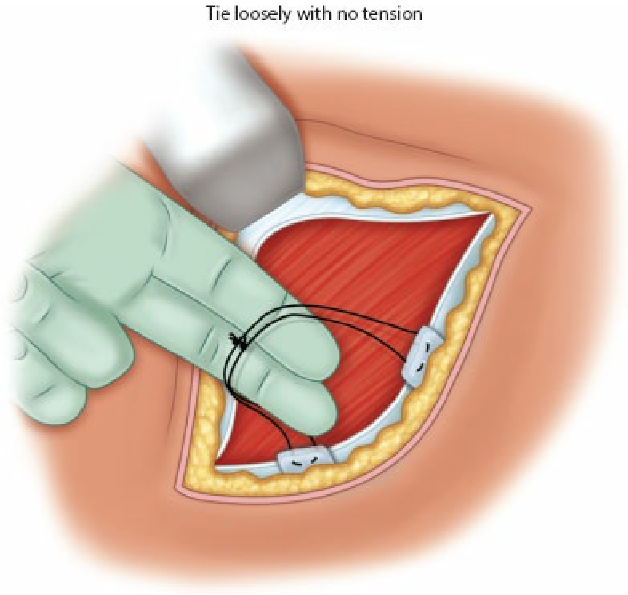

Figure 72.5 After the vaginal incision is closed, sling sutures are tied across the rectus fascia without tension. Typically, an assistant places two fingers between the suture knot and the rectus fascia to ensure tension-free placement. (Reproduced from Blaivas JG and Chaikin D, Pubovaginal fascial sling for the treatment of all types of stress urinary incontinence: surgical treatment and long-term outcome, in Cardozo L and Staskin D, eds., *Textbook of Female Urology and Urogynecology*, Informa, London, U.K., 2006. With permission.)

Postoperative Care

Patients are admitted for overnight observation. The vaginal packing is removed on postoperative day 1 (POD#1) and the urethral catheter is removed when the patient is out of bed and ambulating (usually POD#1). The patient is typically discharged home without a catheter unless she is unable to void or has elevated PVRs >150 mL. In this case, she will return to clinic in approximately 5 days for a repeat voiding trial. Alternatively, patients can perform CIC until voiding improves and PVRs are reduced. Some authors recommend leaving a catheter to drainage for at least 48 hours if the bladder was perforated during needle passage.

All patients are instructed not to lift objects heavier than 3 kg for 6 weeks. Vaginal intercourse is also avoided for at least 6 weeks and not resumed before follow-up physical examination by the surgeon. Frequent ambulation is encouraged, but again strenuous activity is to be avoided for 6 weeks. Follow-up visits are typically at 2 weeks, 6 weeks, 6 months, and annually thereafter.

OUTCOMES OF AUTOLOGOUS PVS SURGERY

Outcomes data for the use of autologous RF and FL as PVS slings are robust. In the earliest modern-day study from 1978, McGuire reported an overall success rate of 80% [9]. Since then, several retrospective studies with long-term follow-up (>48 months) have documented cure rates of 72.9%–94% [10–12]. In 1997, Cross et al. published a retrospective analysis of 150 patients who underwent PVS for urinary incontinence [13]. In their study, 98% of patients had predominantly SUI and 93% of all patients were cured of their incontinence based on the results of in-office questionnaires and telephone interviews. In one study with 7.1 years of mean follow-up of 153 patients, 71.7% were continent and only 3.3% required reoperation for SUI [14].

Studies comparing RF verses FL for use in PVSs have found comparable success rates between the two techniques. Beck et al. noted a 92.4% cure rate measured by absence of leakage on a postoperative cough test in 170 patients who underwent an FL PVS [15]. Similarly, Latini et al. reported that 83% of respondents who had undergone an FL PVS indicated that the procedure had a positive effect on their life, 82% would recommend the surgery to a friend, and 83% would undergo the procedure again [16]. They also noted that 20% of patients who had undergone an FL PVS reported localized numbness, 7% had pain, and 5% had tendonitis at the harvest site 1-week postoperatively.

While the results of these and numerous other studies that document the effectiveness of PVS surgery are encouraging, it is important to note that comparing *cure* rates between various studies is challenging due to variations in the definition of success, outcome criteria, length of follow-up, inclusion and exclusion criteria, incidence of concomitant surgery, and reporting of perioperative complications.

The PVS has also been shown to be an effective treatment for recurrent SUI after a failed corrective surgery. In a retrospective study from 2001, Richter et al. found that rates of postoperative voiding dysfunction were similar in patients getting their first anti-incontinence surgery and in patients who had undergone a previous retropubic suspension (46%) or needle suspension (24%) [17]. Interestingly, 88% of patients in that study felt that the sling improved their quality of life and 82% stated that they would undergo the surgery again; however, 11.8% of patients did require long-term CIC for persistent retention. In another study, Athanasopoulos et al. described outcomes in patients who had failed treatment with a midurethral sling. In this study, 29.9% of the 264 patients had a previously placed midurethral sling that was partially removed at the time of PVS surgery [18]. The overall success rate in terms of markedly improved or cured incontinence in the study was 84.7%. Lastly, in a more recent report by Lee et al., the authors found no difference in outcomes between 36 patients undergoing a primary PVS and 48 patients undergoing a secondary (history of previous major incontinence surgery) PVS procedure [19]. They reported a 76% success rate after a primary PVS procedure and a 69% success rate after a secondary PVS procedure. In summary, PVS surgery demonstrated high success rates in a variety of different types of patients.

Autologous pubovaginal slings also serve an important role during urethral reconstruction surgeries. In the authors' opinion, an autologous PVS provides excellent support to the urethra and decreases persistent or de novo SUI after urethral diverticulectomy surgery. This opinion is supported in the literature through multiple studies that have shown excellent results pertaining to continence and diverticula recurrence after concomitant autologous PVS and urethral diverticulectomy [20–22]. Other authors have published excellent results in terms of continence and spontaneous voiding after using an autologous PVS in conjunction with repair of even more complex urethral damage from etiologies such as protracted obstetrical deliveries, failed anti-incontinence surgeries, aggressive transurethral resections of the bladder neck, long-term indwelling urethral catheters, pelvic trauma, tumors, and radiation [23,24].

COMPLICATIONS OF AUTOLOGOUS PVS SURGERY

Typically, complications after PVS surgery may be effectively grouped by their temporal relationship to the procedure itself. Acute major global perioperative complications such as myocardial infarction, pulmonary embolism, deep vein thrombosis, and death are exceedingly rare [10,15,25–27]. Wound complications such as hematoma, seroma, and hernia formation have been observed in up to 15% of women undergoing an RF sling [28,29]. Thigh wound complications such as hematoma (14%), seroma (4%), and persistent leg pain (3%) have also been reported in patients after fascia lata harvest [15,28,30]. Incisional hernias occur at a rate of 0.8%–1% [10,31]. While several cases of urethral erosion have been reported after autologous PVS surgery, these are most likely a result of overly aggressive periurethral dissection or placement of the sling under excessive tension [32–36].

The most common nonurologic complications from PVS surgery are pulmonary, cardiovascular, neurologic, and gastrointestinal (bowel injury). In 2007, Anger et al. analyzed Medicare claims data for short-term complications after sling (all types) surgery among female beneficiaries aged 65 and older [37]. A total of 1365 sling procedures were included in the analysis. The authors found that 12.5% of women developed surgical or urologic complications in the 3 months after the procedure and 33.6% had a diagnosed UTI. Within the 1-year follow-up period, 6.6% of claims were for bowel injury or obstruction, 9.1% cardiac, 2.6% thromboembolic, 15.3% pulmonary, and 22.1% others. An overall death rate of approximately 3 per 10,000 procedures has been estimated for all SUI procedures (retropubic suspension, transvaginal suspensions, anterior repairs, and PVS) [5].

Voiding dysfunction secondary to bladder outlet obstruction after PVS surgery is often related to detrusor overactivity and impaired detrusor contractility. However, iatrogenic obstruction is also a common cause of postoperative voiding dysfunction and is usually the result of overtightening of the sling that results in hypersuspension of the urethrovesical angle. Transient urinary retention is common after PVS surgery and most patients return to spontaneous voiding with the first 10 days postoperatively [38,39]. The reported incidence of voiding dysfunction after PVS ranges from 2.5% to 35% [40–43]. Kochakarn and Leenanupunth noted that 39% of their patients performed CIC for a mean of 8.9 weeks [44], while Govier et al. noted that women in their study performed CIC for a mean of 3.3 weeks after PVS surgery [45]. In their study, Beck et al. observed postoperative voiding dysfunction for a mean of 2 months after surgery [15]. Additionally, Karram and Bhatia noted that the mean time to spontaneous voiding for women in their study was 20 days [46]. A meta-analysis by the American Urological Association Stress Urinary Incontinence Clinical Guidelines Panel in 1997 reported that the incidence of urinary retention more than 4 weeks after pubovaginal sling placement was 8% and the risk of permanent retention usually does not exceed 5% [2].

Preoperative voiding dysfunction has been shown to affect a patient’s ability to empty after anti-incontinence surgery, and therefore it is important to identify this problem during the initial history and physical examination. Preoperative urodynamic studies may be helpful in identifying patients who mount a low detrusor pressure and rely on valsalva for voiding. Such patients are not strictly excluded from having anti-incontinence surgery but should be counseled on the higher risk of postoperative obstruction and the possible need for long-term CIC. Mitsui et al. found that patients with a PVR greater than 100 mL ($p = 0.05$) or Q_{max} of less than or equal to 20 mL/s ($p = 0.09$) during preoperative urodynamics were more likely to require prolonged CIC (28% of patients required CIC for 4–40 months) [47].

Postoperatively, patients with voiding dysfunction can present with frank urinary retention, subtle irritative symptoms, or urgency incontinence. Recurrent UTIs may also be indicative of obstruction in the otherwise asymptomatic patients. Although no clear cutoff values for obstruction exist, the PVR volume is very important in the evaluation of voiding dysfunction and should be measured in spontaneously voiding patients prior to their discharge from the hospital [48].

Because postoperative obstruction following autologous PVS usually improves or resolves with time, it is appropriate and effective to initially treat persistent voiding dysfunction conservatively (CIC, indwelling catheter, timed voiding, double voiding, biofeedback, pelvic floor muscle training, and anticholinergic therapy). Most physicians advocate waiting 3 months prior to considering repeat surgical intervention for persistent obstructive symptoms.

SURGICAL MANAGEMENT OF VOIDING DYSFUNCTION AFTER PVS SURGERY

Surgical management of bladder outlet obstruction following a PVS traditionally involves a complete urethrolysis by a retropubic, transvaginal, or suprameatal approach. Early in the postoperative course, usually within 6 weeks of surgery, the authors of this chapter have had success with loosening of the sling via caudal pressure applied to the urethra with a cystoscope under anesthesia; however, worsening of the urethral rigidity secondary to periurethral fibrosis is a possible complication of this maneuver [15]. Other early interventions, such as transurethral resection or incision of the bladder neck, have been shown to be an ineffective means of managing postoperative obstruction [49].

Patients with persistent symptomatic obstruction after 6 weeks that requires intervention should undergo either an urethrolysis or a sling incision. Success rates for these procedures for all sling types (autologous, cadaveric, synthetic) range from 65% to 93% [39,40,43,50,51]. Specifically concerning urethrolysis, Foster and McGuire reported that transvaginal urethrolysis was successful in only 50% of PVS obstructions and thus concluded that transvaginal lateral dissection is insufficient in relieving the direct suburethral compressive force of the sling. To better approach the lateral wings of the sling, the authors recommended a suprameatal approach. Petrou et al. reported on a series of 12 patients who underwent such a procedure, 8 of whom had successful results [51]. Likewise, Carr and Webster noted a complete or significant resolution of symptoms in 86% of patients after retropubic urethrolysis [40]. Even in cases of failed urethrolysis, a repeat transvaginal, retropubic, or combined urethrolysis should be able to achieve excellent cure rates of up to 92% as long as the urethra is circumferentially mobilized away from the pubic bone [52].

On the other hand, there are some authors who report that single-sling incision has comparable success rates (84%–100%) and shorter operative time and less morbidity than a formal urethrolysis [53–55]. In 2005, Thiel et al. reported a 100% success rate in 11 women following lateral sling incision, with a 54% rate of recurrent stress incontinence [56]. Goldman also performed simple-sling incision in 14 women with iatrogenic urethral obstruction [57]. This included 3 patients with a midurethral polypropylene mesh sling. In this study, 13 of 14 (93%) patient had complete or significant improvement of voiding dysfunction and 1 (7%) required subsequent urethrolysis. Three patients (21%) developed recurrent SUI, one of which required treatment. In the authors' opinion, the most important factor to consider when deciding on sling incision or formal urethrolysis is the length of time from surgery. Within the first 3–6 months after surgery, a single-sling incision will likely be adequate.

CONCLUSIONS

The PVS surgery has evolved over the past 100 years. With the introduction of novel graft materials and less invasive methods of placement, women undergoing PVS surgery today may enjoy shorter convalescence periods than ever before. However, because synthetic, allograft, and xenograft materials have unpredictable biocompatibility profiles in vivo, these technological advancements bring unique risks. Autologous RF and FL slings induce minimal inflammatory response and are considered the "biocompatibility gold standard" against which all other sling materials are measured. Autologous PVS surgery affords patients cure rates up to 97%. Serious complications are rare and voiding dysfunction after surgery is often transient and can usually be managed conservatively. It is however important to avoid excessive sling tension during placement. As with all surgical procedures, a discussion of the specific risks, benefits, and alternatives to sling surgery is quintessential to obtaining informed consent preoperatively and to ensuring patient satisfaction postoperatively.

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73 Tension-Free Vaginal Tape Procedure For Treatment of Female Urinary Stress Incontinence

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INTRODUCTION

The tension-free vaginal tape (TVT) procedure for the treatment of female urinary stress incontinence is a sling operation. For more than a century, sling operations have been developed and performed with satisfactory degree of success in terms of achieved dryness. The classical sling operations as described by Goebbel [1], Frangenheim [2], Stoeckel [3], and Aldridge [4] are all major invasive surgical procedures, with the inevitable risk of complications, postoperative morbidity, and voiding difficulties. Slings of many different materials—allografts, xenografts, and synthetics—have been used. Classical slings are placed at the bladder neck in order to correct hypermobility and to enhance pressure transmission of intra-abdominal pressure provoked by straining. This mechanism of action is in alignment with the most popular theories of the past century, describing the causes of urinary incontinence [5].

Growing awareness of the magnitude of the urinary incontinence problem in the aging population of the developed world has regenerated increasing interest in finding more effective, less invasive, and more affordable methods of curing incontinence. As hypermobility of the bladder neck correlates poorly with symptoms of incontinence and severity of leakage [6], a shift of interest from correcting anatomical changes to an attempt to restore function of the urethral closure mechanism has occurred. Many findings through the years have identified the midurethra as the focus of interest when dealing with female stress incontinence. Anatomical, physiological, and histological investigations indeed support the concept of the midurethra to be important in maintaining urinary continence in the female.

Pubourethral ligaments, inserting at the midurethra, has been identified by Zaccharin in the 1960s [7] and further nicely demonstrated by DeLancey in the 1990s [8]. Histological evaluation of the female urethra by Huisman revealed prominent vascularization specifically at the midurethra [9].

The early urodynamic investigations by Asmussen and Ulmsten further strengthen the impression of the more distal parts of the urethra playing a major role in the closure mechanism.

The maximal closure pressure is located at the midurethra, and in fertile women, pulsatility can be demonstrated at the same location, indicating strong vascular support [10]. Ingelman-Sundberg found that the ventral parts of the pubococcygeal muscles inserted into the anterior vaginal wall at the site of the midurethra and utilized this finding in his sling plasty [11]. Furthermore, Westby showed elegantly in radiographic experiments how, in continent women, the urethra closes at its middle section on holding urination and that the maximal closure pressure is situated at the same level of the urethra [12].

By combining these findings, a new theory for describing the causes of female urinary incontinence was presented by Petros and Ulmsten, the “midurethral theory” (in early literature, the integral theory) [13]. According to this theory, damage to the pubourethral ligaments supporting the urethra, impaired support of the anterior vaginal wall to the midurethra, and weakened function of the part of the pubococcygeal muscles, which inserts adjacent to the urethra, are responsible for causing stress urinary incontinence. Connective tissue is an important element of the involved structures. The quality of the connective tissue has an influence on continence [14].

DEVELOPMENT OF THE TVT PROCEDURE

The TVT procedure was developed on the basis of the elements of the midurethral theory. The goal was to create a minimally invasive operation, which would reinforce the pubourethral ligaments, strengthen the support of the urethra by the anterior vaginal wall, and achieve conditions that would favor ingrowth of fresh connective tissue into the region. The procedure was performed in local infiltration anesthesia from the very beginning in order to facilitate early same-day discharge of the patients from the hospital.

Several different sling materials were evaluated. The one finally chosen is a synthetic polypropylene monofilamentous mesh, with a pore size between 75 and 150 μm, which is optimal for ingrowth of fibrous tissue and allows leukocytes and macrophages to enter into the mesh, thus avoiding colonization of bacteria. The special weave of this type I mesh has been found to have favorable properties in terms of elasticity and strength [15].

An effort to standardize the operation was made in order to facilitate training of doctors to perform the procedure in a manor, which includes certain built in safety features and makes possible good clinical results. The use of local anesthesia—prilocaine (2.5 mg/mL) with adrenalin (2 μg/mL) diluted with saline to 0.25%—causes vasoconstriction in the operating region, which decreases the risk of intraoperative bleeding and hematoma formation. The volume of 75–100 mL of anesthetics recommended to be used results in hydrodissection of tissues at the operation site and facilitates passage of the specially designed instrument, with the attached polypropylene tape, through the right layers of tissue, thus avoiding complications as bladder injury.

If the local anesthesia is placed only in the region where the tape should be positioned, deviation by the instruments from this safe sector during performance of the operation causes the patient to react and, thereby, guides the surgeon to correct his or her performance. Local anesthesia interferes least with the function of the pelvic floor and allows intraoperative testing of optimal tension-free placement of the tape by a cough test in order to avoid postoperative voiding difficulties.

TVT OPERATION TECHNIQUE

The TVT device consists of an 11 mm wide and 40 cm long tape of polypropylene, which in both ends is attached to stainless steel, specially curved, 5 mm in diameter insertion trocars.

The tape is covered by plastic sheets to protect the tape from contamination and facilitate its passage through the tissues. A reusable handle fits to the trocars and is used to insert the trocars. A rigid catheter guide is placed into an 18 French Foley catheter and helps to deflect the bladder away from the path of the trocar insertion.

In 2010, a modernization of the original TVT device was launched. The TVT exact is used exactly by the technique described for the original TVT procedure. The differences between the two devices are the thickness of the trocar, the original having a diameter of 5 mm, and the TVT exact having a diameter of 3 mm. Both trocars have the same curvature and tip radius and the polypropylene tape has not changed. The narrower trocar reduces the penetration force needed. The TVT exact handle and trocar are combined in one piece, which is disposable.

The patient is placed in a lithotomy position avoiding more than a 70° flexion of the tights. After premedication with, for example, 0.5 mg midazolam, the local anesthetics are placed. The operation requires three small incisions: two 1 cm wide suprapubic skin incisions at the upper rim of the pubic bone, each 2–2.5 cm lateral to the midline, and a vaginal midline incision not more than 1.5 cm wide starting 0.5 cm from the external meatus of the urethra.

Five cc of anesthetics is placed under the skin at the site of the planned skin incisions. Another 20 cc is placed on each side retropubically following closely the posterior surface of the pubic bone down to the urogenital diaphragm. Vaginal infiltration of the anesthetics includes 10 cc on each side paraurethrally up to the urogenital diaphragm and another 5 cc under the vaginal mucosa at the site of the midurethra.

The skin incisions are made to facilitate passing of the trocars through the skin. After the vaginal incision is made, careful, minimal blunt dissection, using Metzenbaum scissors, should be undertaken paraurethrally between the vaginal mucosa and the pubocervical fascia not more than 2 cm deep. The TVT trocar is placed in its starting position within the dissected paraurethral tunnel, with the trocar tip between the index finger of the surgeon's hand in the vagina and the lower rim of the pubic ramus. With a slow controlled pressure, the trocar is brought through the urogenital diaphragm, the space of Retzius, and the rectus muscle fascia using the skin incision as an aim of direction. Attention must be paid to keep the trocar all the time in close contact with the dorsal surface of the pubic bone in order to avoid bladder perforation or entrance into the abdominal cavity. The same procedure is repeated on the other side. After passing each trocar to the extent that the trocar tip is visible at the skin incision, cystoscopy using a 70° optic is performed to assure bladder integrity. If bladder perforation is noted, the trocar is withdrawn and passed once more, paying more careful attention of staying close to the pubic bone and within the safe sector. Once bladder integrity is confirmed, each trocar is brought through and the final adjustment of the tape can take place. The recommendation is to fill the bladder with 300 cc of saline and perform a cough test. The patient is asked to cough vigorously while the tape is adjusted to a point when leakage is only a drop of saline at the urethral meatus. This procedure will assure tension-free placement of the tape and minimize risks of postoperative voiding problems. After the final adjustment of the tape has been made, the plastic sheets are taken off. At this point, it is important to control that no further tightening of the tape occurs by placing Metzenbaum scissors between the urethra and the tape when removing the plastic sheets. No fixation of the tape is performed.

CLINICAL PERFORMANCE OF THE TVT OPERATION

The results of the first clinical trial with the TVT operation were encouraging, showing an objective cure rate of 80% [16]. Thereafter, surgeons of six different centers were given personal hands-on training of the TVT technique, and a multicenter, two-country, prospective clinical trial was initiated. The aim of this study was to investigate the performance of the procedure in normal clinical settings outside the clinics of invention. One hundred and thirty-one carefully selected primary cases of genuine stress incontinence were enrolled. The 1-year follow-up results revealed an objective cure rate of 91% and another 7% to be significantly improved. Only 2% were regarded as failures. The complication rate was low, including one case of bladder injury and one wound infection. Three patients had short-term (≤3 days) voiding problems and only one patient experienced retention symptoms for 12 days [17]. These promising results prompted further studies in unselected groups of women with indications for surgical treatment of their urinary incontinence. In a prospective clinical trial of 161 consecutive TVT operations, which included 28% with prior failed incontinence surgery, 37% with mixed incontinence, and 11% with intrinsic sphincter deficiency, the overall objective cure rate at 16 months of follow-up was 87%, 7% were significantly improved and only 5% were classified as failures [18]. No serious complications occurred. The bladder perforation rate was 3.7% and 4.3% of the women experienced short-term voiding difficulties. De novo urge symptoms were noted in 3% of the women, while as many as 80% of those women who preoperatively complained of urge symptoms were relieved of these symptoms at their 16-month follow-up visit. Later, several reviews and meta-analyses have confirmed these favorable results [19–22].

LONG-TERM RESULTS

Table 73.1 shows the objective and/or subjective cure rates in follow-up trials of 10 or more years thus far published.

Some of the problems of evaluating long-term results of incontinence surgery are the growing number of patients lost to follow-up by time and the fact that in many of these often elderly patients' new illnesses appear that might affect bladder function and thus complicate estimation of long-term effectiveness and safety of an anti-incontinence surgical intervention.

The rate of lost to follow-up in the long-term reports, the results of which are presented in the table, ranges between 8% and 28%. This relatively low rate of lost to follow-up subjects 10 or more years after intervention allows one a reliable picture of the actual performance of the TVT operation over time.

The cure rates even 17 years after surgery are in the same order as those reported in the initial early trials, suggesting minimal decline in effectiveness over the years [29]. An attempt to predict the risk of failure or declining effectiveness of the TVT procedure has been done in many reports without being able to identify any single significant factor. A tendency of higher failure rates seems to be associated with high age at the time of operation and the presence of a low-pressure urethra.

An important finding of the long-term follow-up is the absence of signs of rejection or adverse tissue reaction of the polypropylene tape material. Neither was any erosion of the tape into the urethra or the bladder seen [29].

TVT AFTER FAILED INCONTINENCE SURGERY

The next step was to study the effectiveness of the TVT procedure in special groups of patients. Tables 73.2 and 73.3 show the objective and/or subjective cure rates found in patients with prior failed traditional incontinence surgery and prior failed midurethral sling (MUS) surgery, respectively. From the results, it can be concluded that the performance of the TVT procedure is as good as in primary cases when the primary operation had been a traditional method, mostly colposuspension or a pubovaginal sling [30–36]. When the primary failed operation had been an MUS procedure, the repeat MUS, in this context the TVT procedure, shows favorable cure rates, which though seem to be slightly lower than in primary cases and in which a tendency of decline in cure rate is seen after approximately 4 years [37–40]. The decline is partly explained by the fact that many women over time develop urgency symptoms not necessarily related to the surgery, but affecting their subjective perception of cure of urinary symptoms. A question is often raised: which approach for a repeat MUS preferred, the retropubic or the transobturator? There is no clear answer, but some studies indicate that a retropubic repeat procedure might perform better than a transobturator procedure [37,39,41]. Two meta-analyses arrive at different conclusions, one is that the retropubic approach is more effective than the transobturator one in correcting primary failed MUS surgery [42], and another finding is that there is no difference between the approaches [43].

Table 73.1 Ten or More Years of Follow-Up of the Tension-Free Vaginal Tape Procedure

Authors	**No. of subjects**	**Follow-up (years)**	**Lost to follow-up (%)**	**Cure rate**
Groutz et al. [23]	60	10	13	65% sc
Serati et al. [24]	63	10	8	91% oc 87% sc
Heinonen et al. [25]	191	10	28	90% oc 78% sc
Svenningsen et al. [26]	603	10	20	90% oc 76% sc
Nilsson et al. [27]	90	11	23	90% oc 77% sc
Olsson et al. [28]	147	11	16	84% oc 77% sc
Nilsson et al. [29]	90	17	22	91% oc 87% sc

Abbreviations:oc, objective cure; sc, subjective cure.

Table 73.2 Objective Cure Rate and Time of Follow-Up after Tension-Free Vaginal Tape Surgery in Recurrent or Persistent Stress Incontinence after Traditional Incontinence Surgery

Authors	**No. of subjects**	**Follow-up (months)**	**Cure rate (%)**
Rezapour et al. [30]	34	48	82
Azam et al. [31]	67	12	81
Lo et al. [32]	41	12	83
Kuuva et al. [33]	51	25	90
Liapis et al. [34]	33	20	70
Ala-Nissilä et al. [35]	60	96	86
Sivaslioglu et al. [36]	23	12	62

Table 73.3 Objective (oc) or Subjective (sc) Cure Rate and Time of Follow-Up after Tension-Free Vaginal Tape Surgery in Recurrent and Persistent Stress Incontinence after a Primary Midurethral Sling Procedure

Author	**No. of subjects**	**Follow-up (months)**	**Cure rate**
Lee et al. [37]	31	12	92% oc
Palva et al. [38]	20	60	75% sc
Stav et al. [39]	77	50	72% sc
Verbrugghe et al. [40]	80	45	64% oc

TVT IN CASES OF INTRINSIC SPHINCTER DEFICIENCY

Intrinsic sphincter deficiency (ISD) can be defined in many ways, for example, as a low-pressure urethra (<20 cmH_2O) and/or a Valsalva leak point pressure less than 60 cmH_2O or stress urinary incontinence in the absence of urethral hypermobility. The majority of clinical reports dealing with ISD and TVT surgery define ISD as maximal urethral closure pressure (MUCP) less than 20 cmH_2O. Some add a low Valsalva leak point pressure to their definition, while the absence of urethral hypermobility seems to be a criterion not currently relevant. ISD has been regarded as a severe form of stress incontinence with poorer outcome after traditional incontinence surgery (as colposuspension) compared to cases with MUCP >20 cmH_2O. Clinical reports on cases of ISD treated by TVT surgery found cure rates close to 80%, rates that are close to the rates found in cases with higher values of MUCP [44–47]. Three comparative studies have compared TVT with a transobturator procedure in cases of ISD [47–50]. All three studies find a statistically significant poorer outcome with the transobturator procedure than with the TVT operation (Table 73.4).

TVT IN OBESE WOMEN

Obesity is a growing problem worldwide. It is a risk factor of developing urinary incontinence. One might, therefore, postulate that incontinence surgery results in poorer outcome in obese individuals than in normal-weight persons. As MUS surgery has become the gold standard of incontinence surgery and a vast majority of incontinence surgery performed worldwide is MUS surgery, it has become important to investigate the performance of MUS surgery in obese women with stress incontinence. Table 73.5 summarizes some of the few studies comparing obese women with normal-weight women treated with the TVT procedure because of stress incontinence. It can be seen that the cure rates in obese women are somewhat lower than in normal-weight women, with an average cure rate of slightly over 70%; the follow-up time period was mostly 2 years or less [51–54]. The report by Hellberg et al., with a follow-up of more than 5 years, reveals a statistically significant (p = 0.0005) 30% lower cure rate than in controls, a finding that might indicate that over time the obese women have a declining cure rate after TVT surgery [53].

Table 73.4 Objective or Subjective Cure Rate in Intrinsic Sphincter Deficiency Cases after Tension-Free Vaginal Tape Surgery Compared to Transobturator or Control Cases

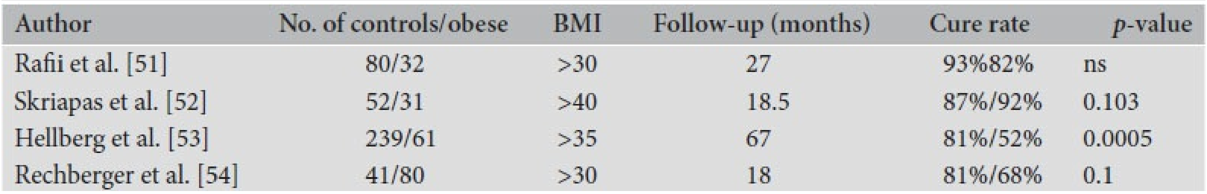
Author	**No. of TVT/controls**	**Follow-up (months)**	**Cure rate**
Liapis et al. [44]	37/0	22–30	73% oc
Meschia et al. [45]	61/204	31	77%/86% sc
Segal et al. [46]	54/0	1–35	79% sc
Jeon et al. [48]	94/72 TOT[a]	24	86%/35% sc $p < 0.0001$
Güngördük et al. [49]	180/120 TOT	31	78%/52% sc $p < 0.0001$
Choo et al. [47]	47/89	50	77%/75% sc
Schierlitz et al. [50]	82/82 TOT	36	99%/82% oc[b] $p < 0.001$

Abbreviations:sc, subjective cure; oc, objective cure.

[a] Comparison with a transobturator procedure.

[b] % not requiring repeat incontinence surgery.

Table 73.5 Cure Rates after Tension-Free Vaginal Tape Surgery in Obese and Normal-Weight Women



Author	No. of controls/obese	BMI	Follow-up (months)	Cure rate	*p*-value
Rafii et al. [51]	80/32	>30	27	93%82%	ns
Skriapas et al. [52]	52/31	>40	18.5	87%/92%	0.103
Hellberg et al. [53]	239/61	>35	67	81%/52%	0.0005
Rechberger et al. [54]	41/80	>30	18	81%/68%	0.1

Abbreviation:ns, not significant.

TVT IN CASES OF MIXED INCONTINENCE

Mixed urinary incontinence is a condition when a patient suffers simultaneously of both stress and urgency incontinence. Mixed incontinence can be divided into cases with either predominant stress or predominant urgency incontinence assessed by subjective parameters or into urodynamically proven mixed incontinence with signs of leakage at stress and detrusor activity. Surgery for mixed incontinence is mostly recommended for cases with stress incontinence predominating mixed incontinence, with or without urodynamically proven detrusor overactivity. Study reports on the outcome of TVT surgery in cases of mixed incontinence are difficult to compare and interpret as the definition of mixed incontinence varies greatly and cure rates are expressed as overall cure, cure of the stress component, or cure of the urgency component. Table 73.6 gives the overall cure rates after TVT in subjects with mixed incontinence of the few reports from which these parameters could be extracted. A rather recent meta-analysis looking at the cure rate after MUS surgery indicates that there is a persistent and good cure of the stress component, while the cure of the urgency component is variable and less than the stress component between 30% and 85% at a follow-up of a few months up to 5 years [61]. From the studies with a longer follow-up, it seems as if cure rates decline with time [57,59]. This decline is not necessarily caused by the failure of the TVT procedure as the stress component does not show tendencies of recurrency. It is mostly the symptoms of urgency that increase, which in turn might be the consequence of concomitant illnesses evolving during follow-up.

COMPLICATIONS

Quality of life has become an important concept when discussing the outcome of incontinence surgery. The quality of life of the incontinent women is not solely reigned by the absence of urinary leakage, but as much by the absence of voiding difficulties, urinary tract infections (UTIs), and other adverse symptoms caused by complications associated with the surgical procedure. Minimal invasiveness and standardization of a surgical intervention is a means of bringing down the rate of complications. Systematic prospective registering of complications is the only possibility to get an accurate picture of the risk and the rate of specific complications.

Table 73.6 Cure Rates after Tension-Free Vaginal Tape in Women with Mixed Incontinence

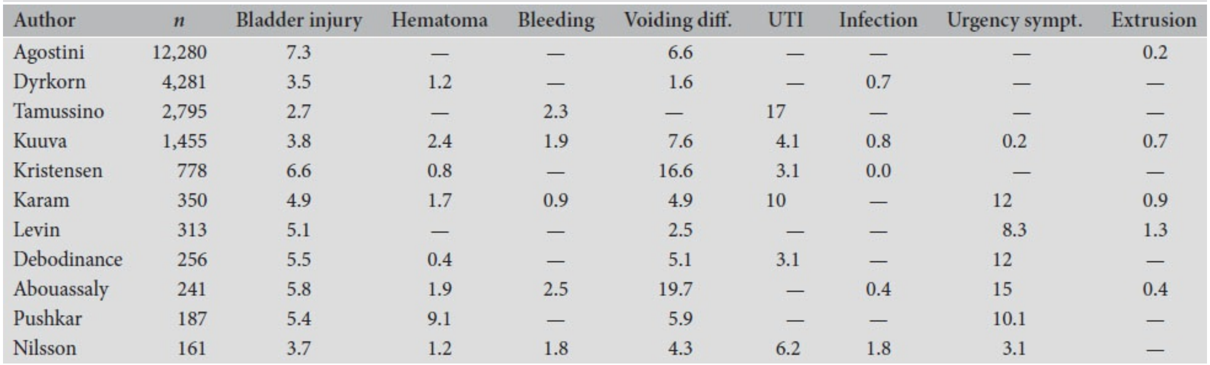
Author	**No. of subjects**	**Follow-up**	**Cure rate (%)**
Segal et al. [55]	65	Not stated	64
Abdel-Hady et al. [56]	128	6 months	89
Holmgren et al. [57]	112	48 months	60
Paik et al. [58]	72	11 months	82
Kulseng-Hanssen et al. (2008) [59]	258	38 months	80
Palva et al. [60]	89	36 months	72

Fortunately, a few such registers have been established and published [62–65]. The one from Finland is unique as it comprises every single TVT procedure performed in the country as it was introduced to the clinics within a systematic hands-on training program [62]. The Finnish material also includes the learning curve of all the surgeons involved. A French retrospective survey of complications associated with the TVT procedure was obtained by asking 92 urologists and gynecologists about the frequency of complications. All together, the survey included 12,280 TVT procedures [65] and is the most comprehensive survey of complications. The Norwegian register including 4281 TVT procedures is a prospective follow-up of complications associated with the TVT operation [64]. Another registry from Austria included 2795 cases, but does not involve all the clinics of the country [63]. A few other more comprehensive studies also focusing on the complication rates have been published [66–71]. The rate of the most common complications associated with incontinence surgery of these studies and the four registries are shown in Table 73.7. Interesting is to note that the rate of bladder injury is rather consistent in these reports, being on average 4.9%. The definition of voiding difficulties varies between the reports but mostly refers to the need for short-time intermittent catheterization within the first two postoperative days. The average rate of the reported postoperative voiding difficulties was 7.5%. In the report by Abouassaly et al., with the highest rate of voiding difficulties, only one patient needed an indwelling catheter for more than 48 hours [68]. The risk of postoperative UTI varies also somewhat, with the highest rate reported in the Austrian material. This might be caused by the fact that a policy of using an indwelling catheter postoperatively (63% of the cases) was adhered to. The average rate of UTI was 5.2%. The recommendation is to perform the TVT operation in local anesthesia, a condition that does not necessitate the use of a postoperative catheter in the bladder. In a report by Bodelsson et al., it was found that the risk of bladder perforation was three times higher if the TVT operation was performed in spinal anesthesia compared to local anesthesia [72].

The TVT operation has been found to be effective in the treatment of women with stress incontinence complicated by the simultaneous existence of urge symptoms or/and urge incontinence. In these cases of mixed incontinence, the cure rates reported are more than 80% [18,56,58]. Preexisting urge symptoms resolve in 50%–80% of the cases [18,61]. Occurrence of de novo urge symptoms varies between 0.2% and 15% (Table 73.7). Seventeen years of follow-up suggests that there is no risk of an increasing number of cases with de novo urge problems over time, the rate of these symptoms being 6% seven years postoperatively [29].

Although the TVT operation is partly a blind procedure, the risk of excessive (>200 mL) intraoperative bleeding and retropubic hematoma formation is rare. Excessive bleeding occurs on average in 2% of the cases (Table 73.7) and is mostly managed by manual compression and tamponade. In a systematic evaluation of the occurrence of postoperative retropubic hematoma formation, Flock et al. reported a rate of 4.1% among 249 consecutive cases, with only four cases exceeding 300 mL and requiring surgical intervention [73].

Table 73.7 Rate of Complications (%) after Tension-Free Vaginal Tape Surgery



Author	*n*	Bladder injury	Hematoma	Bleeding	Voiding diff.	UTI	Infection	Urgency sympt.	Extrusion
Agostini	12,280	7.3	—	—	6.6	—	—	—	0.2
Dyrkorn	4,281	3.5	1.2	—	1.6	—	0.7	—	—
Tamussino	2,795	2.7	—	2.3	—	17	—	—	—
Kuuva	1,455	3.8	2.4	1.9	7.6	4.1	0.8	0.2	0.7
Kristensen	778	6.6	0.8	—	16.6	3.1	0.0	—	—
Karam	350	4.9	1.7	0.9	4.9	10	—	12	0.9
Levin	313	5.1	—	—	2.5	—	—	8.3	1.3
Debodinance	256	5.5	0.4	—	5.1	3.1	—	12	—
Abouassaly	241	5.8	1.9	2.5	19.7	—	0.4	15	0.4
Pushkar	187	5.4	9.1	—	5.9	—	—	10.1	—
Nilsson	161	3.7	1.2	1.8	4.3	6.2	1.8	3.1	—

Abbreviation:—, not reported.

A potentiality of more serious vascular complications exists with a partly blind procedure. The incidence of such has been very low. The rate of serious vascular complications in the Finnish registry report was 0.07% and the Austrian registry reported a bowel perforation rate of 0.04%.

SUMMARY

Available data obtained from published clinical reports show that the TVT operation is effective in curing stress incontinence. In prospective trials where strict criteria for cure and significant improvement have been used, approximately 95% of women having a TVT operation are found to be cured or significantly improved of their stress incontinence. Furthermore, the TVT procedure seems to perform well in all categories of patients on whom incontinence surgery traditionally is recommended, that is, in primary cases of stress incontinence, in cases of prior failed incontinence surgery, and in cases with mixed incontinence, in those with intrinsic sphincter deficiency, and in overweight and obese women. The risk of intraoperative and short-term postoperative complications is low if proper training is provided and the operation is performed in its standardized way. No long-term adverse effects of the procedure have been reported.

In a cost-utility analysis by Manca et al., the TVT operation was found to be cost saving compared with open colposuspension [74].

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* Deceased

74 Transobturator Tape for Surgical Treatment of Stress Urinary Incontinence: Outside-In Technique

Emmanuel Delorme and Jean-François Hermieu

INTRODUCTION AND HISTORY

In 1990, Mouchel [1] was the first to attempt to recreate the natural urethral supportive system with a mesh for the treatment of stress urinary incontinence (SUI). At about the same time, DeLancey [2,3] described the anatomy of the pelvic–pubic fascia and theory of the occlusion of the urethra on this retrourethral fascia by the pressure generated by exertion. More recently, Petros and Ulmsten [4,5] applied DeLancey's law clinically and introduced the notion of tension-free tape, describing the retropubic tape (RPT). The tape is held in place solely by friction with the tissues through which it passes.

The concept of the transobturator sling links the aforementioned concepts and clinical experience: it reproduces, in location and orientation, the effect of the suburethral fascia covering the urogenital gutter, behind the urethra, from one puborectalis muscle to the other one.

The transobturator tape (TOT) sling is held in place by friction between the tape and the musculoaponeurotic structures of the obturator foramen. It is a perineal procedure. The procedure is performed in the space between the aponeurosis of the levator ani muscle above, the perineal membrane below, the obturator foramen laterally, and the urethra and paraurethral space medially (Figure 74.1). This perineal space does not contain any vascular, nervous, or visceral structures. The transobturator urethral suspension pathway is flatter than for retropubic suspension.

Compared to RPT, the first aim of transobturator route was to decrease the risk of visceral (bladder, digestive structures), vascular (Santorini's plexus, iliofemoral vessels), and neurological (obturator and pudendal nerves) problem. The second aim was to reduce voiding dysfunction because a horizontal urethral suspension is theoretically less likely to cause dysuria than a retropubic suspension.

The first TOT was implanted in 1999 and the first retrospective series was published in 2001 [6].

ANATOMY

The first anatomical studies published or communicated on TOT were based on the work of Delmas [7]. The obturator foramen is constituted by, from outside in, the middle adductor muscle, the external obturator muscle, the obturator membrane, and the internal obturator muscle. On its medial aspect, the obturator foramen is divided into two parts by the parietal insertion of the levator ani muscle. The upper part, above the levator, is the pelvic area. It contains, at the level of its superolateral angle, the obturator canal that is crossed by the obturator pedicle. At this level, the obturator foramen is very close to the bladder that rests on the levator ani muscle. The lower part of the obturator foramen is under the obturator insertion of the levator ani muscle (Figure 74.2). The perineal space is located under the superior aponeurosis of the levator ani muscle, above the perineal membrane, and from bottom to top is laterally bound by the ischiopubic ramus and the internal obturator muscle; its medial limit consists of the paraurethral space and urethra. This perineal space does not contain any vascular, nervous, or visceral structures. The tape should be located within this perineal space (Figures 74.1 and 74.2). In this perineal part of the obturator foramen, only two anatomical structures could cause some risks during placement of the tape:

The urethra, which must be identified and protected by the finger when passing the tunneling device.

The pudendal pedicle and more specifically its terminal branch, the dorsal nerve of the clitoris. This nerve follows the medial side of the ischiopubic ramus from back to front.

When introducing a surgical instrument into the obturator foramen from outside in, the bony ramus protects the pudendal nerve.

Outside the obturator fossa, in the groin, the two terminal branches of the obturator nerve are located. The anterior branch is away from the area where the TOT is done, but the posterior branch is internal and close to the groin passage of the TOT. This is the reason why the groin route of the TOT must be very close the ischiopubic bone [8].

SURGICAL TECHNIQUE (TUNNELING DEVICE FROM OUTSIDE TO INSIDE)

Prosthesis and Surgical Instruments

The tunneling device is a needle with the functional part shaped into a suitable curve, fitted with a fastening system enabling traction of the tape through the obturator foramen. There are various types of tunneling devices with different systems for securing the tape to their tip. The tape is usually made of knitted monofilament polypropylene. The tapes are either highly elastic, requiring a plastic sheath for placement, or low-elasticity tapes that do not require a plastic sheath.

Anesthesia

Any type of anesthesia is acceptable, as the adjustment of the position of the tape does not necessarily require patient participation. The anesthesia can be general, regional (spinal), or local.

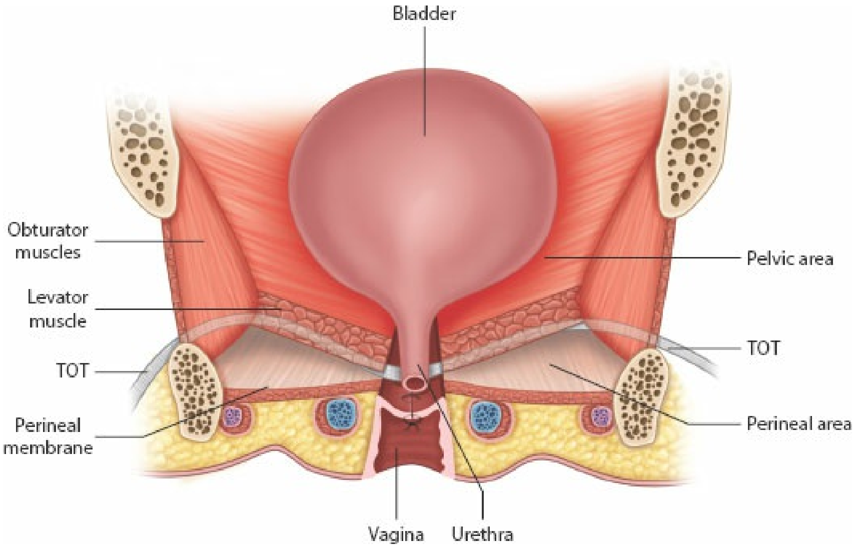


Figure 74.1 Transobturator tape is a perineal tape (with permission from Abiss).

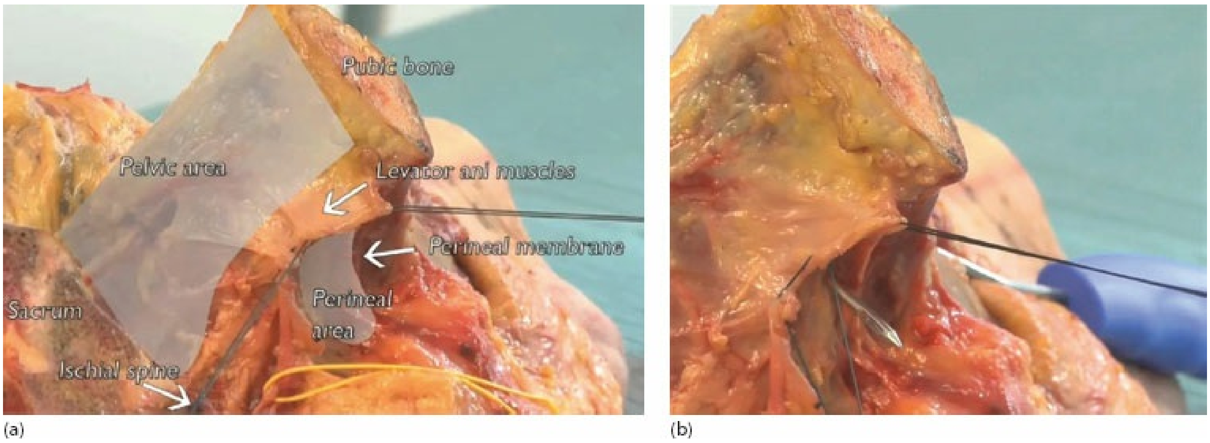


Figure 74.2 (a) Anatomy; (b) the needle is in the perineal area under the levator muscle.

Patient Position

The patient is placed in the dorsal lithotomy position. In this position, the hips are slightly less flexed avoiding risk of neural injury.

Surgical Technique

For operative guidance, a urethral catheter may help to manually locate the urethra more easily.

The sagittal retrourethral incision, which crosses the full thickness of the vaginal wall, must be wide enough to insert a finger (Figure 74.3). From this incision, dissect the vagina laterally on either side of the urethra. The dissection continues up to the ischiopubic ramus. The dissection is made in the deep anatomical plane, between the suburethral fascia and the urethra and not in the superficial surgical plane between the suburethral fascia and the vaginal skin. The lateral dissection should not disrupt the perineal membrane.

A puncture skin incision is made 15 mm laterally to each ischiopubic ramus at the horizontal level of the clitoris (Figure 74.4).

The tip of the tunneling device should emerge lateral to the middle third of the urethra. This course is controlled by aiming for the urethral meatus with the tunneling device (Figure 74.5). A finger is inserted as a guide inside the incision, laterally to the urethra, but above and behind the pubic bone. In conclusion, it is the arrival point of the tip of the tunneling device on either side of the urethra that determines at which level the tape will be positioned (Figure 74.5).

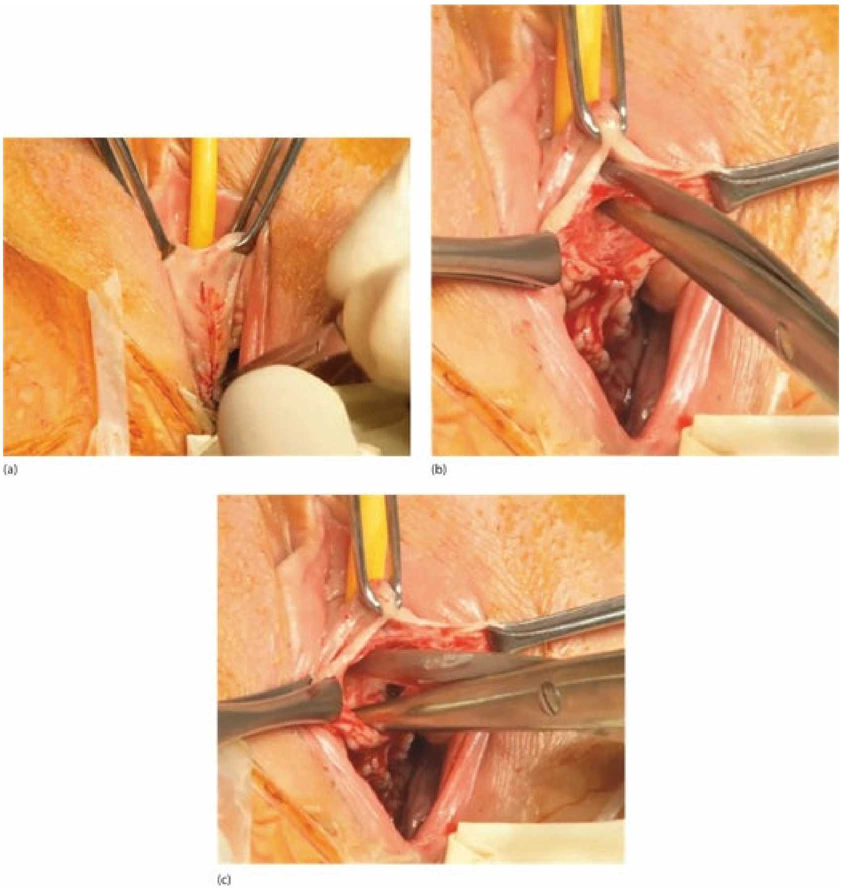


Figure 74.3 Vaginal incision and dissection: (a) mucosal incision; (b) suburethral fascial incision; (c) dissection between urethra and fascia, respecting the perineal membrane.

The tip of the tunneling device is guided inward, toward the urethra, aiming for the urethral meatus beneath the ischiopubic bone. The safest method is to guide the tunneling device around the ischiopubic ramus keeping it in close contact with the bone. When the tip of the tunneling device leaves contact with the bone, the needle crosses the obturator muscles, and immediately it can be felt by the operative finger behind the pubic bone (there remains only the perineal membrane for the needle to cross to be in close contact with the finger). The "blind" path of the needle is very short when using this method. The course of the tunneling device is a horizontal route and the needle comes out laterally to the urethra (in an acute angle between the ischiopubic bone and the urethra [Figure 74.6]). By applying this technique, the tape will be behind the middle third of the urethra, away from the bladder neck. The aim of this movement is to trace a perineal trajectory with the surgical instrument while staying underneath the superior fascia of the levator ani muscle. An index finger in the incision is used to ensure that the tunneling device does not come through the vagina and does indeed pass above the lateral fold at a distance from it. The tip of the index finger in the vaginal incision is used to push the urethra back upward and inward, protecting it from the needle. The finger will thus come into contact with the tip of the tunneling device laterally under the pubic overhang. The latter is then guided by the finger into the vaginal incision. The "blind" path when the tunneling device leaves the bone and comes into contact with the finger is very short (less than 15 mm). If it seems longer, then it is advisable to withdraw the tunneling device and start again. Once complete, it is advisable to look and check that the vagina has not been pierced by the tunneling device.

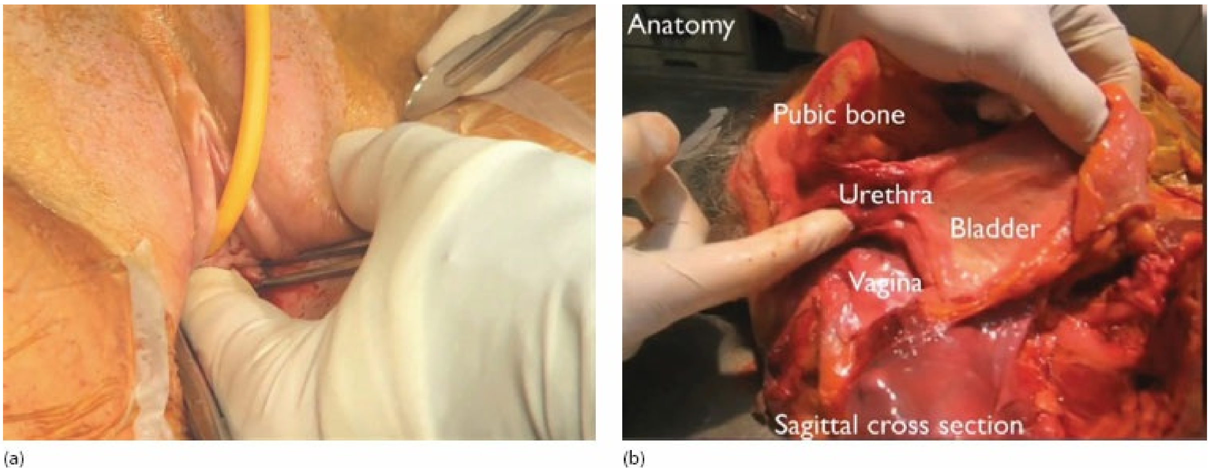


Figure 74.4 (a) Finger lateral to the urethra pushes the perineal membrane behind the pubic bone. (b) The obturator incision is at the horizontal level of the clitoris, close to and outside the ischiopubic bone.

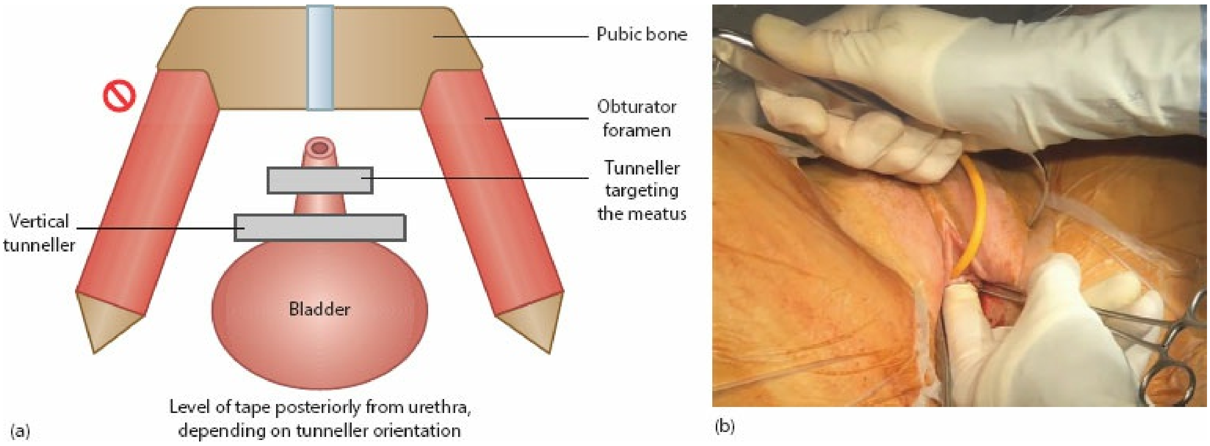

Pubic bone
Obturator foramen
Tunneller targeting the meatus
Vertical tunneller
Bladder
Level of tape posteriorly from urethra, depending on tunneller orientation
(a)
(b)

Figure 74.5 (a and b) Tunneler horizontally targeting the urethral meatus.

The tip of the tape is secured onto the tip of the needle/trochar and then drawn into place.

Adjustment of the tape behind the urethra can also be achieved using anatomical parameters. Two points are important when adjusting the position of the tape, to reduce the risk of urethral compression that can induce dysuria:

1. With a low-elasticity tape, a visible space must be left between the tape and urethra (around 5 mm) (Figure 74.7).
2. With a high-elasticity tape, the tape must be resting against the urethra without pressing on it.

The surplus tape outside the skin is cut off. The vaginal incision is closed with a few simple resorbable sutures. The obturator incisions do not need to be sutured—take care to separate the skin from the tape. If they are point-like and vertical, they will tend to close up naturally when the lower limbs are brought into the horizontal position at the end of the procedure. Suture material at this level can cause discomfort. It is not necessary to insert a vaginal mesh.

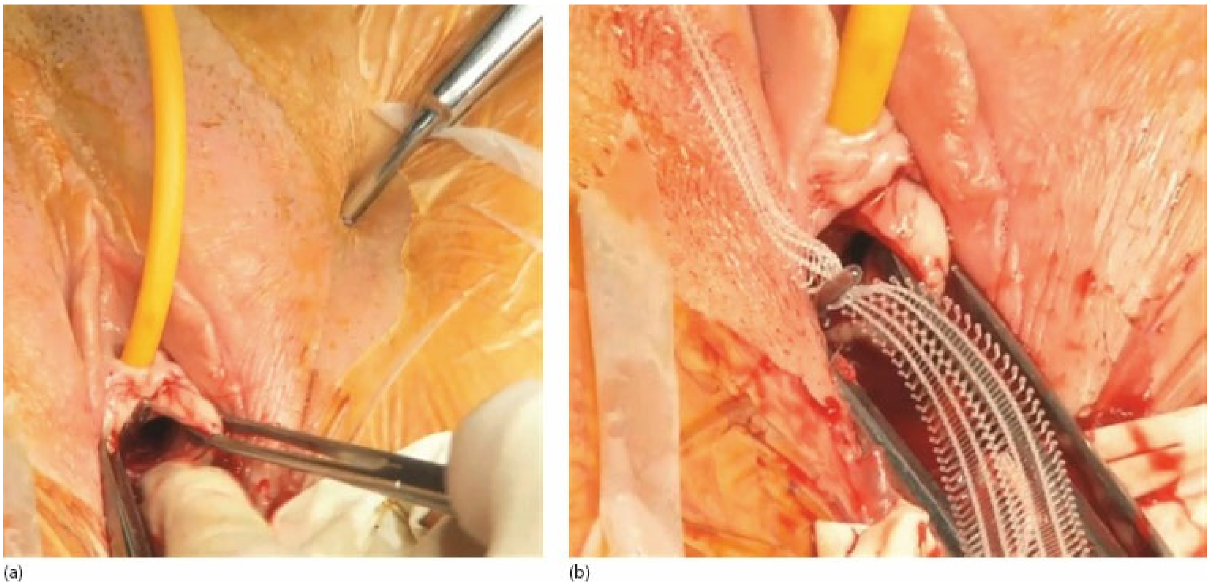


Figure 74.6 (a) The tunneller crosses the obturator fossa and (b) is outside the incision.

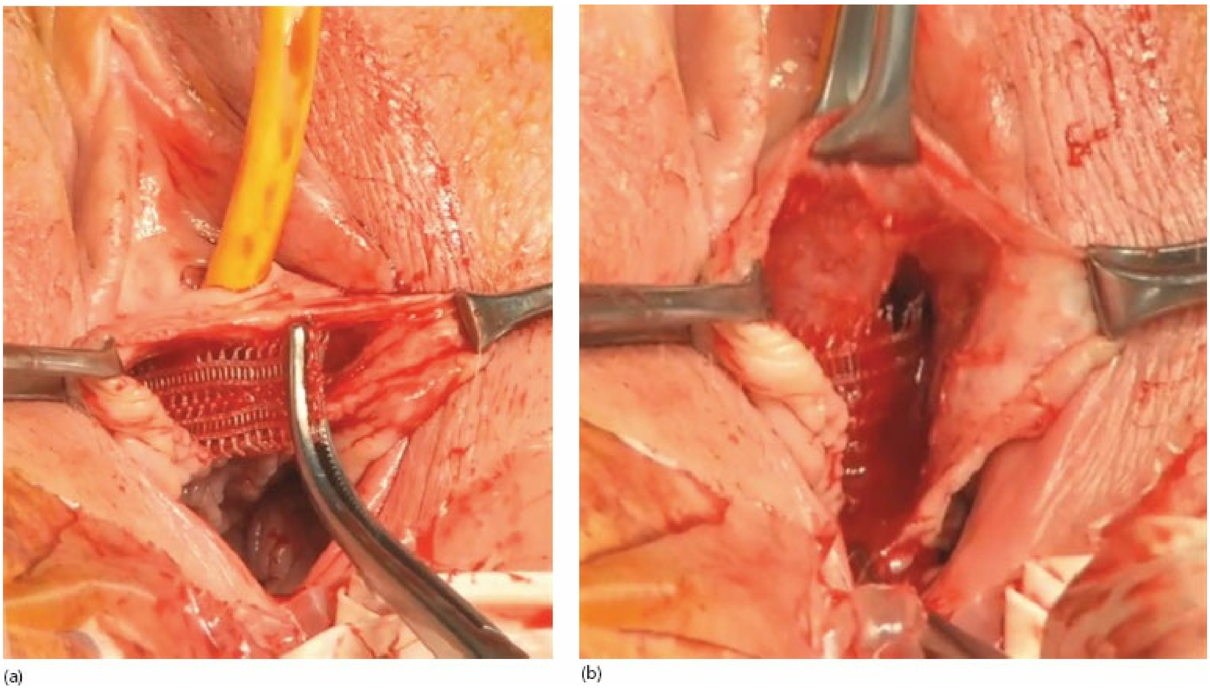


Figure 74.7 (a) Adjustment of the tape behind the urethra; the technique depends on the elasticity of the tape (a low-elasticity tape should be adjusted 5 mm away from the urethra). (b) Tape in place.

Postoperative Care

The catheter is usually removed at the end of surgery or the day after the procedure. Postmictional residue is measured with ultrasound or catheterization. If there is no significant postmictional residue, which is usual, the patient can be discharged.

CLINICAL PERFORMANCE OF TOT

This study is based to a large extent on the French recommendations on treatments for urinary incontinence using suburethral tapes published in 2010 by J.F. Hermieu [9–12].

Outside-In TOT, History, Results, and Compilations

Our preliminary series of patients who have undergone surgery for SUI with TOT® was only a retrospective feasibility study with follow-up generally of less than 1 year [6,13]. This study proved the feasibility of the intervention.

The synthetic material used (nonwoven polypropylene with silicone) later proved to cause vaginal erosion and sometimes severe infections.

The outcomes with the series of tapes placed by the transobturator route were spoiled by a higher number of cases of vaginal erosion and infections than the retropubic sling. This was essentially secondary to the use of materials unsuited to the vaginal route—multifilament polypropylene or heat-welded sprayed polypropylene. Meschia [14] reports in a comparative study on tension-free vaginal tape (TVT)/IVS erosion rates of 0% and 9%, respectively. Other publications report infectious complications with this type of material [15,16].

The consensus is currently to use for TOT® polypropylene monofilament knitted mesh [17] as defined by Ulstem for the retropubic route.

The rate of vaginal erosion with polypropylene monofilament knitted mesh tapes is 0.1%–2.4% [18,19] with a slight advantage for the retropubic route.

The TOT® route has been specified, thanks to anatomical studies [7]. Concerns about perioperative lesions to the obturator pedicle have been lifted by dissection work that has showed that the tunneler, then the tape, passed through the lower part of the obturator foramen, that is to say 2.2–2.5 cm from the pedicle with an average of 2.6 cm [20]. The TOT® is in the perineal space between the perineal membrane and the levator ani muscles.

The series published on the outside-in transobturator route confirm the anatomical data. The risk of perioperative complications is low, bladder wounds exceptional (0%–0.8%), and urethral wounds rare (0%–2.5%) [21,22].

In our prospective study [23] on 185 patients, there were no perioperative complications and no immediate revision surgery was performed. There were 23 immediate postoperative complications. Intermittent catheterization involved a total of 16 patients. For 14 of them, catheterization was necessary for less than 10 days. Two patients suffered from EVA > 3 postoperative pain. The same two patients continue to suffer from chronic pelvic pain with, respectively, 12 and 18 months follow-up. Four patients suffered from urinary tract infections and one patient suffered from pyelonephritis. There were no cases of late-onset serious complications (urethral or vaginal erosion), visceral injuries, or bleeding.

The average median follow-up was 23 months. For 68 patients follow-up has been demonstrated for more than 36 months. SUI was cured in 85.3% of cases and improved in 91.2% of cases. Among the urinary urgency patients in the preoperative phase, with urge urinary incontinence or without leakage, urinary urgency was cured in 51.4% of cases, improved in 22.9%, and unchanged in 25.7% of cases.

The de novo dysuria rate amounted to 3.3% at 3 months and 4.4% at over 36 months.

The efficacy of TOT® for treating SUI and its low morbidity have been reported in numerous publications (see Table 74.1) and confirmed by the most recent work [24–26].

Comparison of Outside-In TOT® with Other Types of Suburethral Tapes

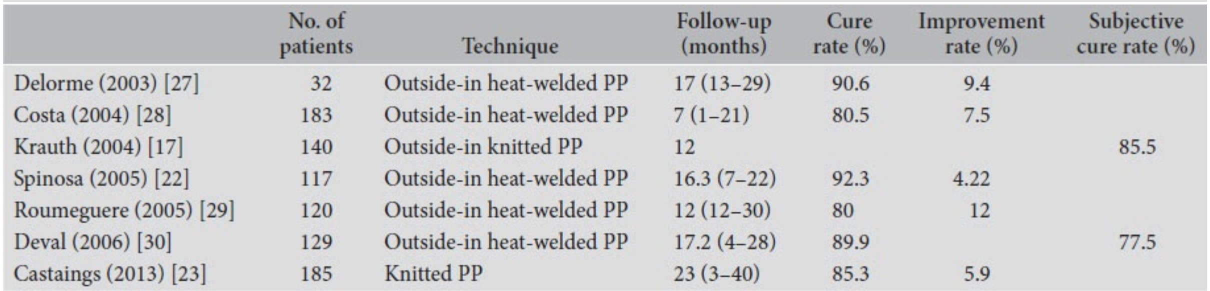
Inside-Out TOT®

In 2003, de Leval [31] proposed an inside-out transobturator route with the following objectives: to retain the advantages of the transobturator route and to avoid the supposed disadvantages of the outside-in transobturator route (exceptional risk of bladder wounds, risk of urethra wounds caused by the introducer device passed from the outside in, to avoid an incision and excessive dissection of the vagina in order to insert a finger as far as the bone guiding the needle as it emerges in order to avoid any bladder/urethra injury).

Anatomical studies have shown that the pathway of the tape was closer to the pudendal pedicle and the posterior terminal branch of the obturator nerve than in the *outside-in* route [8,32]. The clinical studies have shown that this route is safe when technically it is implemented in line with the initial description. The rate of perioperative complications was identical to that of the *outside-in* route [33].

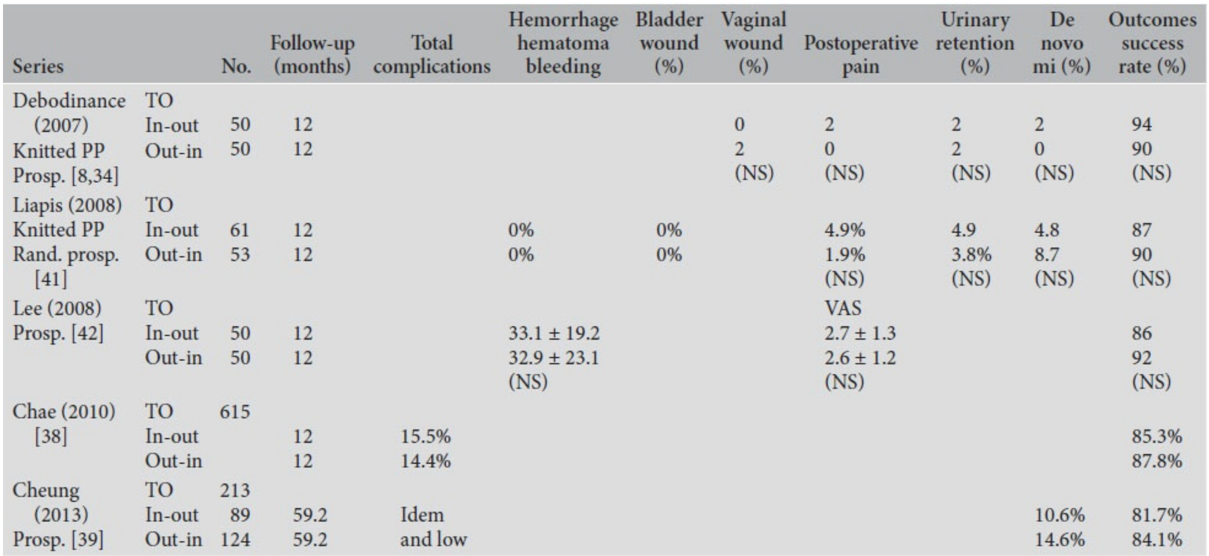
The Debodinance study [34] is a nonrandomized prospective study of a series of 100 women. At 1-year follow-up, he does not report any significant difference in terms of perioperative or late-onset complications, postoperative dysuria, or de novo urge incontinence. The 1-year cure rate is 94% in the inside-out group and 90% in the outside-in group (NS). These data are confirmed not only by Liapis [35], Lee [36], and Vervest's series [37] but also by Chae (series of 640 patients with 1-year follow-up) [38] and Cheung's [39] series with 5-year follow-up. For the majority of authors, the comparative study of the complications for the *inside-out* and *outside-in* routes does not show any significant difference between the two [40] (cf. Table 74.2).

Table 74.1 Outcomes for Outside-In TOT®



	No. of patients	Technique	Follow-up (months)	Cure rate (%)	Improvement rate (%)	Subjective cure rate (%)
Delorme (2003) [27]	32	Outside-in heat-welded PP	17 (13–29)	90.6	9.4	
Costa (2004) [28]	183	Outside-in heat-welded PP	7 (1–21)	80.5	7.5	
Krauth (2004) [17]	140	Outside-in knitted PP	12			85.5
Spinosa (2005) [22]	117	Outside-in heat-welded PP	16.3 (7–22)	92.3	4.22	
Roumeguere (2005) [29]	120	Outside-in heat-welded PP	12 (12–30)	80	12	
Deval (2006) [30]	129	Outside-in heat-welded PP	17.2 (4–28)	89.9		77.5
Castaings (2013) [23]	185	Knitted PP	23 (3–40)	85.3	5.9	

Table 74.2 Comparison Inside-Out and Outside-In TOT®



Series		No.	Follow-up (months)	Total complications	Hemorrhage hematoma bleeding	Bladder wound (%)	Vaginal wound (%)	Postoperative pain	Urinary retention (%)	De novo mi (%)	Outcomes success rate (%)
Debodinance	TO										
(2007)	In-out	50	12				0	2	2	2	94
Knitted PP	Out-in	50	12				2	0	2	0	90
Prosp. [8,34]							(NS)	(NS)	(NS)	(NS)	(NS)
Liapis (2008)	TO										
Knitted PP	In-out	61	12		0%	0%		4.9%	4.9	4.8	87
Rand. prosp.	Out-in	53	12		0%	0%		1.9%	3.8%	8.7	90
[41]								(NS)	(NS)	(NS)	(NS)
Lee (2008)	TO							VAS			
Prosp. [42]	In-out	50	12		33.1 ± 19.2			2.7 ± 1.3			86
	Out-in	50	12		32.9 ± 23.1			2.6 ± 1.2			92
					(NS)			(NS)			(NS)
Chae (2010)	TO	615									
[38]	In-out		12	15.5%							85.3%
	Out-in		12	14.4%							87.8%
Cheung	TO	213									
(2013)	In-out	89	59.2	Idem						10.6%	81.7%
Prosp. [39]	Out-in	124	59.2	and low						14.6%	84.1%

Transobturator Tape or Retropubic Tape

In Sung's meta-analysis [43], over 303 references were identified. Unfortunately, 285 of them were not comparative studies, did not have a control group, or were not explicit enough to be used. The meta-analysis was only able to use 18 articles, 6 randomized studies (representing 492 women), and 12 cohort studies (representing 2009 women).

It was not possible to clearly evaluate the objective cure rate due to evaluation criteria that were unclear and varied from one study to the other. The relative risk of subjective curing of SUI by the transobturator route compared to the retropubic route is 0.82 (CI 95%, 0.19–0.83). The relative risk of perioperative complications with the transobturator route compared to the retropubic route is 0.40 (CI 95%, 0.19–0.83) when it is based on randomized studies and 0.21 (CI 95%, 0.10–0.44) when it is based on cohort studies. The most common complication is bladder perforation (3.5% with the retropubic route, 0.2% with the transobturator route), followed by hematoma (1.6% vs. 0.08%), and then infection (less than 1% in both groups).

The relative risk of de novo urge incontinence at 1-year follow-up with the transobturator route compared to the retropubic route is 0.63 (CI 95%, 0.12–3.33) when it is based on randomized studies and 0.48 (CI 95%, 0.23–1) when it is based on cohort studies.

This meta-analysis, however, is open to criticism. Its results are based on studies that include some that are indisputably biased. The results are determined based on several variables (route first of all, but also type of tape). The lengths of the follow-up are not homogeneous.

Latthe’s meta-analysis [44] uses five randomized trials comparing TVT-O and TVT and six trials comparing TOT® and TVT. These studies are not all included in Sung’s meta-analysis. The subjective cure rate for the transobturator route, whether outside-in or inside-out, at 2- and 12-month follow-up, was no better than for the retropubic route (OR 0.85; 95% CI 0.60–1.21). Complications such as bladder injury (OR 0.12; 95% CI 0.05–0.33) and voiding dysfunction (OR 0.55; 95% CI 0.31–0.98) are less frequent than for the retropubic route. On the other hand, pain in the root of the thigh (OR 8.28; 95% CI 2.7–25.4) and vaginal wounds as well as exposure of the mesh (OR 1.96; 95% CI 0.87–4.39) are more common after placing the sling by the transobturator route.

A certain number of recent studies have confirmed the comparable efficacy and low morbidity of the RPT and the TOT® after a short follow-up period (3 months) [45]. Over a longer follow-up period, the outcomes remain comparable and stable: 2 years [46], 5 years for Angioli [47] with 71% of patients cured of SUI, but only 60% of patients satisfied in each group, but this is a small series (72 patients). The risk of de novo urgency would appear to be significantly lower after placing a TOT® than a RPT even with a long follow-up period for some [48], but this is not found in all the series of patients [49] (Table 74.3).

Table 74.3 Comparison TOT®/RPT

Series		No.	Follow-up (months)	Hemorrhage hematoma bleeding	Bladder wound (%)	Vaginal wound (%)	Postoperative pain	Urinary retention (%)	Erosion (%)	De novo mi (%)	Outcomes success rate (%)
Mellier (2004)	RP	99	29.5	10%	10					3.4	90
Knitted PP	TO	94	12.8	2%	0					4.1	95
Retrosp. [50]											(NS)
David Montefiore	RP	42	1	4.8%	9.5	0	(NRS)			4.8	92.9
(2006)	TO	46		0%	0	10.9	2 ± 2			8.7	93.5
Knitted PP				(NS)	$p = 0.03$	$p = 0.03$	0.8 ± 1.4			(NS)	(NS)
Rand. prosp. [51]							$p = 0.03$				
Liapis (2006)	RP	46									89
Knitted PP	TO	43									90
Rand. prosp. [52]	In-out										(NS)
Dietz (2006)	RP	56	9								73.2
Knitted PP	TO	58									94.8
Retro. [53]											$p = 0.0018$
Laurikainen (2007)	RP	136	2	(NS)			1.5			2.2	98.5
Knitted PP	TO	131					16			2.3	95.4
Rand. prosp. [54]	In-out						$p < 0.01$			(NS)	(NS)
Andonian (2007)	RP	80	12	3.8%	13.8		(%)	7.5	0		86
Knitted PP/	TO	78		2.6%	0		6.3	7.8	2.6		83
ht-welded PP				(NS)			3.9				(NS)
Random. prosp. [55]											
Porena (2007)	RP TO	73	31	(NS)	2.7	0		(NS)	(NS)	14	71.4
Rand. prosp. [56]		75			1.33	5.33				11	77.3
											(NS)
Paick (2007)	RP	252	10.8		4.8			15.1			92.1
Retrosp. [57]	TO	212			0			6.6			84.9
					$p = 0.001$			$p = 0.004$			$p = 0.015$
Lee (2007)	RP	60	13	40 ± 23.8	3.3		(NS)	10		0	86.8
Knitted PP	TO	60		31.1 ± 28.6	0			13.3		6.6	86.8
Rand. prosp. [36]	In-out			(NS)	(NS)			(NS)		(NS)	(NS)
Zullo (2007)	RP	35	12	38.9 ± 9.4 mL	5.7	2.7		2.7	0	9	91
Knitted PP	TO in-out	37		42.5 ± 8.6	0	0		0	0	0	89
Rand. prosp. [58]				(NS)						(NS)	(NS)
Barry (2008)	RP	107	3	64 mL	8.5			(NS)	1.2		78
Knitted PP	TO	80		49 mL	0				5.4		82.8
Rand. prosp. [59]				$p < 0.05$	$p < 0.05$				(NS)		(NS)
Aigmüller (2014)	RP	480	3								87%
Prosp. [45]	TO										84%
George (2010) [46]	RP				1.3%			9.2%[a]/2.6%[b]			97.4%
	TO				0%			4.1%[a]/1.4%[b]			94.5%
Angioli (2010)	RP	72	60								72.9%
Rand. [47]	TO										71.4%

[a] Less than 1 week after surgery.

[b] More than 1 week after surgery.

In conclusion, overall TOT® and RPT have similar outcomes in the treatment of SUI. The use of RPT is accompanied by a risk of bladder injury that does not exist with TOT®. The TOT® has an increased risk of inguinal pain compared to RPT—the majority of publications reporting inguinal pain concern inside-out TOT® series [60,61].

TOT® and Pain

The transobturator route and more particularly the inside-out route may be implicated in the etiology and pathogenesis of postoperative pain [62–64] and traumatic neuropathy [62]. The risk of nerve injuries to the pudendal nerve and the posterior terminal branch of the obturator nerve is controversial from the anatomical point of view for the inside-out transobturator approach [7,65]. Pudendal nerve damage has been proven in some studies on the *inside-out* approach [66]; however, the rarity of this complication does not lead to a conclusion that there is a greater neurological risk with *inside-out* than with *outside-in* approach. The risk of injury to the posterior terminal branch of the obturator nerve has been demonstrated anatomically [32]. When using the inside-out technique, passing as close as possible to the external side of the ischiopubic ramus limits the risk of injury to the posterior terminal branch of the obturator nerve.

Poorly discriminated pain in the groin and root of the thigh region, usually transient, is more common in inside-out procedures [44]. Passing through the pelvic insertion of the adductor longus muscle may be responsible for postoperative pain [32].

Inguinal pain is found in most of the *inside-out* TOT® series, but is found or described less often in *outside-in* series [61,67]. In our first series [6], no patients had inguinal pain; in our second series published [23] at 3-year follow-up, only two patients had pain worse than 3 on a scale of 0–10.

Cases of dyspareunia have been described after a TOT® procedure, although studies on sexuality before and after a TOT® procedure objectively show an overall improvement in the quality of patients' sex lives after a TOT® as SUI interferes with their sex lives [68].

Pain can have several other etiologies: infection of the implant requiring its removal and also idiopathic retraction of the implant. Chronic inflammatory reactions have also been described and perhaps painful scar neuromas during prosthetic ingrowth [69]. Treatment of such pain requires the removal of the sling straps [70,71].

SPHINCTER DEFICIENCY

The urodynamic definition of sphincter deficiency varies from one study to another. It is difficult to compare the different series of patients.

For some, tapes give less good results in treating sphincter deficiency than SUI [57]. The TOT® is less effective than RPT in cases of sphincter deficiency [23,26,72].

Although tapes have lower efficacy on sphincter deficiency than on SUI, they still have their uses in the treatment of sphincter deficiency; for Goktolga, 57.4% of patients are satisfied after 5 years [73].

Some studies show that placing a tape by the retropubic route is more effective in the short and medium term than the transobturator route, when there is sphincter deficiency (86.94% compared to 34.89%) [74–76].

The RPT has been proposed to treat TOT® failure, with 75% long-term success [77]. This is confirmed by Schierlitz's [78] prospective comparative study, which proves the greater efficacy of RPT compared to TOT® in treating sphincter deficiency at 3-year follow-up. The median time to repeat surgery for TOT® was 15.6 months compared with 43.7 months for RPT ($p < 0.001$).

Urethral hypermobility seems to be a criterion, much more decisive than sphincter deficiency, in the efficacy of tape and particularly of TOT®. Fixity of the urethra is a factor of failure of TOT® [79,80].

CONCLUSION

Surgical Technique

The surgical technique for the implantation of a TOT (*outside-in* procedure), although simple, should be very strict. The following technical points must be respected to ensure the safety of the procedure:

- The vaginal incision must be deep to ensure that the dissection is performed in the anatomical plane between the urethra and retrourethral fascia.
- The trajectory of the tunneling device should be oriented toward the middle third of the urethra; this is achieved by aiming for the urethral meatus until it can be felt with the finger at the top inside the vaginal incision, behind the pubic bone; the needle's path is horizontal.
- The tunneling device should remain in close contact with the bony ischiopubic ramus throughout its trajectory.
- The tip of the finger must be inserted into the incision, to protect the urethra and then to accompany the tip of the tunneling device into the vaginal incision.

Clinical Conclusions

The most significant advantage of the TOT procedure compared to RPT is the lower risk of visceral complications and hemorrhaging. There is tendency for less dysuria and urgency after placing a TOT than with an RPT.

The TOT seems to have three weaknesses compared to the RPT:

1. There is a greater risk of vaginal erosion, in particular laterally, but this is due to poor insertion technique.
2. The TOT seems to be less effective than the RPT in treating sphincter deficiency.
3. The risk of postoperative pain appears to be greater after placing a TOT. More postoperative pain is reported in publications for tapes placed by the *inside-out* route than after the *outside-in* TOT approach.

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75 Single-Incision Minislings

Mickey Karram and Radhika Sharma

INTRODUCTION

In 2006, the single-incision synthetic midurethral sling (MUS) was introduced as a modification to traditional retropubic and transobturator MUSs. These slings were designed to require less dissection in the midurethral area without the need to make additional incisions suprapubically or in the groin. They are placed entirely through an incision in the vagina having no exit point. They were designed to minimize the risk of bladder perforation associated with traditional retropubic MUS and the risk of groin discomfort or other issues related to the inner thigh associated with passage of transobturator slings through the obturator membrane and adductor compartment. Single-incision minislings are anchored into the obturator internus muscles or connective tissues of the endopelvic fascia of the retropubic space behind the pubic bone, and more recently, some are anchored directly into the obturator membrane.

Early SIMS had decreased efficacy compared to standard MUS and long-term data were lacking. However, recently, long-term outcome data have become available regarding the effectiveness of SIMS as compared to their standard MUS counterparts.

A survey of urologists in the United States suggests that 10% of practicing urologists have already adopted this technology for regular use in patients with primary stress urinary incontinence (SUI). However, the U.S. Food and Drug Administration (FDA) has recently required the manufacturers of SIMS pursue additional studies to further document long-term efficacy and safety. This mandate leads to the voluntary withdrawal from the market of at least two commercially available SIMS. These studies, which will be ongoing over the next 2 years, will determine the future of these devices.

INDICATIONS AND PATIENT SELECTION

Indications for SIMS are similar to the indications for the more traditional MUS in that they can be offered as an initial, definitive treatment of SUI. Because the minisling is less invasive than a retropubic or transobturator MUS, it may be desirous for some special patient populations. Because it avoids the retropubic space, the minisling may be considered specifically in patients who have undergone previous retropubic and abdominal procedures and may be at higher risk for significant pelvic adhesions. Because it does not entail complete passage of trocars to the skin level, it may be considered in patients with significant soft-tissue mass or obesity in the areas of traditional MUS trocar site exit (i.e., truncal or intertrigonal obesity) that may surpass the length of the trocar. Because single-incision minisling procedures can be done under local anesthesia, they can also be considered in patients with significant comorbidities in whom general anesthesia is contraindicated.

DESCRIPTION OF VARIOUS TYPES OF SINGLE-INCISION SLINGS

Five SIMS are commercially available at the present time in the United States: MiniArc single-incision sling (SIS) system, MiniArc Precise SIS system, MiniArc Pro SIS system (American Medical Systems, Minnetonka, MN), Solyx SIS system (Boston Scientific Corp., Natick, MA), and Altis SIS (Coloplast, Minneapolis, MN).

The MiniArc SIS (Figure 75.1) is a polypropylene mesh (8.5 cm × 1.1 cm) with permanent self-fixating tips that is deployed with a supplied metal 2.3 mm needle/trocar. The mesh is connected to the tip of the needle before insertion; the mesh and needle are inserted; and the needle is removed, leaving the mesh behind. Self-fixating tips are constructed of polypropylene and have two anchoring barbs that help resists up to 5.5 lb of pullout force to remove the mesh. A redocking maneuver can be set up before insertion to allow retrieval and reinsertion of the mesh if necessary.

The MiniArc Precise has a similar setup and procedure to the MiniArc SIS. The advantage of the

Precise sling is preventing mesh rotation and disengagement. This mesh is also geared at improving the control of sling tension that had been lacking in previous models of the single-incision synthetic slings.

The MiniArc Pro system varies with its earlier two counterparts by incorporating a visual feedback system allowing repeatable, standardized control. A feedback system has been employed that utilizes a stationary scale and an indicator that moves relative to the scale if the mesh is elongated or tensioned. This marking system allows for the placement of the sling under the portion of the urethra being supported in a consistent manner.

The Solyx SIS system (Figure 75.2) includes a polypropylene mesh tape (9 cm in length) with permanent barbed self-fixating tips and a metal and plastic delivery device or trocar. This system is designed similarly to the MiniArc SIS system, in that each tip of the sling is sequentially attached to the end of the delivery device for mesh placement, which is removed after insertion. The edges of the center 4 cm of the mesh (advertised as the suburethral portion) are bonded together to potentially reduce irritation and the possibility of mesh erosion or extrusion.

The Altis SIS system (Figure 75.3) is a macroporous, knitted, monofilament polypropylene sling (7.75 cm) spanning between the obturator membrane complexes. The sling has a low elasticity at 7.5% similar to collagen fibers; it also has a radiopaque coating for imaging. Affixed to each side of the sling is a monofilament suture. The anchors on the sling are designed to secure maximum pullout force while allowing a flexible secure placement. The tensioning sutures on either end of the mesh allow for a movable anchor with two-way adjustability. This theoretically is meant to prevent sling movement during the healing period.

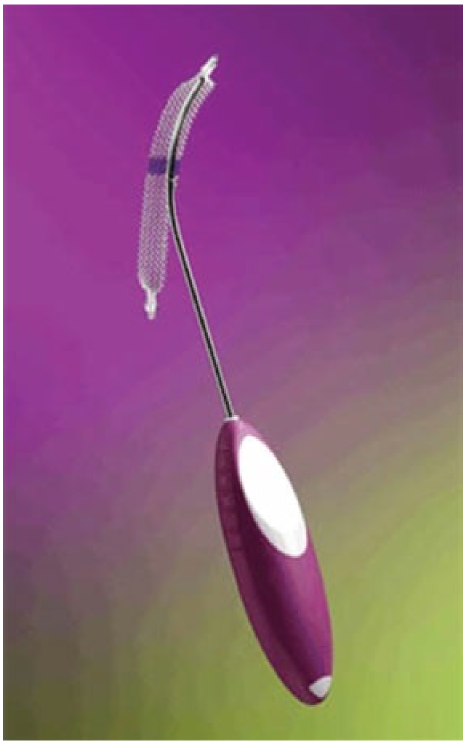

Figure 75.1 MiniArc single-incision sling. (Reproduced by courtesy of American Medical Systems, Minnetonka, MN.)

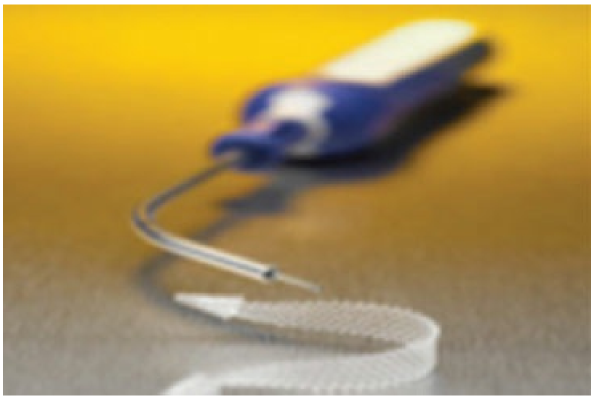

Figure 75.2 Solyx single-incision sling. (Reproduced by courtesy of Boston Scientific Corporation, Natick, MA.)

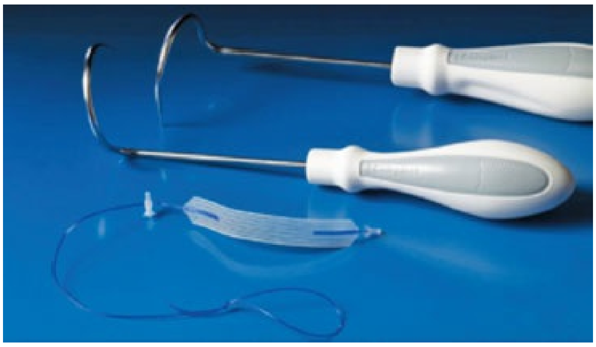

Figure 75.3 Altis single-incision sling. (Reproduced by courtesy of Coloplast, Minneapolis, MN.)

SURGICAL TECHNIQUE

1. *Preoperative considerations*: Insertion of a minisling may be performed under many different types of anesthesia, including general, spinal or epidural, regional, and local. Perioperative antibiotics (e.g., fluoroquinolone or first-generation cephalosporin) are generally administered before the incision.
2. *Patient positioning*: The patient is positioned in the dorsal lithotomy position with legs in stirrups. The perineum and vagina are sterilely prepared and draped so as to exclude the anus. Lateral labia majora retraction stitches may be placed or a self-retaining retractor may be used to improve vaginal exposure. A weighted vaginal speculum is placed, and bladder drainage is accomplished with a Foley catheter.
3. *Vaginal incision*: A 1–1.5 cm midline incision is marked starting 1 cm below the urethral meatus, and the area is infiltrated with injectable grade saline or 1% lidocaine with epinephrine for hydrodissection of the periurethral tissues. An Allis clamp may be placed distal to the incision, with care taken not to traumatize the urethral meatus, to facilitate visualization. An incision is made sharply with a scalpel.
4. *Vaginal flap dissection*: Dissection of lateral vaginal flaps proceeds in a standard fashion with attention to developing an appropriately robust and well-vascularized vaginal flap, while not jeopardizing the thickness of the periurethral tissue. This flap is carried laterally and anteriorly until the endopelvic fascia is encountered, but the retropubic space is not entered (Figure 75.4a and b).
5. *Preparation of the Sling*: The sling is prepared by inserting the tip of the delivery device or needle into the self-affixing end of the mesh apparatus, ensuring that the mesh is oriented on the outside of the delivery needle.
6. *Insertion of sling*: To place the MiniArc SIS or Solyx SIS, the tip of the delivery needle with mesh assembly attached is inserted into the previously dissected vaginal space and aimed along a path 45° from the midline (Figure 75.5). The placement should be immediately posterior to the

ischiopubic ramus; the needle can be “walked off” the posterior aspect of the bone, maintaining a close proximity to the posterior surface of the bone. The tip should be advanced until the midline marking on the mesh is situated under the middle of the urethra. The needle is removed from the mesh, attached to the other end of the mesh device, and inserted on the contralateral side in a similar manner, ensuring the mesh lies flat under the urethra, until the proper degree of desired tension is achieved. The delivery device is disengaged and removed. The MiniArc SIS can be arranged with a delivery/inserter needle to facilitate reconnecting the needle tip into the self-affixing tip of the mesh device. This arrangement allows for the mesh to be inserted further, if more tension is desired. The redocking procedure entails threading a 2–0 polypropylene suture through the tip of the mesh assembly and then through the tip of the delivery device, knotting one end. This end of the mesh is placed first, in the usual fashion, and then the delivery needle is removed, leaving the suture in place. The opposite side is also placed in the usual fashion. If further tensioning is warranted, the free end of the suture is reinserted into the end of the delivery needle, and the needle is advanced along the suture, sliding into the tip of the mesh device. Once docked, the entire mesh device can be advanced further into the patient.

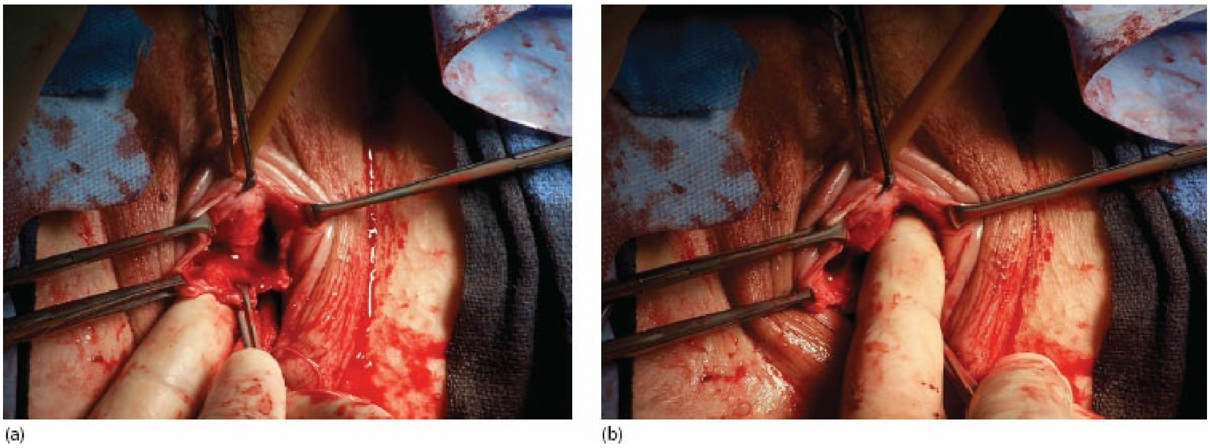

Figure 75.4 (a) Distal anterior vaginal wall incision made prior to passage of a single-incision sling. (b) Note the index finger of the surgeon is used to palpate the lower edge of the inferior pubic ramus.

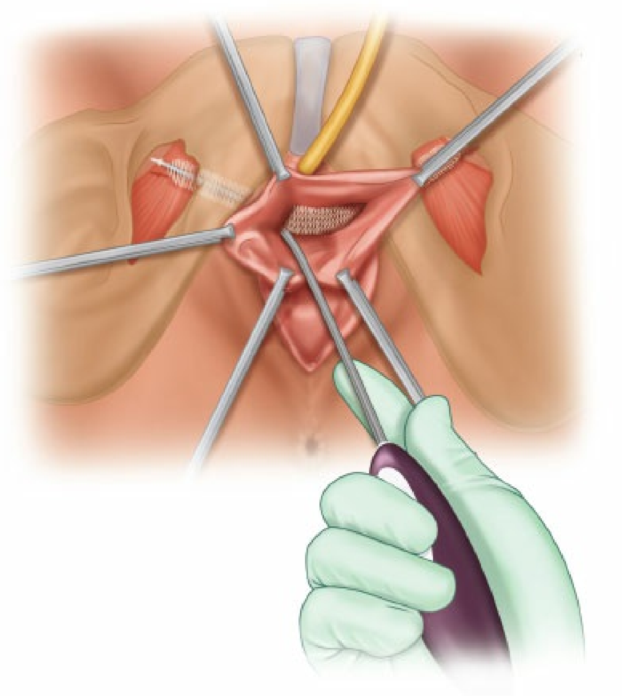

Figure 75.5 Technique for placement of the MiniArc single-incision sling. The sling is placed directly into the obturator internus muscle. (Reproduced from Baggish MS and Karram MM, *Atlas of Pelvic Anatomy and Gynecologic Surgery*, 3rd ed., Elsevier, St. Louis, MO, 2011. With permission.)

The placement of the Altis adjustable SIS proceeds by the same initial steps (steps 1–4) as previously outlined. After appropriate dissection is completed, the fixed anchor is pushed into the tissue until it is slightly beyond the ischiopubic ramus. The handle is pivoted toward the obturator internus muscle and membrane. A metal tip of the trocar extends past the anchor allowing for an easier placement of the anchor into the obturator membrane. The fixed anchor is pushed through the obturator internus muscle and membrane. Gentle traction is applied to the suburethral sling to confirm proper fixation. The adjustability of the sling is independent of its insertion and does not lock, which allows the loosening of the sling should it be found to have been set too tightly.

7. *Cystoscopy*: Cystoscopy should be performed to evaluate for bladder injury.
8. *Vaginal closure*: The vaginal incision is closed in the same way as described previously in which the anterior sulcus is trimmed, and the vaginal incision is closed.

Outcomes

Up until recently, very little data existed on the outcomes of SISs especially when compared to more traditional transobturator and retropubic MUS. Table 75.1 reviews outcome data on single-incision MUSs. All studies were compared to either retropubic or transobturator MUS. Outcomes of the studies were objective and subjective and assessed at 12 and 24 months postoperatively. Objective outcomes encompassed negative cough stress test (CST) and the 1 hour pad test. Subjective cure rates included the reported episodes of leaking following the procedure, subjective reports of SUI, self-assessment of cure, overall satisfaction with results, and resolution of symptoms. Randomized control trials included the use of MiniArc, Ajust, Ophira, and Solyx slings. Studies on tension-free tape (TVT)-Secur were excluded from Table 75.1.

Abdel-Fattah's recent meta-analysis of randomized controlled trials comparing SISs (after excluding TVT-Secur) to transobturator and retropubic MUS showed no difference in patient-reported outcomes and objective cure rates. The analysis also revealed lower postoperative pain scores and earlier return to normal activity in the SIS groups.

Table 75.1 Outcome Data on Single Incision Mus

Study, dates	Design	Enrolled	Inclusion criteria	Intervention	Outcome and follow-up
Enzensberger et al., 2010	RCT Austria	95	+CST, subjective SUI	MiniArc vs. TOT	MiniSling noninferior to TVT-O in objective cure rate. Postoperative pain at 48 hours, length of operation shorter for minisling.
Oliveira et al., 2008	RCT Portugal	60	Clinical and urodynamic SUI	MiniArc vs. TVT-O	Objective and subjective cure rates equivalent.
Merali et al., 2012	RCT Canada	37	All participants SUI	MiniArc vs. TOT	Objective cure rates at 12 months postoperatively were equivalent.
Schellart et al., 2009–2011	RCT Multicentered Netherlands	193	Urodynamic SUI	MiniArc vs. TOT	1 year follow-up MiniArc noninferior to Monarc subjective and objective cure rate, less postoperative pain with MiniArc.
Basu et al., 2009–2012	RCT United Kingdom	71	SUI symptoms and objective evidence of SUI, or failed conservative treatment	MiniArc vs. TVT	3-year failure rate significantly higher for single-incision sling vs. retropubic sling; both procedures had reduced efficacy over time.
Mostafa et al., 2009–2010	RCT Multicenter United Kingdom	137	SUI, failed or declined pelvic floor physical therapy, or primary continence procedure	Ajust vs. TOT	Lower postoperative pain profile in Ajust group, subject, and objective cure rates did not differ between Ajust and TVT-O slings.
Djehdian et al., 2008–2011	RCT Brazil	130	SUI, no prolapse > Stage I	Ophira vs. TOT	Minisling was inferior to TOT, minisling shorter operative time, and less postoperative thigh pain.
Piccione et al., 2008–2010	Prospective multicenter	95	Clinically symptomatic and urodynamic SUI	Ajust	Objective and subjective cure rates improved in patients treated with Ajust sling.

COMPLICATIONS AND SURGICAL TIPS

Complications that can occur are similar to the complications that can occur with retropubic and transobturator MUS. These include bladder injury or perforation, bleeding, vaginal mesh extrusion, urinary tract mesh erosion, voiding dysfunction, and urinary retention. Viscous organ damage and major vascular injury still may occur but in theory should be much less common because the needle/trocar trajectory through the retropubic or obturator space is significantly more truncated by design of the minisling.

Bladder perforation may occur at the time of sling insertion; the self-affixing points of the MiniArc SIS and Solyx SIS may make removal and reinsertion of the device difficult because these slings are not designed to be removed. Removal of the MiniArc SIS may be facilitated by setting up the redocking procedure with a suture. If bladder perforation occurs and is discovered on cystoscopy, the sling should be immediately removed. A secondary insertion should not be attempted at that operative time. In the authors' opinion, cystoscopy should be routinely performed at the time of placement of a SIS.

Because of the shorter length of inserted mesh, more tension is placed on the minisling at the time of insertion than is placed on other types of MUS. The implanted sling should be in close apposition to the urethra with no laxity in the material. The surgeon should use a clamp or right angle to determine that there is no redundancy in the sling material.

CONCLUSION

SISs were reported to have higher failure rates with increased rates of mesh erosion; however, several recent trials have demonstrated the efficacy of SISs to be comparable to more traditional transobturator and retropubic MUS. Specifically, the MiniArc when compared to standard MUS demonstrated similar efficacy. This could be secondary to improved design with alteration of the trajectory as well as improved surgeons' understanding of the minisling procedure. The compilation of recent outcome data demonstrates that there may be a role for SISs given their lower postoperative pain score, more favorable recovery time and earlier return to normal activities. However, further long-term outcome and safety data as mandated by the FDA will most likely ultimately determine the fate of these procedures.

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76 Readjustable Slings: Safyre and Remeex

Paulo C.R. Palma and Cassio Riccetto

INTRODUCTION

Slings have been the chosen option for most of the patients complaining stress urinary incontinence (SUI) for a long time. Synthetic slings have turned major surgeries into minimally invasive procedures and also reduce operative time and hospital stay as well as postoperative discomfort and the recovery period. Complex patients include those with multiple recurrences after the previous treatment attempts, specially using mesh, with dysfunctional voiding due to fixed urethra, and with previous urethral reconstructive surgery. Until recently, autologous material was mostly used for this subset based on two major concerns: risk of prosthetic implant infection and urethral erosion leading to pain and urethral fistulas [1]. Readjustable slings were proposed to allow for a safe and effective management of complex incontinence. In this chapter, we will focus on two most popular commercially available adjustable slings: Safyre and Remeex.

SAFYRE

The readjustable and self-anchoring Safyre sling (Promedon, Argentina) is a tension-free, synthetic sling, placed at the midurethra that makes urethral erosion unlikely. It was developed in the 1990s according to the integral continence theory [2]. This device allows for tension readjustment if postoperative persistent urinary leakage or retention occurs [3,4].

Features

From a conceptual standpoint, Safyre corresponds to a sling. So, the creation of a suburethral support zone increases urethral resistance and diminishes the rotational as well as the descending movement of the urethra when abdominal pressure increases. Additionally, it improves the coaptation of the urethral lumen at rest and under stress. However, contrary to the classical pubovaginal slings, the Safyre is applied in the middle third of the urethra, where the pubourethral ligaments, responsible for natural stability of the urethra, are inserted [2].

Safyre consists of a polypropylene monofilament mesh that acts as a urethral support, held between two self-anchoring tails made of polydimethylsiloxane polymer (silicon) (Figure 76.1). The Safyre self-anchoring system is created by a sequence of 4 mm cones displayed in a palm tree trunk conformation, creating a hooklike effect and attaching to the surrounding structures as the pelvic fascias and the abdominal rectus muscle as well. These tails are the key for the readjustable self-anchoring system. In order to minimize the surgical damage to pelvic floor natural support structures, a special 3.5 mm in diameter needle allows for retropubic placement, through both suprapubic and transvaginal approaches, according to the surgeon's best skills. The versatile needle is assembled for transvaginal approach when the hooked extremity is introduced inside the needle holder, and for suprapubic approach when assembled the other way (Figure 76.2). A special curved needle with a hooklike extremity is used for the transobturator approach (Figure 76.3). For this unique feature, i.e., universal approach, Safyre is the only sling so far that allows for comparing retropubic and transobturator procedures using the same device, in regarding to efficacy, safety, and complications.

In a comparative study, Safyre VS and Safyre T were analyzed. After a mean follow-up period of 18 months (ranged from 12 to 36 months), according to Blaivas and Jacobs criteria, 116/126 patients (92.1%) who underwent Safyre VS procedure and 94/100 (94%) who underwent Safyre T were found continent, and 3/126 (2.4%) and 2/100 (2%), respectively, reported significant improvement. In the same study, the impact on quality of life was assessed using the International Consensus of Incontinence Questionnaire Short Form (ICIQ-UI-SF), which showed significant improvement in all questions compared with preoperative assessment (90% of patients reported that they had less urinary symptoms after surgery, in both groups). At the end of follow-up period, the stress test was negative in all the continent and incontinent patients, and the incontinent group was using one pad per day at the most [5].

Retropubic Placement through Transvaginal or Suprapubic Approach (Safyre VS)

Two 0.5 cm transverse incisions are made close to the superior aspect of the pubic bone 5 cm apart from each other. A longitudinal vaginal incision 1.5 cm in length is made, starting 1 cm from the urethral meatus. Notice that this incision is not allowed encroaching on the bladder neck. Dissection is done to create a 1 cm tunnel lateral to the urethra for the introduction of the needle. First, the needle is advanced through the vaginal tunnel until the perforation of pelvic floor at the level of the midurethra. Then, it is redirected against the back of the pubic bone and advanced continuously to the previously made landmarks in the suprapubic area. Cystoscopy is performed to rule out bladder perforation. After the removal of the holder, Safyre VS is attached to the needle and pulled out to the suprapubic area. The same maneuvers are repeated on the other side. The proper tension of the sling is adjusted maintaining a Metzenbaum scissors between the urethra and the sling, to prevent undue tension. The extremities of the sling are cut and the Metzenbaum scissors removed. No further fixation is needed and the incisions are closed in the usual manner (Figure 76.4). An indwelling catheter is left in place overnight.

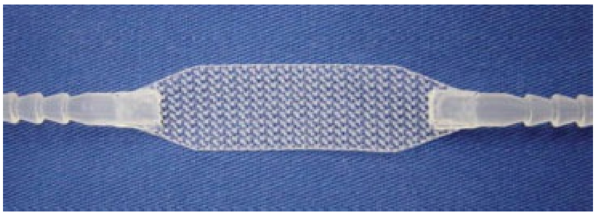

Figure 76.1 Safyre consists of a polypropylene mesh that acts as a urethral support, held between two self-anchoring tails made of polydimethylsiloxane polymer.

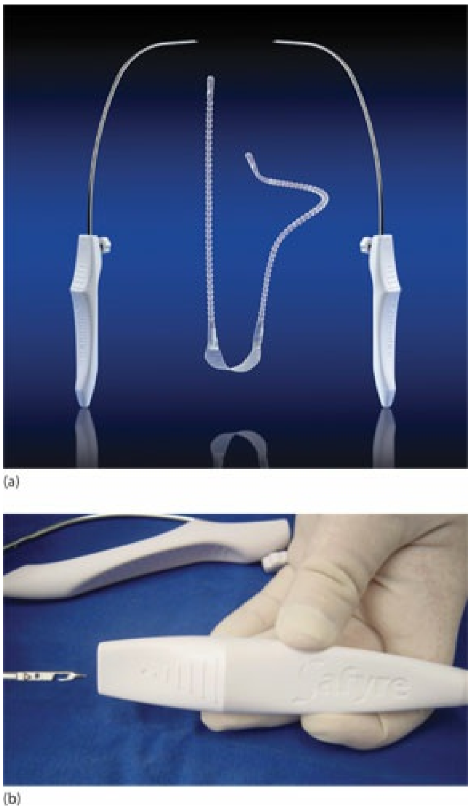
(a)
(b)

Figure 76.2 (a) Safyre VS set. (b) Safyre's needle can be assembled for retropubic transvaginal approach when the hooked extremity is introduced inside the needle holder and for suprapubic approach when assembled the other way.

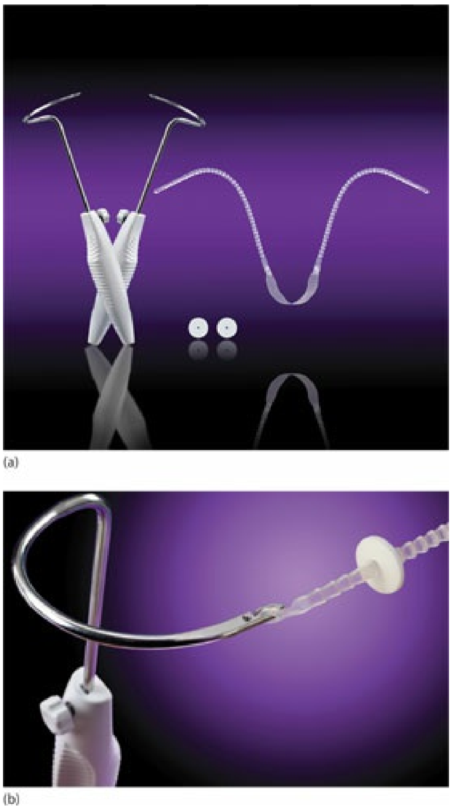

Figure 76.3 (a) Safyre T Plus set. (b) Detail of the helical needle, with a hooklike extremity is used for the transobturator approach.

Transobturator Approach (Safyre T)

Safyre T is a monofilament polypropylene mesh, which is held between two self-anchoring silicone columns that associate the universal approach with readjustability [6]. A 2 cm long vertical vaginal incision is performed at 0.5 cm from the urethral meatus. Minimal vaginal dissection is performed laterally toward the inferior ramus of the pubic bone; this minimal dissection avoids damage to the urethral innervations and allows for the passage of the needle and the anchoring columns. Skin punctures are made bilaterally in the genitofemoral folds at the level of the clitoris. The needle is passed around and under the ischiopubic ramus through the skin, obturator membrane, and muscles and finally out through the vaginal incision. This is accomplished by introducing the needle vertically in the previously made skin incision until the obturator membrane and muscle are perforated. Next, the needle is brought to a horizontal position with the tip heading to the surgeons index finger in the vaginal incision. This maneuver allows the surgeon to bring the needle safely to the vaginal incision. Safyre T sling is then hooked by the tip of the needle and brought to the previously made incision. The same maneuvers are repeated on the other side. A forceps or scissors is placed between the tape and the urethra during intraoperative adjustment, avoiding any tension of the tape. The exceeding silicon columns are cut leaving five cones over the skin. This extra length is introduced in the subcutaneous tissue, toward the labia majora for safety and to facilitate the anchoring tails postoperative identification should it be necessary. The skin and vaginal incisions are closed in the usual manner (Figure 76.5). Cystoscopy should be performed if there is any concern about bladder injury [5,6]. Foley catheter was left in place overnight.

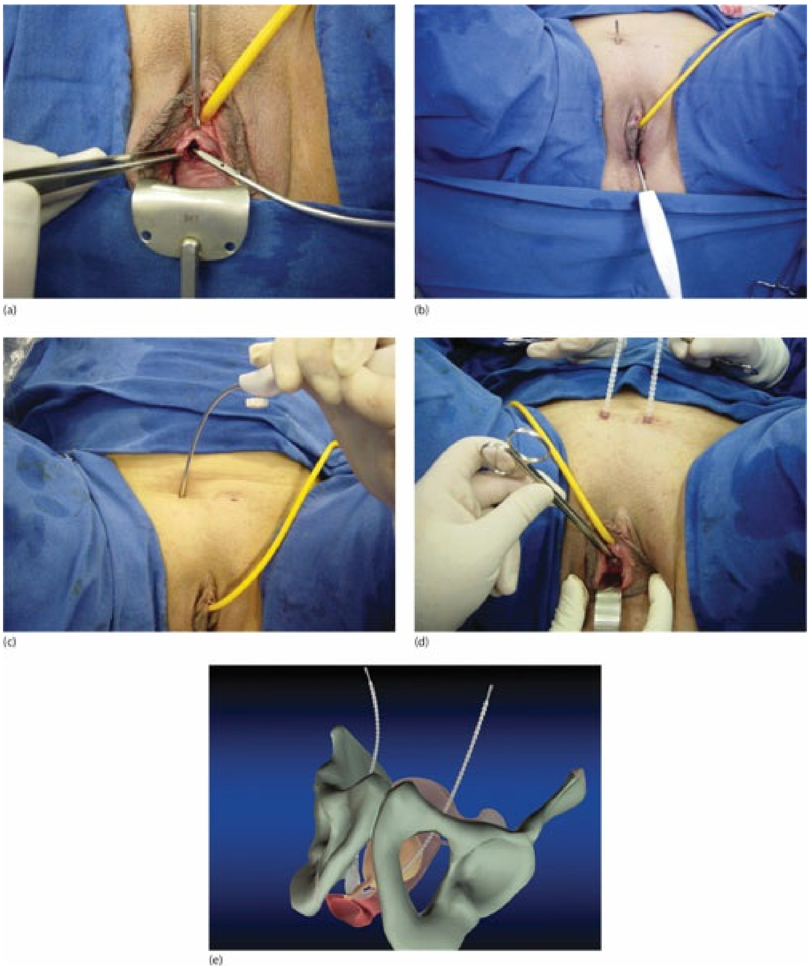

Figure 76.4 Safyre VS technique. (a) Vaginal incision. (b) In the transvaginal, the needle is inserted through the vaginal incision, laterally to the urethral approach. (c) Otherwise, in the suprapubic technique, the needle is inserted through the suprapubic punction and guided by the surgeon's finger until the vaginal incision. (d) The proper tension of the sling is adjusted maintaining a Metzenbaum scissors between the urethra and the sling to prevent undue tension. (e) Scheme of the standard technique.

Safyre T and Urethral Reconstruction

Exceptionally, we advised the placement of Safyre T at the same moment of urethral reconstruction in selected patients as shown in Figure 76.6 based on the need to provide suburethral support for the neourethra. For this, a Martius flap is gentile interposed between the neourethra and Safyre T, which was left loosened. In this situation, we used to keep patients with a thin Foley catheter (12 or 14 French) for 21–28 days and then take it out and start adjustments if necessary.

Readjustment Technique

Tightening

The procedure to tighten Safyre can be performed under local or spinal anesthesia. As the extremities of the polydimethylsiloxane tails can be easily palpable in the subcutaneous tissue, local anesthesia with lidocaine 1% solution seems to be the method of choice. Usually, the readjustment of only one tail is enough, avoiding the risk of significant deviation of the urethral axis.

A small incision is made over the palpable tail extremity (close to the superior aspect of the pubic bone or genitofemoral folds), and it is gently dissected out and pulled carefully, until proper tension is achieved (Figure 76.7). The bladder is filled with 300 mL saline solution before the procedure, so the patient can be asked to cough and do repeated Valsalva maneuvers to check if leakage occurs. Generally, the readjustment is ideally made within 30 days from the surgery, but, theoretically, it can be done at any time after the procedure, because of the formation of a fibroblastic pseudocapsule surrounding the polydimethylsiloxane tail of the Safyre that permits easy dissection and mobilization of the tails inside this pseudocapsule, whenever it is necessary.

Loosening

The procedure to loosen the Safyre should be done in the first month to avoid fibrosis and can be performed under spinal, intravenous, or local anesthesia. A longitudinal vaginal incision 1.5 cm in length is made, starting 1 cm below the urethral meatus, and the polypropylene mesh is dissected out from the urethropelvic fascia. The tails are dissected bilaterally, grasped with hemostatic clamps and pulled back, until a Metzenbaum scissors or a right-angle clamp can be comfortably interposed between the mesh and the urethra. A Foley catheter is left in place overnight.

Comments

The retropubic approach has becoming the most popular approach for Safyre implant due to its preferable use in complex and recurrent patients, but as the transobturator approach avoids the scarred retropubic space in patients with previous failed procedures, it should be considered when retropubic area is considered inaccessible. The transmuscular insertion of transobturator Safyre, through the obturator and puborectalis muscles, along with the subcutaneous tunnel, provides good fixation and anatomical reinforcement of the urethropelvic ligaments, reproducing the natural suspension fascia of the urethra. Among the advantages of this technique, safety, short-operative time, and short hospital stay should be highlighted [7].

Safyre is a hybrid sling for readjustability that is based on the pseudocapsule induced by the silicone columns that allows for moving the anchoring tails upward or downward as needed. As opposed to TVT or other polypropylene minimally invasive slings, the smooth surface of Safyre mesh allows for easy primary adjustment during the implant and even during eventual readjustment, besides keeping its resistance and shape due to its low deformity rate. Moreover, the elasticity of polymetylsyloxane tails can provide fine movements according to the changes of patient’s abdominal pressure, acting as a dynamic support. We have previously reported the good results using either the retropubic [4] or transobturator approach. In our series, readjustments were performed under local anesthesia with almost 60% of cure or improvement of residual incontinence.

Other study compared the efficacy and safety of synthetic transobturator and aponeurotic retropubic slings for the treatment of SUI in women. Forty patients were randomized for Safyre T transobturator sling or aponeurotic retropubic sling. Healing rate was 90.5% (19/21) and 95% (19/20), respectively, after 12 months. The transobturator group presented lesser complications rate than the retropubic group. Authors concluded that the transobturator and the aponeurotic slings techniques were equally effective, but the transobturator sling has shown fewer complications and lesser surgical time than the aponeurotic sling [8].

The diagnosis of obstruction is frequently underestimated and most of patients who do not develop complete urinary retention tend to be diagnosed in the late postoperative period, usually after they had presented with urinary tract infection. Although retention can subside after 4 weeks postoperatively, we advise the loosening procedure within this period in order to avoid fibrotic reaction around the sling and to allow for the patients to resume them as soon as possible. Safyre self-anchoring system is unique as far as postoperative readjustability is concerned. The procedure is minimally invasive and no large abdominal incision is required for harvesting fascia. Sling fixation to the aponeurosis of the abdominal rectus muscle as in classical slings is also unnecessary. Its late adjustments of sling tension are possible in patients presenting persistent incontinence or urinary retention, avoiding major surgeries such as urethrolysis or the need for another sling insertion. The readjustment rate in our series was 10% leading to a success of 40% of the cases and improvement in 20% of this subset of patients [5]. It is our understanding that sling tightening in incontinent patients may be done at any time; on the other hand, loosening the sling must be done between 4 and 6 weeks at the latest to avoid bladder outlet obstruction caused by fibrosis.

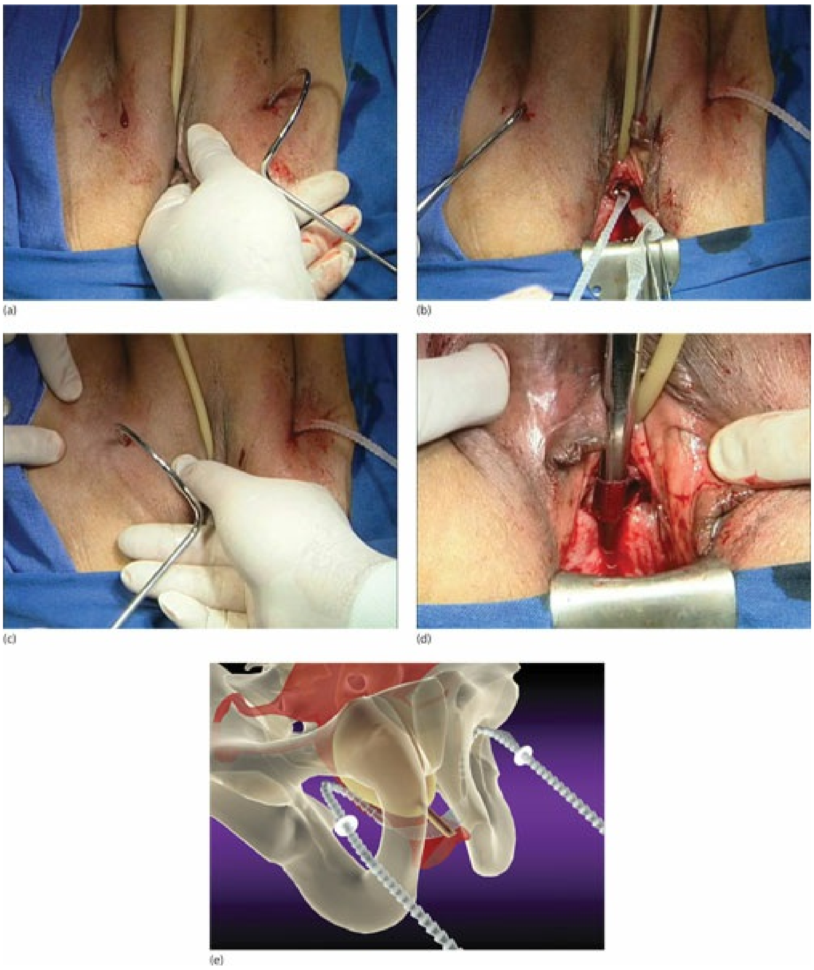

Figure 76.5 Safyre T technique. (a) The needle is passed around and under the ischiopubic ramus through the skin, obturator membrane, and muscles and finally out through the vaginal incision. (b) The same maneuvers are repeated in the other side. (c) Safyre T sling is then hooked by the tip of the needle and brought to the previously made incision. (d) A forceps or scissors is placed between the tape and the urethra during intraoperative adjustment, avoiding any tension of the tape. (e) In selected cases, a special silicon washer can be used to keep the proper sling adjustment in the postoperative period.

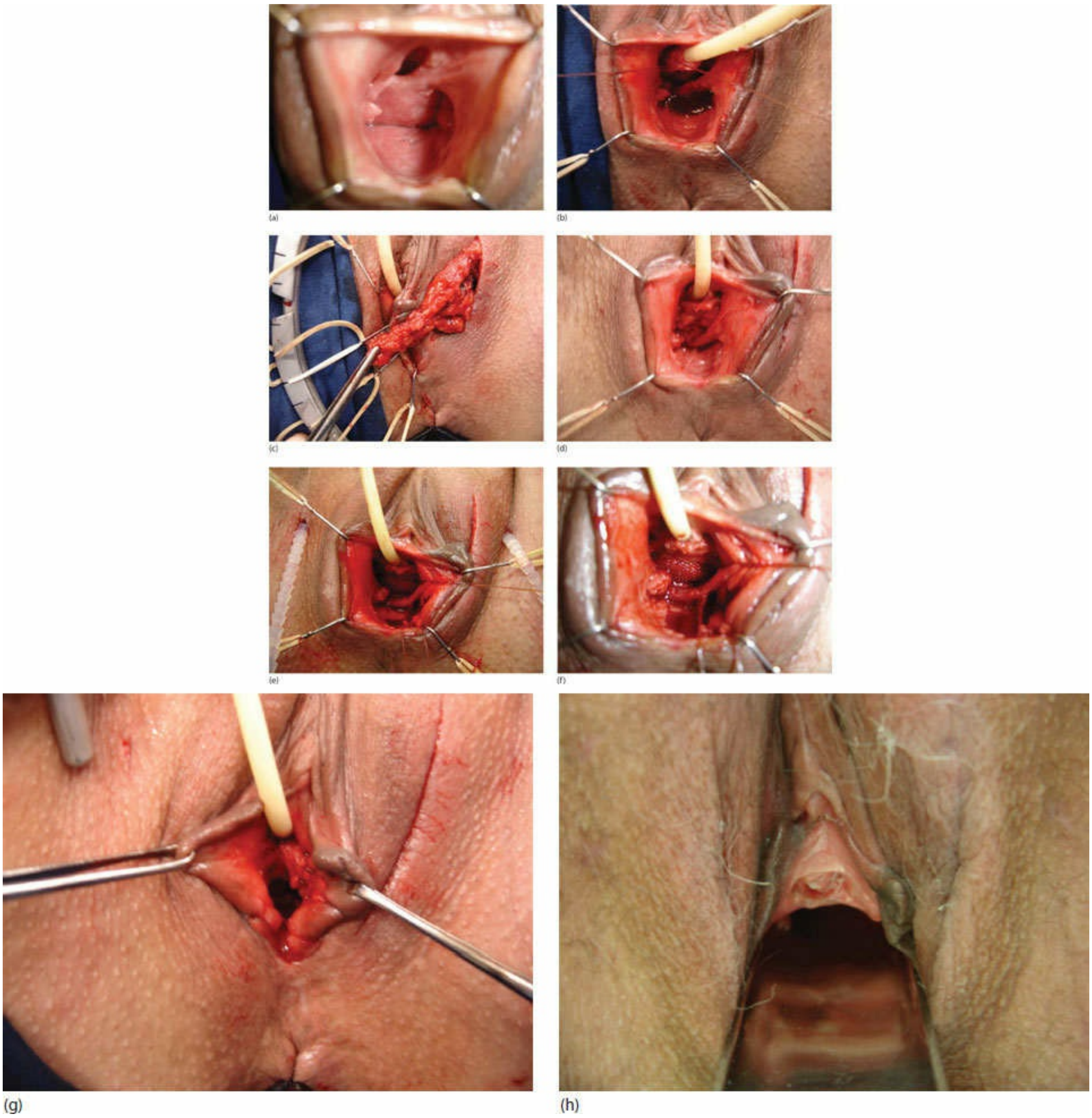

Figure 76.6 Single-procedure urethroplasty plus Safyre T implant. A Martius flap is interposed between the neourethra and Safyre to prevent neourethral erosion. Safyre was left loosened and adjustment can be performed after 30–40 days postoperative, if necessary. (a) Preoperative. (b) Urethroplasty with vaginal wall (double layer). (c) Harvesting of Martius flap. (d) Placement of Martius flap. (e and f) Safyre implant.

Regarding complications, there were no vascular, bowel, or obturator plexus injuries. No patients reported voiding symptoms after 4 weeks of the procedure, confirming the low “de novo” detrusor overactivity rate.

In conclusion, results showed that transobturator approach is as effective as the retropubic procedure in the management of female SUI providing high cure rate along with a significant improvement in the quality of life. Safyre combines the advantages of the transobturator approach with readjustability and may be an attractive surgical alternative.

SAFYRE T CROSSOVER

In spite of improvement in techniques and devices, there is a subset of patients who fail to respond to corrective standard anti-incontinence procedures. These patients have lost completely the urethral sphincteric function and the urethra acts solely as a conduct. The subset of patients may benefit from undergoing a more obstructive sling that may be fixed with more tension than usually required or ideally by using a standard sling [5]. In this scenario, patients must be informed about the possible need for postoperative intermittent self-catheterization and urinary symptoms that may occur subsequently. We first described transobturator crossover readjustable sling for treating these complex cases [9].

Technique

The procedure is performed using the Safyre T Plus. This hybrid sling consists of a monofilament polypropylene mesh that acts as a urethral support held between two self-anchoring columns that are made of an implant grade polydimethylsiloxane polymer. These columns are the basis of the readjustable self-fixing system. The kit has also two soft and radiopaque silicone washers that not only improve fixation when tension is necessary but also allow for easy identification should readjustment become necessary.

The procedure is performed with the patient in lithotomy position. An 18F Foley catheter is placed to empty the bladder. A 2 cm vaginal incision is made, 1 cm below the urethral meatus. The vaginal wall is dissected from the underlying periurethral fascia, bilaterally to the inferior ramus of the pubic bone. The urethra is identified and a right angle clamp is passed between the pubic bone and the urethra, exiting on the other side. One of the extremities of the sling is grasped and brought about behind the urethra to the contralateral side. The same maneuvers are repeated on the other side. Next, bilateral skin punctures are made in the genitofemoral fold at the level of the clitoris, and curved needles are introduced through the obturator foramen. The path is made through the skin, obturator membrane and muscles, around the ischiopubic ramus, and finally out through the vaginal incision. The sling is hooked by the tip of the needle and brought out through the previously made incision. These steps are made on the opposite side to create a spiral sling for better coaptation of the urethra. Silicone washers are used to facilitate latter adjustments should it become necessary. The incisions are closed in the usual manner, and a Foley catheter is left in place overnight (Figure 76.8). In Figure 76.9 is demonstrated the final position of the crossover sling using tridimensional helical computer tomography.

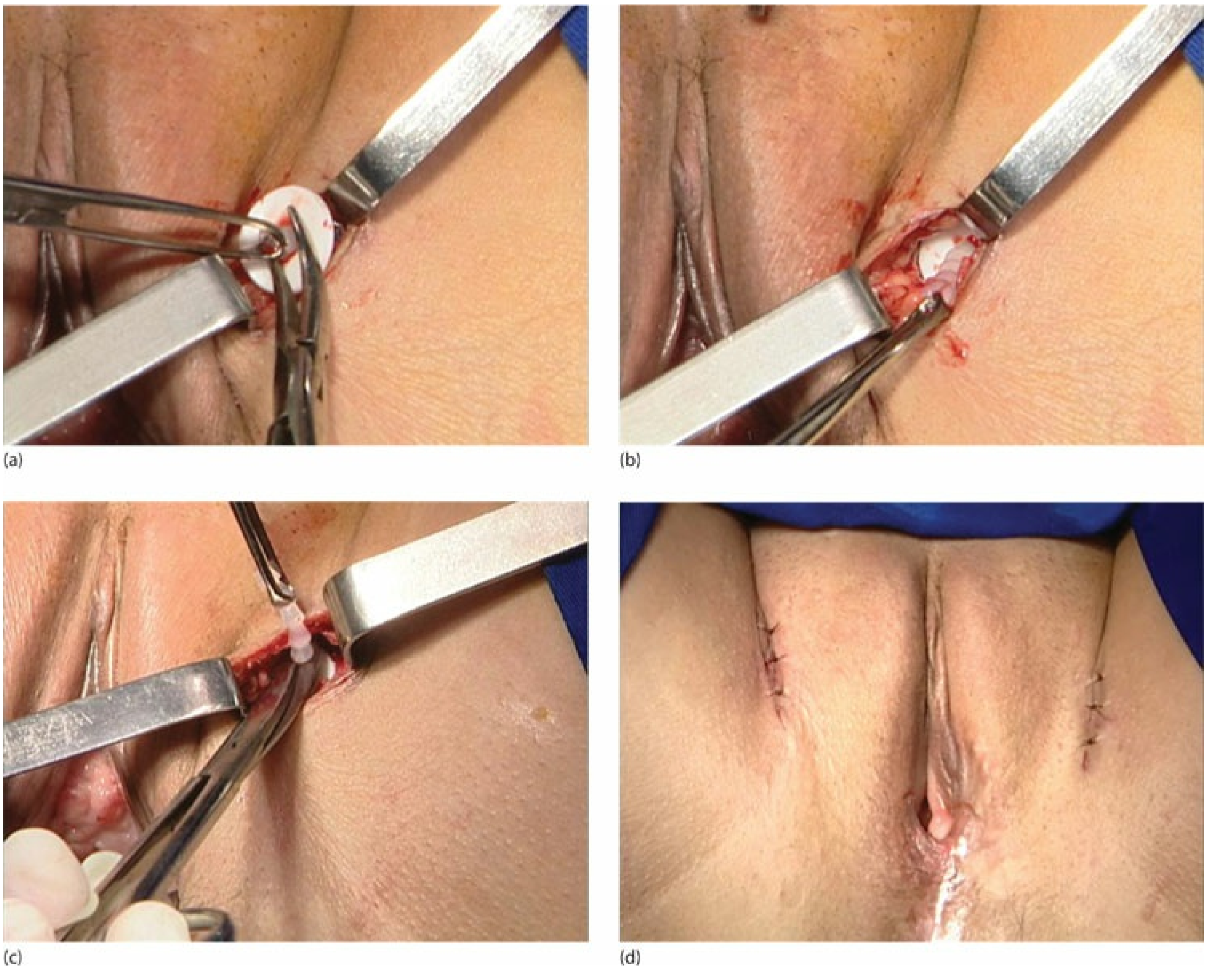

Figure 76.7 The procedure for tightening Safyre is similar, even when retropubic or transobturator approach was used. A small incision is made over the palpable tail extremity (close to the superior aspect of the pubic bone or genitofemoral folds), and it is gently dissected out and pulled carefully, until proper tension is achieved. (a) Dissection of the tail extremity and insertion of silicon washer. (b) Adjustment of the sling tension. During this procedure, the patient can be asked to cough or perform a Valsalva maneuver. (c) The extremity of silicon tail is then cut. (d) The procedure can be performed at one side or bilaterally, taking care to avoid deviation of the urethral axis.

For readjustment, local anesthesia is applied in the region (2% lidocaine with epinephrine). A longitudinal incision is made of 2.5–3 cm in the previous surgical scar. Fat tissue is bluntly dissected and an attempt is made to reach out the silicon cones. These cones are often easily found but in some cases; they may be found underneath the aponeurosis of adductor longus muscle, making an incision necessary. After identifying the silicon column, its extremity is grasped with an Allis clamp, pulled out, and the washer is moved downward increasing coaptation until no urine leakage is seen during Valsalva maneuver. After continence is achieved, the exceeding cones are trimmed off.

Our first published series that included 16 patients after 12-month follow-up, 15 women were continent by subjective and objective assessments, and only 1 remained incontinent. This patient denied any further treatment. If we defined failure as a patient report of less than 50% improvement, with subsequent need for further surgery, the failure rate would be 1 out of 16. The cure rate was 93.7%. Complications included one urethral perforation that was solved by primary closure of the urethral wall; “de novo” urge incontinence developed in 2/16 patients. One patient became incontinent 1 month after the procedure and underwent a successful sling readjustment. The readjustment was performed under local anesthesia. In the same series, there were two patients had undergone a neourethral reconstruction associated to a Martius flap procedure to avoid vaginal erosion with good clinical outcome. These two patients experienced urinary retention after receiving the crossover sling and were put on clean intermittent self-catheterization for 2 weeks. There was no urethral or vaginal erosion during the follow-up [9].

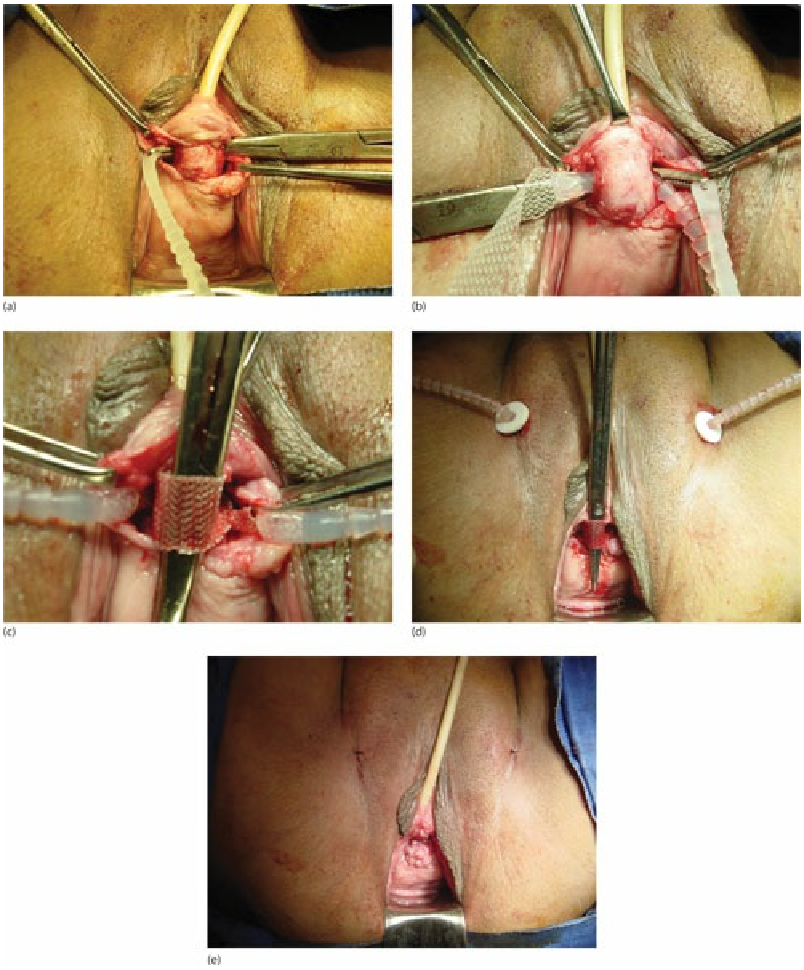

Figure 76.8 Safyre T crossover technique. (a) The urethra is identified and a right-angle clamp is passed between the pubic bone and the urethra, exiting on the other side. (b) One of the extremities of the sling is grasped and brought about behind the urethra to the contralateral side. The same maneuvers are repeated on the other side. (c) Bilateral skin punctures are made in the genitofemoral fold at the level of the clitoris; the silicon tails are pushed in the same manner of in a transobturator sling, creating a spiral sling for coaptation of the urethra. (d) Silicone washers are used to facilitate latter adjustments should it become necessary. (e) The incisions are closed in the usual manner.

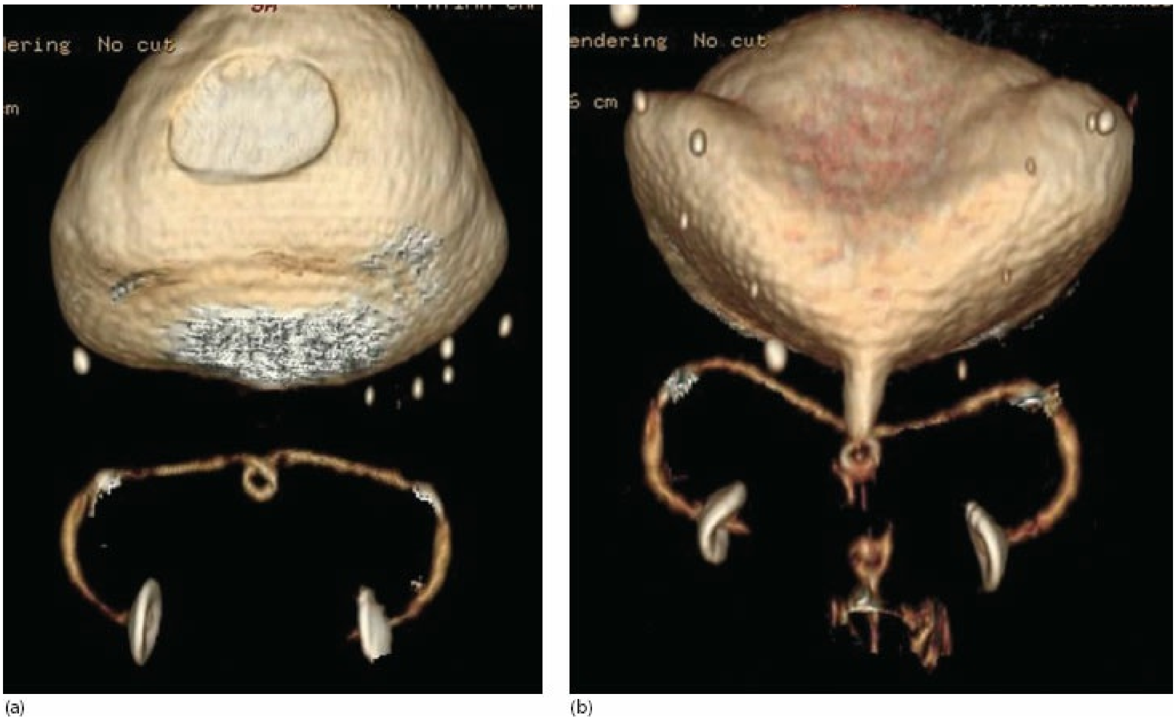

Figure 76.9 Tridimensional helical computer tomography showing final position of the crossover sling. (a) Rest. (b) Stress.

Comments

Patients with multiple prior anti-incontinence procedures represent a difficult population to treat. They often have an incompetent, difficult to compress urethra, likely because of a combination of urethral denervation and violation of the periurethral fascia as well as their underlying risk factors for SUI [10]. They typically had an “open” urethra with low VLPP.

The transobturator crossover sling is a relatively simple alternative to major operative procedures in women requiring salvage anti-incontinence surgery. The transobturator approach allows for the anatomical reconstruction of the natural support of the urethra and at the same time, avoids the scared retropubic space in patients with previous failed procedures. The insertion, through the obturator muscle and membrane and the adductor longus muscle aponeurosis, along with the washers, provides good fixation and anatomical reinforcement of the urethropelvic ligaments, reproducing the natural suspension fascia of the urethra. Readjustment can be easily performed under local anesthesia, and only one patient required readjustment in our first published series. Among the advantages of this technique, we can mention that it avoids retropubic dissection, can be performed in a short operative time with short hospital stay. We also treated two patients with neourethral reconstruction because of the urethrovaginal fistula resulting from a complicated labor. These patients had no previous anti-incontinence procedure but did have a nonfunctional neourethra after urethral reconstruction. In selected patients with severe SUI and failed multiple prior surgeries, we have performed transobturator crossover sling surgery as a salvage procedure. In our first published data, this technique has proved to be easy to perform and effective and had minimal complications, which led us to conclude that it was a significantly less-morbid alternative to bladder neck closure and continent diversion. Also, we describe a new transobturator procedure that provides circumferential coaptation of the urethra for SUI treatment in this difficult patient population. Rutman et al. [11] described a circumferential retropubic sling procedure using a 1 cm × 15 cm piece of soft polypropylene mesh prepared with a zero polyglactin suture applied at each end mostly for neurogenic patients. A clamp was used to pass the mesh between the urethra and pubis. There was a mean 87% overall improvement in symptoms. Of the 37 patients described, 92% remained dry between catheterizations.

As the management of failed slings may be a difficult situation, spiral sling may be an attractive procedure, especially in patients with normal detrusor function. We believe that crossover sling supports the midurethra, preventing urethral hypermobility and improving coaptation.

REMEEX

TRT Remeex System (Neomedic International) was first described by Iglesias et al. and claimed to allow for postoperative adjustments that could be made hours, months, or even years after surgery [12,13], which means that the surgeon could provide a long-term continence and avoid reoperating again a patient with a sling failure. The TRT Remeex System provides the surgeon with the experience of adjusting the sling urethral support with the patient in standing up position and doing the efforts that drives her to incontinence. This unique property provides the surgeon the ability to adjust the sling to the desired urethral support level, thus avoiding urine leakage or retention. Also, it is supposed to have a dynamic pressure transmission system. According to this concept, when coughing, the patient advances the rectus muscle, advancing the varitensor, and increasing the sling urethral support while it’s needed. This reconstructs the intra-abdominal pressure transmission system of normal continent patients. The readjustment is made while the patient is standing up and doing the efforts that drives her to incontinence.

The system is composed basically of five components (Figure 76.10):

- Monofilament polypropylene mesh 1.25 cm × 2.5 cm attached to a polypropylene 1.0 filament (traction thread).
- Varitensor is the regulator mechanism. It is made of Chirulen (ultrahigh-molecular-weight polypropylene) and titanium.
- Manipulator must be attached to the varitensor to manipulate the regulation mechanism. Rotation either clockwise or counterclockwise elevates or lowers the level of the sling.
- Disconnector allows for connection/disconnection of the manipulator to the varitensor.
- Trocar (traction thread passer).

Technique

Patient positioning and preparation are the same as described previously for the Safyre VS. Surgical technique can present minimal variations according to surgeon preference, but can be standardized as follows. A suprapubic transversal incision of about 3–4 cm in the lower abdomen is made until exposure of the rectus muscle aponeurosis is accomplished.

The anterior vaginal wall is incised for 3–4 cm longitudinally at the level of the urethrovesical junction and dissected out laterally. The needles are then driven at each side of the urethra up toward the abdominal wall, tangent to the posterior aspect of the pubic bone, after puncturing through the endopelvic fascia. At this point, cystoscopy is performed and the needles are repositioned in case of bladder perforation. Polypropylene sutures are then connected to the needles and pulled up until they appear in the abdominal incision. With the varitensor positioned at 10 cm above the level of the abdominal aponeurosis, the sutures are inserted into the varitensor and their ends are knotted to each other. While maintaining the varitensor in the horizontal position, the manipulator is rotated clockwise until the varitensor is positioned 3 cm above the aponeurosis. Both abdominal and vaginal incisions are closed in the usual manner. Urethral catheter is left in place (Figure 76.11).

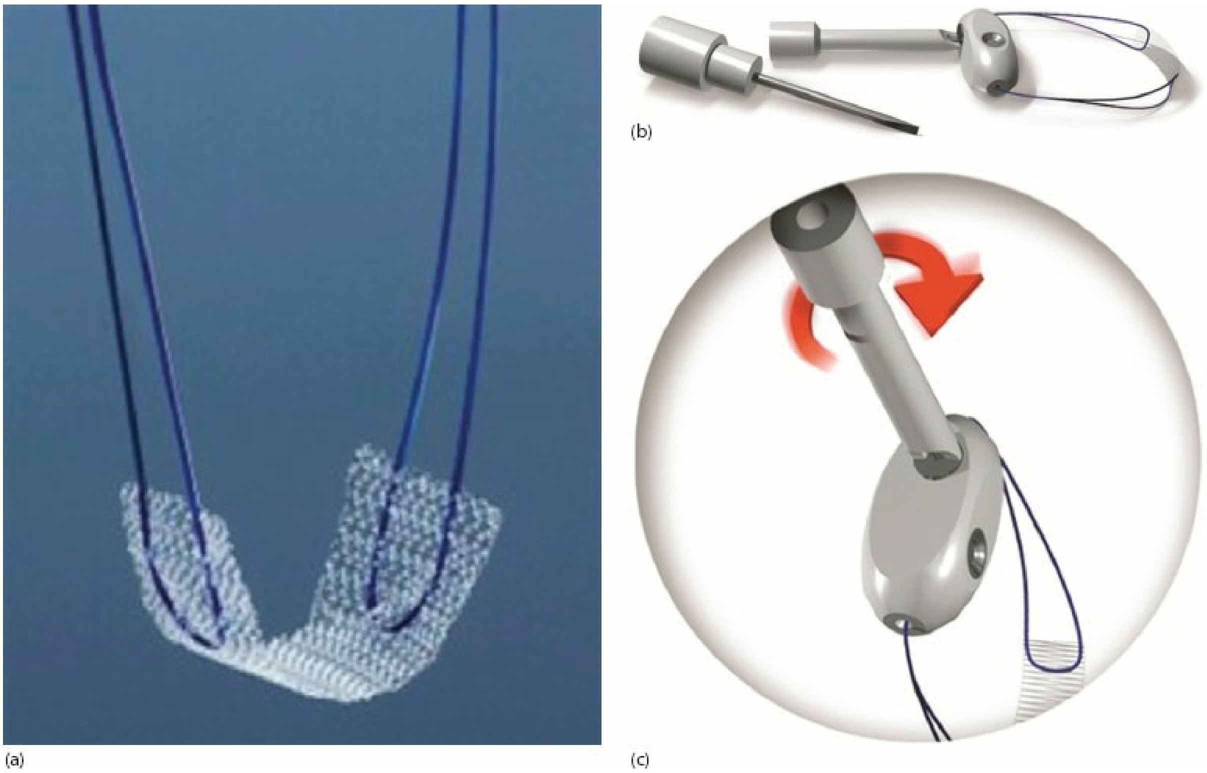

Figure 76.10 TRT Remeex System. (a) 1.25 cm × 2.5 cm monofilament polypropylene mesh attached to a polypropylene 1.0 traction thread. (b) Manipulator and varitensor attached to the sling and disconnector. (c) Manipulator in place showing a clockwise rotation for adjustment.

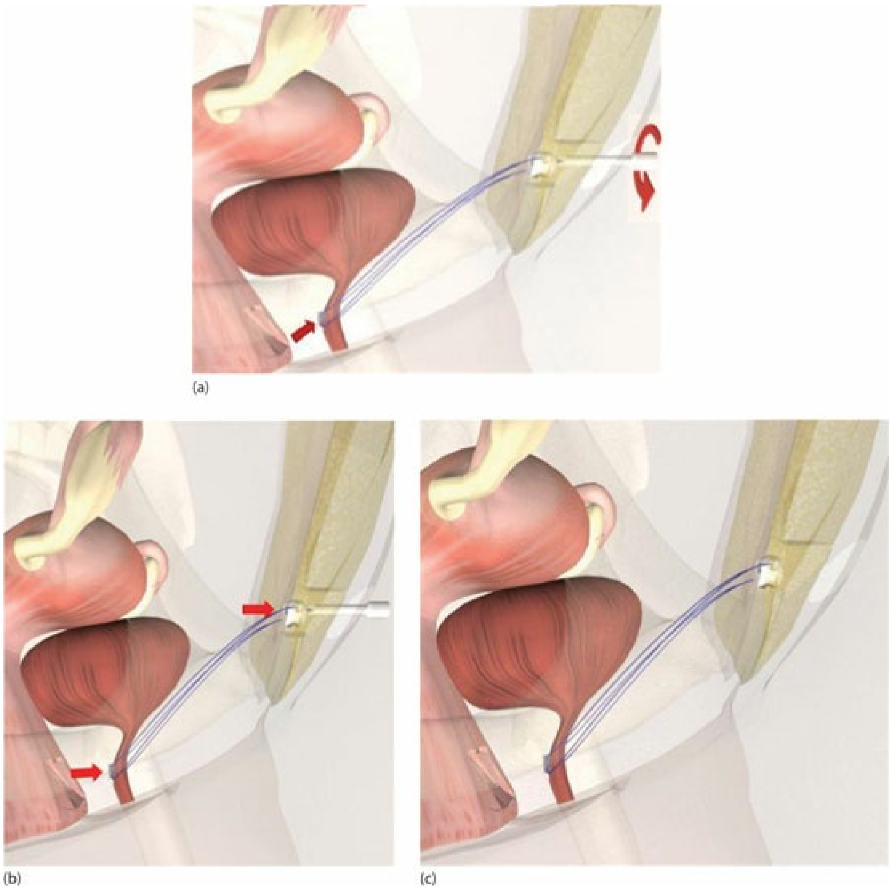

Figure 76.11 TRT Remeex System technique. (a) Remeex prosthesis in place. (b) With a quarter of a turn, the manipulator and the disconnector are withdrawn. (c) The varitensor remains in place. The sling support level can be modified if needed by replacing the manipulator and the disconnector under local anesthesia. (Reproduced by permission of Dr. Antoni Castello.)

For adjustment, the bladder is filled with 300 mL in the next day following surgery and Foley catheter is removed. The patient is oriented to perform Valsalva maneuver and straining. If urine loss is documented, making four complete turns on the manipulator and repeating the provocative maneuvers make adjustment of the sling support. Additional adjustment is carried out in the same manner if needed. After urine loss is resolved, the patient is tested for spontaneous void and postvoid residual. If more than 100 mL is left as residual urine, the sling is loosened. If not, the manipulator is turned 90° in any direction, and the disconnector manipulator is easily removed from the varitensor, which stays buried in the fat above the aponeurosis of the rectus muscle as a permanent regulation mechanism, which can be used at anytime as needed [14]. The sling adjustment is made step-by-step (checking continence every four turns of the manipulator). When the patient is continent, we know that four turns before she was incontinent. This allows the surgeon to provide the minimum necessary urethral support for that particular patient under stress and no more.

Comments

The TRT Remeex System implantation technique has been associated to advantages such as ease to apply, lack of the morbidity presented by the abdominal techniques, allowance of late-term readjustments under local anesthesia if needed, and satisfying results at short- and midterm follow-up [14].

Iglesias et al. observed a subjective satisfaction rate of 90.5% using the TRT Remeex System for treating female SUI. However, the studied population was small, follow-up time was considerably short (mean 12 months) and 62% of patients had a previous unsuccessful anti-incontinence procedure, but were analyzed altogether along with the rest of the cohort who had no previous surgery. Also, objective assessment of incontinence improvement was not performed, but only by subjective self-reported patient impression [12]. Authors emphasize the technique should be recommended for patients with intrinsic sphincteric deficiency or previous surgical failure.

Martinez et al. reported on a success rate of 93% after using the TRT Remeex System in women with a diagnosis of SUI associated to pelvic organ prolapse. However, short follow-up time (average 8 months), a small cohort (29 patients), and the lack of an objective assessment to define success (self-reported improvement) allow for no definitive conclusion whatsoever [15].

More consistent results were shown for the use of the TRT Remeex System in the treatment of male urinary incontinence. Sousa-Escandon et al. reported on a prospective, multicenter study involving 51 patients with urinary incontinence mainly due to radical prostatectomy. There were 65% of patients considered cured (use of no pads, small pads, or security napkins) and 20% significantly improved at a mean follow-up of 32 months. No major intraoperative complications occurred and postoperative pain was minimal and successfully controlled by oral analgesics [16].

According to the Spanish TRT Remeex System Registry XII–2004, 92% of patients were continent under stress and 7% improved after undergoing TRT Remeex System implant [13].

A prospective evaluation reported by the Fundacio Puigvert involving 125 patients and a mean follow-up of 38 months reported a cure rate of 87% based on pad test, clinical, and urodynamic criteria. Twenty-one patients benefited from readjustment of the sling during the follow-up. The tension was increased in 17 cases (continent at discharge) due to recurrence of stress incontinence, and reduced in 4 due to obstruction. The varitensor was removed in one case due to infection [17].

More recently, long-term results after 5 years were presented in a cohort of 30 patients, most of them with severe intrinsic sphincter deficiency and fixed urethra. In this series, according to objective evaluation (pad text and cough stress test), 93% were considered cured/improved. Only two patients (7%) underwent readjustments during the follow-up [18].

CONCLUSION

Adjustable slings have shown to provide satisfying success rates, to be associated to minimal intraoperative complications and to be a safe procedure. Readjustments can be done under local anesthesia at immediate or delayed follow-up as needed. However, the evolution of transobturator prosthesis and the emerge of minislings have moved adjustable slings for restrict subset of patients.

As the devices presented are used in specific situations nowadays, the reports are rarely published. So, more studies are needed for both techniques to corroborate the existing data in a sense to provide longer follow-up and more precise success criteria assessments.

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77

Nonsurgical Transurethral Radio Frequency Collagen Denaturation of the Bladder Neck and Proximal Urethra for the Treatment of Stress Urinary Incontinence

Saad Juma, Elizabeth Timbrook Brown, and Roger R. Dmochowski

INTRODUCTION

Stress urinary incontinence (SUI) is characterized by involuntary urine loss during physical activity such as coughing, sneezing, laughing, exercise, or lifting [1,2]. A common cause of SUI in women is the rotational descent of the bladder neck and proximal urethra (bladder neck hypermobility) resulting in the inappropriate opening of the proximal urethral lumen during periods of increased intra-abdominal pressure [1,2].

Although SUI is not a life-threatening disorder, it can greatly affect a patient’s quality of life (QoL). Thus, patient input in the selection of treatment is paramount. There is no existing pharmacotherapy approved by the U.S. FDA for the treatment of SUI. Available treatment options for women with SUI include Kegel exercises, behavioral modification, biofeedback, transurethral injection of bulking agents, and various forms of midurethral slings and retropubic suspensions. Currently, there is a clinical trial assessing the safety and efficacy of suburethral injection of autolougous muscle-derived cells for SUI [3]. Nevertheless, midurethral sling procedures are currently considered the standard of care in treating women with SUI. To add to the armamentarium of less invasive treatment options for SUI, the use of radio frequency energy has been explored.

HISTORY OF RADIO FREQUENCY THERAPY

Electromagnetic energy, when transmitted to biologic tissue, can cause heating of the target. The degree of heating and the physical effects vary according to the frequency and wavelength of the electromagnetic energy as well as the duration of exposure. High-frequency electromagnetic energy (radio frequency) is the basis for radio transmissions, while very high (microwave) levels are used in radar or, more familiarly, in microwave ovens. Light at high frequencies and wavelengths, as produced by lasers, can also have a rapid heating effect of its target.

Application of radio frequency, microwave, or laser energy results in excitation of water molecules and rapid heating of biologic fluids and tissue, with subsequent tissue remodeling or destruction. The controlled application of electromagnetic energy at radio frequency and microwave frequency levels has been widely used to treat a spectrum of medical conditions. High levels of radio frequency, as in electrocautery, are commonly used for hemostasis [4]. Application of high-energy radio frequency is also widely used for the thermal destruction (ablation) of arrhythmic cardiac tissue [5], shrinkage of excessive soft palate tissue [6], shortening of injured spine and joint ligaments [7,8], shrinkage of joint cartilage [9], reduction of liver tumors [10], and reduction of benign hyperplastic prostatic tissue [11,12]. Such procedures utilize relatively high levels of radio frequency energy to heat body tissues to the point of necrosis, which results in gross tissue shrinkage.

In contrast, the application of lower levels of radio frequency energy generates lower tissue temperatures (65°C–75°C). As a result, tissue necrosis and gross shrinkage do not occur. Instead, application of controlled, low-level radio frequency energy results in acute, focal collagen denaturation (Figure 77.1), with subsequent microremodeling of the affected collagen upon cooling and healing (Figure 77.2) and without associated gross tissue necrosis or neurovascular injury. After healing, the denatured collagen results in reduced dynamic compliance of the surrounding untreated tissue without stricture formation. Lower levels of radio frequency energy have successfully been used to treat conditions such as fecal incontinence (e.g., the Secca procedure) [13], gastroesophageal reflux disease (e.g., the Stretta procedure) [14], and arthritis [15].

RADIO FREQUENCY TREATMENT FOR SUI

Radio frequency therapy may be used to treat women with SUI, offering them a minimally invasive treatment option. Two forms of radio frequency technology have been used for the treatment of SUI in female patients: high-energy transvaginal and low-energy transurethral radio frequency treatment.

Transvaginal Radio frequency Therapy

Transvaginal radio frequency bladder neck suspension (SURx; Cooper Surgical, Trumbull, CT), originally performed laparoscopically, is a surgical procedure wherein two parallel vaginal incisions are created lateral to the urethra at the level of the proximal urethra. The vaginal mucosa is dissected off the underlying endopelvic fascia to expose the surface area for treatment. Subsequently, a transvaginal probe is used to apply high-energy radio frequency to heat and shrink the underlying tissues [16,17]. Radio frequency energy is delivered until blanching or charring of the tissues is noted. Similar energy is applied on both sides of the proximal urethra, always maintaining position 1 cm lateral to the urethra. The goal of this procedure is to shrink the endopelvic fascia, thereby increasing support for the bladder neck [16].

In an early study of the procedure performed laparoscopically in 94 women (mean age, 48.7 years) with proximal urethral and bladder neck hypermobility, 81.2% of 85 patients at 1 year reported improved or complete continence. Urodynamic evaluation showed no leakage during the Valsalva maneuver in 78% of patients. A 12-month, multicenter, single-arm trial of transvaginal high-energy radio frequency therapy using general anesthesia was conducted in 120 women with SUI who were treated as outpatients [17]. Among 86 patients who underwent urodynamic testing at baseline, 76% demonstrated improvement in the Valsalva leak point pressure (LPP) at 12 months. Additionally, 64% of patients reported improved continence or no change in continence status, while 19% experienced increased frequency of SUI episodes. Further studies were unable to reproduce earlier successful results and high rates of additional treatments were required [18–20]. It was determined that transvaginal radio frequency ablation is too dependent on precise technique, and it is no longer marketed [21].

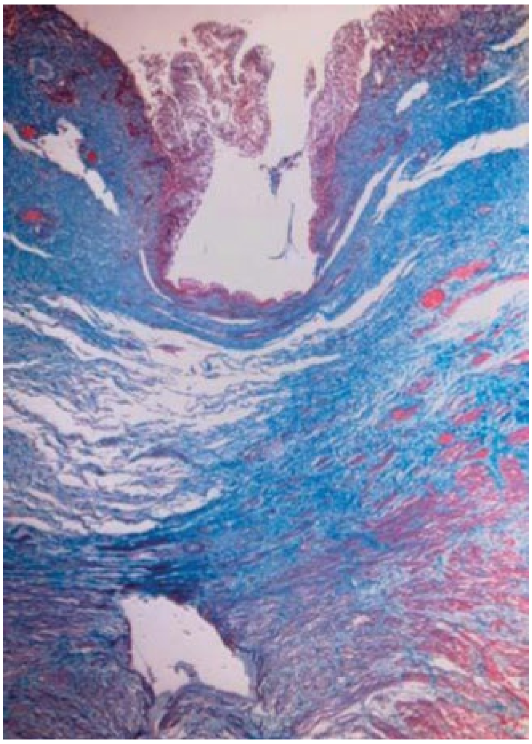

Figure 77.1 Acute histology (trichrome stain) through needle electrode path in porcine urethra immediately following radio frequency energy treatment. Viable, denatured submucosal collagen stains bright blue and small vessels are undamaged. (Courtesy of Novasys Medical, Inc., Newark, CA.)

Transurethral Radio frequency Collagen Denaturation

Transurethral radio frequency collagen denaturation (Renessa; Novasys Medical, Inc., Newark, CA) is approved by the FDA for treating women with SUI due to bladder neck hypermobility. This procedure differs in several ways from transvaginal radio frequency bladder neck suspension. Unlike the high-energy transvaginal radio frequency procedure, transurethral radio frequency collagen denaturation is applied through four small needle electrodes and does not require surgical incisions. Additionally, in high-energy radio frequency ablation, target tissue is heated to produce tissue necrosis followed by gross shrinkage of the endopelvic fascia [16,17,22]. In contrast, transurethral radio frequency causes collagen denaturation and does not produce tissue necrosis, resulting in a functional (reduction in tissue compliance) rather than an anatomic change. Initial animal studies of transurethral collagen denaturation of the bladder neck and proximal urethra evaluated its gross and histologic impact, and physiologic effect demonstrated its feasibility and safety, suggesting a beneficial effect [23].

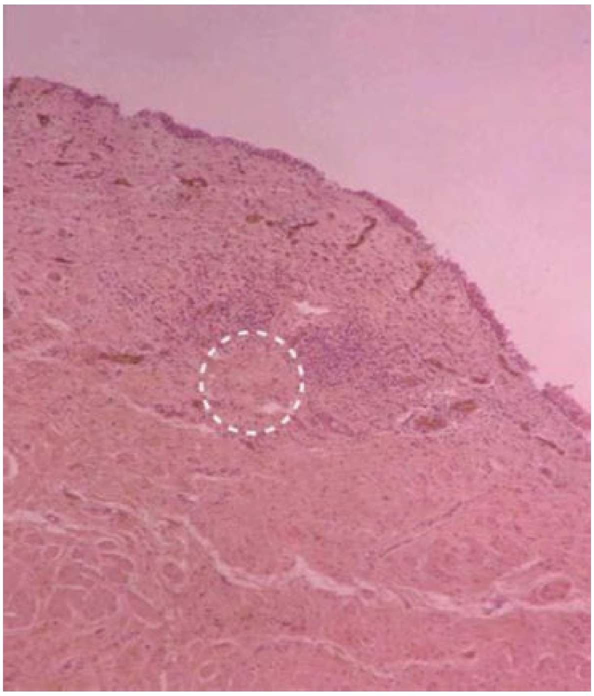

Figure 77.2 Porcine bladder neck histology (H&E stain) at 2 months following radio frequency collagen denaturation. The tiny submucosal sphere of denatured collagen (*circle*) deep in the unaffected mucosa is only identified by chronic inflammatory cells clustered on its superior border. (Courtesy of Novasys Medical, Inc., Newark, CA.)

Indications and Contraindications

Transurethral radio frequency collagen denaturation offers women with SUI due to hypermobility an office-based, minimally invasive treatment option. It is not meant to replace existing treatment options, but to complement the spectrum of available treatments. Radio frequency collagen denaturation is indicated for the treatment of anatomic SUI (bladder neck hypermobility). Patients with SUI, secondary to intrinsic sphincter deficiency, are not good candidates for this treatment. Women with anatomic SUI who have failed Kegel exercises, who are not good surgical candidates, or who wish to avoid or postpone surgery are ideal candidates for radio frequency collagen denaturation of the bladder neck and proximal urethra. Additionally, patients who experience suboptimal primary surgical results may benefit from transurethral radio frequency collagen denaturation.

Women who have undergone a surgical procedure and experience residual or recurrent incontinence must be carefully evaluated before considering further treatment options. Although radio frequency collagen denaturation is sometimes considered following suboptimal surgical results, this technique is not specifically approved by the FDA for use in this setting.

Anesthesia

Transurethral radio frequency collagen denaturation can be performed in the office setting using local anesthesia, with the option to administer pretreatment oral sedation. The feasibility, safety, and comfort of using oral instead of intravenous sedation were demonstrated in two prospective trials [24,25]. In a study by Lenihan and colleagues, the first six patients received an oral sedative plus an oral analgesic, as well as a local periurethral anesthetic block using 2% lidocaine. The remaining 10 patients (63%) received only an oral sedative or analgesic. Postoperatively, patients classified their pain on a visual analog scale from 0 ("no pain") to 10 ("terrible pain") [24]. The mean score was 1.8, with 38% of patients selecting zero. Subsequently, Wells et al. performed a multicenter, single-arm study in 33 women who received only a mild oral sedative (diazepam 10 mg) administered 60 to 90 minutes prior to treatment, along with a bilateral periurethral block using 10 cc total of 2% lidocaine [25]. This in-office anesthetic regimen using oral sedation allowed for treatment completion in all patients without the need to convert to intravenous sedation (100% feasibility). Postoperatively, the patient-rated mean pain score was 1.4 (±1.8), including 42% of patients who rated their pain as zero.

Technique

A prophylactic oral antibiotic is administered, and the patient may opt to receive an oral sedative. Once the patient is placed in the low lithotomy position, she is given a periurethral lidocaine block (Figure 77.3). The bladder is drained with a urinary catheter, after which 30 cc of sterile, room-temperature water is instilled into the bladder and the catheter is removed. The transurethral radio frequency probe (Figure 77.4) is inserted until the probe tip is within the bladder lumen. The balloon at the probe tip is then insufflated and the device gently withdrawn until the balloon is anchored palpably within the bladder neck, at which time the length of the urethra is measured. During treatment, four 23-gauge nickel titanium needle electrodes are then deployed from the probe shaft immediately distal to the balloon, traversing the mucosa and positioning the tips within the submucosa of the bladder neck and proximal 1 cm of the urethra (Figure 77.5). The probe, connected to a radio frequency generator (Figure 77.6), delivers radio frequency energy for a 60-second cycle while sterile, room-temperature water simultaneously irrigates the mucosa to prevent thermal injury. The submucosa immediately surrounding the four needle tips is heated and maintained at 65°C for a minimum of 30 seconds, resulting in microscopic, focal collagen denaturation without substantial tissue necrosis. The probe is repositioned after each treatment cycle, and the cycle is performed nine times, using simple deployment and rotational maneuvers, resulting in collagen denaturation of 36 circumferential, microscopic focal sites within the bladder neck and proximal urethral submucosa. Once the final cycle is completed, the needles are retracted, the balloon is deflated, and the radio frequency probe is removed. The patient is asked to void immediately after treatment.

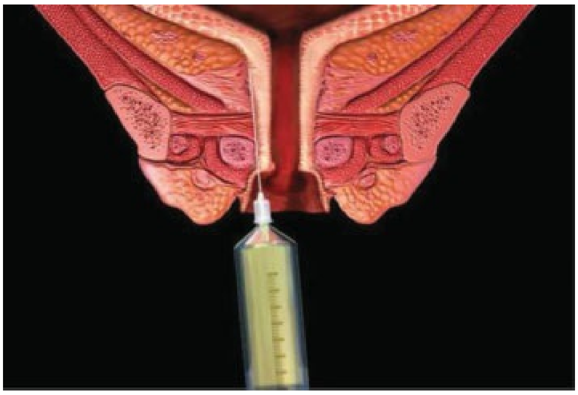

Figure 77.3 A sterile 25-gauge 1.25 in. needle is fully inserted parallel to the urethral wall. After injection of 2–3 cc of 2% lidocaine into the tissue adjacent to the bladder neck, an additional 2 cc was injected during the first 1 cm of needle withdrawal, anesthetizing the proximal urethral tissues. Similar bilateral injections were administered. (Courtesy of Novasys Medical, Inc., Newark, CA.)

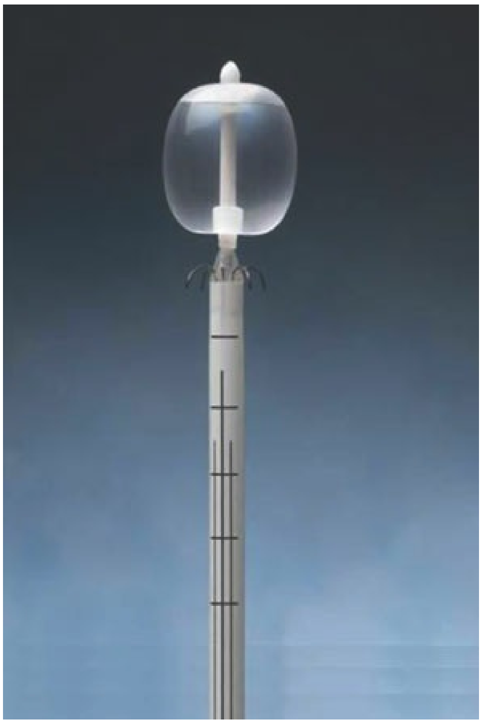

Figure 77.4 The transurethral radio frequency probe, which is inserted until the probe tip is within the bladder lumen. The balloon at the probe tip is then insufflated and the device gently withdrawn until the balloon is anchored palpably within the bladder neck. (Courtesy of Novasys Medical, Inc., Newark, CA.)

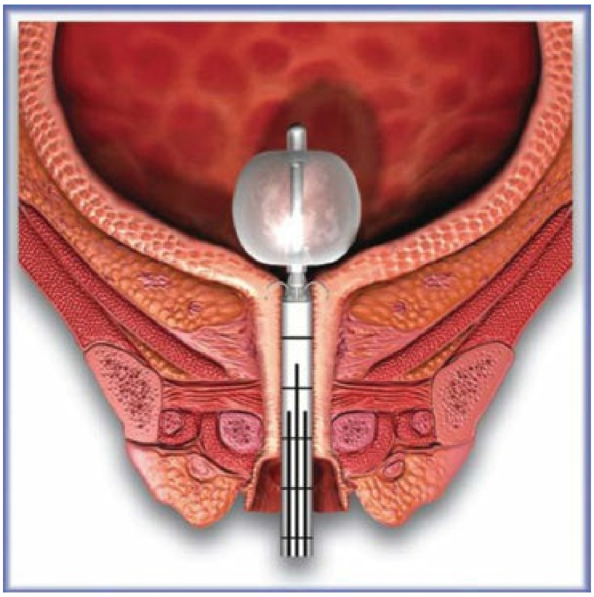

Figure 77.5 Radio frequency collagen denaturation of the proximal urethral submucosa is performed after the anchoring of the device balloon within the bladder neck, followed by deployment of four small needle electrodes into the submucosa (two needles inserted perpendicular to the plane of the image and are not shown). (Courtesy of Novasys Medical, Inc., Newark, CA.)

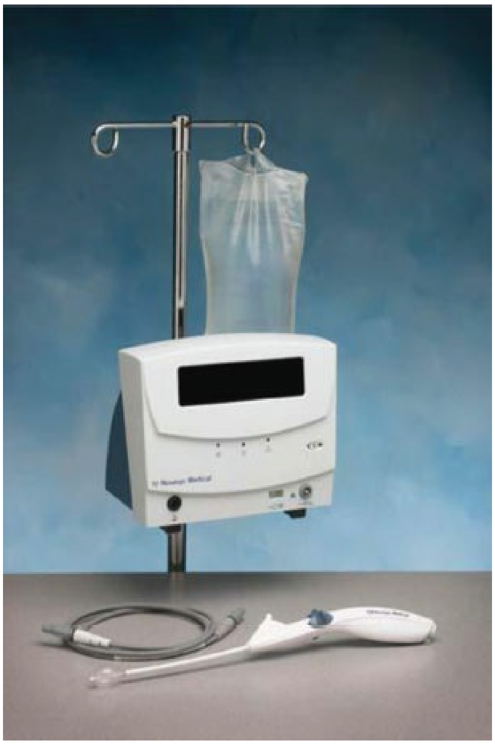

Figure 77.6 The generator used during transurethral radio frequency collagen denaturation employs automatic safety features that monitor tissue temperatures and impedance. (Courtesy of Novasys Medical, Inc., Newark, CA.)

Postprocedure Care and Recovery

Since no incisions are required for radio frequency collagen denaturation and general anesthesia is not used, posttreatment recovery is typically rapid and uncomplicated. Most patients complete the procedure under local anesthesia and leave the physician's office within 1 hour. In an ongoing 36-month trial, approximately one-third of patients resumed normal daily activities within hours to 1 day following the procedure, while 91.9% of patients returned to normal activities within 2 days [26]. Indwelling or intermittent catheterization was not required by any patient at discharge.

Efficacy

The pilot trial of transurethral radio frequency collagen denaturation evaluated safety and the effect of this procedure on incontinence episode frequency and patient QoL [27,28]. In addition, this trial analyzed the outcomes of four treatment regimens that differed in total number and anatomic locations of radio frequency applications within the lower urinary tract. In a study of 41 women (mean age, 48.8 years) with SUI and evidence of bladder neck hypermobility [27], patients were randomized to receive one of four radio frequency regimens: (1) group 1 (n = 10), radio frequency energy was administered at 24 sites in the proximal urethra, with a total radio frequency duration of 7.5 minutes; (2) group 2 (n = 10), 36 sites including 12 in the vesicourethral junction and 24 in the proximal urethra, with a total duration of 10.5 minutes; (3) group 3 (n = 11), 48 sites including 24 in the distal bladder neck and 24 in the proximal urethra, with total duration of 12.0 minutes; and (4) group 4 (n = 10), 60 sites including 24 in the distal bladder neck, 12 in the vesicourethral junction, and 24 in the proximal urethra, with a total duration of 15.0 minutes. Following the procedure, preexisting urinary tract infections were identified from screening urine cultures in three women, and one patient at baseline had active urge symptoms and was using anticholinergic medication. Consequently, these four patients were excluded from the efficacy analysis, but included in the safety assessment. Patients were evaluated at 2 weeks, 2–3 months, and 6 months posttreatment. Change from baseline in the incontinence quality of life (I-QoL) score was the primary efficacy variable. The I-QoL instrument, a disorder-specific, validated questionnaire [29,30], generates an overall score from 0 to 100 (0 indicates worst possible I-QoL), as well as three subscale scores.

Six months after the procedure, there were increases in mean overall I-QoL scores in all four treatment groups, with significant improvements in groups 2 ($p = 0.004$) and 4 ($p = 0.02$) (Table 77.1) [27]. The majority of patients in all groups experienced at least a 10-point increase in overall I-QoL scores. With the exception of group 1 (who received the fewest number of radio frequency applications, all isolated to the proximal urethra), patients reported varying reductions in daily incontinence episodes, with significant decreases noted in groups 2 ($p = 0.04$) and 4 ($p = 0.004$). In addition, daily pad use with moderate to severe baseline SUI experienced at least a 10-point improvement in I-QoL scores compared with similar patients in the sham group (50%; $p = 0.03$) [31].

Table 77.1 Changes from Baseline to 6 Months Posttreatment in the Pilot Study of Transurethral Radio frequency Collagen Denaturation in Women with Stress Urinary Incontinence

	Group 1 ($n = 8$)	Group 2 ($n = 9$)	Group 3 ($n = 11$)	Group 4 ($n = 9$)
Mean I-QoL scores				
Baseline	44.1	53.9	54.9	53.6
6 Months	54.3	76.6	66.4	80.6
Increase ≥10 points, %	63	78	70	67
Mean daily incontinence episodes				
Baseline	2.6	4.6	2.9	3.9
6 Months	2.6	2.1	1.9	0.7
Change from baseline[a]	0.0	−2.5	−1.0	−3.2
Mean daily pad usage				
Baseline	1.9	2.1	1.6	2.0
6 Months	2.0	1.4	0.8	0.0
Change from baseline[b]	0.1	−0.7	−0.8	0.1

Source: Sotomayor M and Bernal GF, *Int Urogynecol J Pelvic Floor Dysfunct*, 14, 373, 2003.

Abbreviation:I-QoL, incontinence quality of life questionnaire.

[a] Negative numbers indicate decrease in incontinence episodes.

[b] Negative numbers indicate decrease in pad usage.

At 12 months, 87 (79.1%) patients in the radio frequency-treated group and 49 (77.8%) patients in the sham group underwent LPP testing [31]. There were no significant differences regarding demographic or other baseline characteristics between these two evaluable populations. Women in the radio frequency-treated group experienced a 13.2 cm H_2O increase in LPP at 12 months compared with a 2.0 cm H_2O decrease in those in the sham group ($p = 0.02$) (Table 77.2).

A retrospective analysis of the results of this controlled trial sought to determine whether menopausal status and/or use of hormone replacement therapy (HRT) had any effect on the outcome as measured by the percent of patients that at least decreased in all groups, with improvement reaching statistical significance in group 4 ($p = 0.03$).

In a subsequent retrospective analysis [28], the incidence of I-QoL overall score improvement of at least 10 points ranged from 44% to 70% among all groups. The percentage of patients who experienced at least a 50% reduction in daily incontinence episode frequency ranged from 63% to 89%, and the “cure” rate (defined as “no incontinence” episodes or pad use between 6 and 12 months) ranged from 22% to 67%.

A 12-month, randomized, controlled trial compared the transurethral radio frequency collagen denaturation with a sham procedure [31]. In total, 173 women with SUI due to hypermobility (mean age, 50 years) were randomized to receive active radio frequency treatment ($n = 110$) or sham procedures ($n = 63$). The sham procedure differed from active treatment in that the probes lacked needle electrodes and the generator, while appearing and sounding similar, did not actually deliver radio frequency energy. All procedures were performed in an outpatient setting under conscious sedation.

Impact on patient QoL was based on the incidence of a 10-point or greater improvement in I-QoL scores at 6 and 12 months. Objective treatment efficacy was evaluated through Valsalva LPP testing at 6 and 12 months. At 12 months, 89 (80.1%) patients in the radio frequency-treated group and 53

(84.1%) patients in the sham group underwent QoL assessments. The 12-month analysis excluded 21 women lost to follow-up; 8 women with I-QoL changes that could not clearly be attributed to the study procedure, owing to a change in medical history (e.g., hysterectomy during the trial period, urinary tract infection at 12 months); and 2 women with baseline I-QoL scores of at least 90 points who could not numerically achieve a 10-point or greater score improvement. The percentage of patients with at least a 10-point improvement from baseline in overall I-QoL scores is shown in Table 77.2. When all patients were included regardless of baseline severity of SUI, there was no significant between-group difference at 12 months. In contrast, significantly more radio frequency-treated patients (74%) had a 10-point improvement over baseline in I-QoL scores [32]. In the radio frequency-treated group, 43 women had moderate to severe SUI including 13 (30%) premenopausal women, 23 (53%) postmenopausal women using HRT, and 7 (16%) postmenopausal women not using HRT. There was no significant difference in the 12-month incidence of a 10-point or greater I-QoL score improvement between postmenopausal women using HRT (70%) and those not using HRT (71%). Likewise, no significant differences in a 10-point or greater score improvement occurred between premenopausal women and either postmenopausal women using or not using HRT.

Table 77.2 Percent of Patients with At Least a 10-Point Improvement from Baseline in Incontinence Quality of Life Scores and Change from Baseline in Valsalva Leak Point Pressure in a 12-Month Controlled, Randomized, Sham Procedure–Controlled Trial

	Radio frequency collagen denaturation	**Sham procedure**
≥10-point improvement in I-QoL scores		
All patients (n = 142)	48%	44%
Mild SUI[a] (n = 69)	22%	35%
Moderate to severe SUI[a] (n = 73)	74%	50%
Change in Valsalva^{LPP} (*cm* H_2O)	+13.2 ± 39.2	−2.0 ± 33.8

Source: Appell RA et al., *Neurourol Urodyn*, 25, 331, 2006.

Abbreviations: I-QoL, incontinence quality of life questionnaire; SUI, stress urinary incontinence; LPP, leak point pressure.

[a] Severity at baseline based on I-QoL score: 0–60 points, moderate to severe SUI; 61–90, mild SUI.

A separate retrospective analysis to determine long-term efficacy was conducted in 21 women in the radio frequency group who had not undergone additional SUI treatment in the interim and were available for follow-up at least 3 years posttreatment [33]. Patients completed the 3-day diaries and the I-QoL questionnaire. Diary analysis revealed that 56% of patients had at least a 50% reduction in SUI episodes at follow-up. Evaluation of I-QoL scores showed a significant improvement versus baseline, with a mean score improvement of 12.7 points (p = 0.04). Results demonstrated that the effectiveness of this procedure at 1 year was maintained for at least 3 years in more than half of patients.

The long-term efficacy of nonsurgical transurethral radio frequency collagen denaturation was assessed in a multicenter, prospective, open-label, single-arm trial in 136 women with SUI secondary to bladder neck hypermobility. Patients had failed earlier conservative treatment and had not received surgical or bulking agent therapy. Interim results after 12 months were initially reported [26].

Intent-to-treat analysis revealed significant reductions compared with baseline in the number of daily and weekly leakage episodes due to activity ($p < 0.0026$ for both), with 50% of patients reporting at least a 50% reduction in activity-related leaks (Table 77.3). As measured by stress pad weight tests, 69% of women exhibited at least a 50% reduction in leaked urine volume (median reduction, 15.2 g; $p < 0.0001$). Furthermore, 45% of women were dry (29% no SUI; 16% <1 g leakage). There were also significant improvements in the median scores on the I-QoL questionnaire ($p < 0.0001$) and in the mean scores on the urinary distress inventory (UDI-6; $p < 0.0001$) (Table 77.4). In total, 71.2% of women exhibited I-QoL improvement including 50.3% with at least a 10-point improvement, and 61.8% of patients reported improvement on the UDI-6 (Table 77.4). A subsequent study provided a 36-month follow-up for these patients showing a mean I-QoL score improvement of 17 points from baseline (p = 0.0004), suggesting a durable QoL improvement up to 3 years [34] (Table 77.5).

In a recent study, a Markov model was used to compare the cost effectiveness of transurethral radio frequency collagen denaturation with sling or Burch procedures for treating SUI in patients who had previously failed conservative therapy. There was a 17%–30% lower mean cost for radio frequency relative to comparative sling or Burch procedures [35]. In this analysis, radio frequency appears to have a lower cost with fewer adverse events (AEs) compared with surgical treatments, though this study did not include long-term follow-up or cost of treatment for recurrent SUI.

Thus, preliminary trials suggest a treatment advantage for transurethral radio frequency collagen denaturation compared to sham procedures in the treatment of SUI [36]. However, there have not been randomized trials comparing this approach to other alternative treatments to date.

Safety

In the pilot study, no serious adverse events (SAEs) were associated with the procedure or identified up to 6 months afterward [27]. The most common AEs recorded during the procedure, recovery, and 30-day posttreatment period are listed in Table 77.6. One case of urinary retention presented 24 hours following discharge and required an indwelling catheter for 48 hours, with no further retention episodes. No other AE required therapeutic intervention, and no patient found her symptoms distressing enough to request an unscheduled physician visit. Over 12 months posttreatment for each of the radio frequency regimens in this study, no SAEs were reported [28]. Between 6 and 12 months, 8% of patients reported at least one episode of dysuria and 22% noted at least one episode of urgency, although none of these AEs affected patient QoL.

Table 77.3 Changes from Baseline in Median Number of Leaks Caused by Activity in 12 Months from a 36-Month Trial (Intent-to-Treat Population, *n* = 136)

	Baseline	**12 months**	**Change**
Leaks/day, *n* (range)	2.1 (0.1–35.0)	1.1 (0.0–20.0)	−0.6 (−34.3 to 18.9)
Leaks/week, *n* (range)	15.0 (1.0–245.0)	7.5 (0.0–140.0)	−4.0 (−240.0 to 132.0)
Patients with ≥50% fewer leaks, %	—	68 (50.0)	—

Source: Elser DM et al., *J Minim Invasive Gynecol*, 16, 56, 2009.

Table 77.4 Changes from Baseline in Adjusted Incontinence Quality of Life and Urogenital Distress Inventory Scores at 12 Months (Intent-to-Treat Population, *n* = 136)

	Baseline	**12 months**
I-QoL[a]		
Median total score (range)	53.0 (0.0–85.0)	63.0 (33.0–97.0)
Median change (range)		+9.5 (−66.0 to 91.0)
p value[b]		<0.0001
Patients with ≥10-point improvement from baseline, *n* (%)	—	68 (50.3)
UDI-6[a]		
Mean score ± SD	52.5 ± 16.0	38.4 ± 22.3
Mean change ± SD	—	−14.1 ± 24.7
p value[c]		<0.0001
Patients with any improvement from baseline, *n* (%)	—	84 (61.8)

Source: Elser DM et al., *J Minim Invasive Gynecol*, 16, 56, 2009.

Abbreviations:I-QoL, incontinence quality of life; UDI-6, urogenital distress inventory; SD, standard deviation.

[a] For I-QoL scores, increase indicates improvement; for UDI-6 scores, decrease indicates improvement.

[b] Wilcoxon signed-rank test.

[c] Paired student t test.

Table 77.5 Incontinence Quality of Life Questionnaire ≥ 10-Point Improvement, Imputed Results by Severity at Baseline throughout a 36-Month Study Period

Visit	Mild ($n = 50$)	Moderate ($n = 65$)	Severe ($n = 24$)
3 months	42% (21)	60% (39)	79% (19)
6 months	36% (18)	62% (40)	83% (20)
12 months	34% (17)	63% (41)	83% (20)
18 months	32% (16)	78% (51)	79% (19)
24 months	38% (19)	66% (43)	79% (19)
36 months	36% (18)	69% (45)	88% (21)

The randomized, sham procedure–controlled trial supported the safety of this procedure [31]. No SAEs were reported. Except for dysuria, wherein the incidence was numerically but not significantly greater among women in the radio frequency-treated group, there were no significant between-group differences in the incidence of all other AEs (Table 77.7). All cases of dysuria, hematuria, and hesitancy were transient and mild to moderate, and all urinary tract infections were simple and resolved with antibiotic therapy. In general, the safety profile for transurethral radio frequency collagen denaturation was comparable to that of the sham procedure.

Table 77.6 Adverse Events Reported during the Pilot Trial of Transurethral Radio Frequency Collagen Denaturation ($n = 37$)

During procedure or in recovery room, n (%)	
Any serious event	0 (0)
Dysuria	1 (3)
Gross hematuria	1 (3)
Anesthetic reaction	1 (3)
30 days posttreatment, n (%)	
Any serious event	0 (0)
Dysuria	23 (62)
Urgency or pain	19 (51)
Gross hematuria	16 (43)
Urinary retention (requiring 48 hours indwelling catheter)	1 (3)

Source: Sotomayor M and Bernal GF, *Int Urogynecol J Pelvic Floor Dysfunct*, 14, 373, 2003.

Table 77.7 Twelve-Month Prevalence of Adverse Events in the Randomized, Sham Procedure–Controlled Trial

Adverse Event	Radio frequency Treatment ($n = 110$)	Sham Treatment ($n = 63$)
Dysuria	9.1% (10)	1.6% (1)
Hematuria	0.9% (1)	0.0% (0)
Urinary retention	0.9% (1)	0.0% (0)
Urinary tract infection	4.5% (5)	4.8% (3)
Hesitancy	0.0% (0)	1.6% (1)
Asymptomatic detrusor overactivity	1.8% (2)	6.3% (4)
“Dry” overactive bladder	7.3% (8)	3.2% (2)
“Wet” overactive bladder	10.0% (11)	9.5% (6)

Source: Appell RA et al., *Neurourol Urodyn*, 25, 331, 2006.

In the 36-month study, transurethral radio frequency collagen denaturation was safe and well tolerated [26,34]. At 3 days posttreatment, the most common AEs were dysuria ($n = 7$; 5.2%), urinary retention ($n = 6$; 4.4%), pain ($n = 4$; 2.9%), and urinary tract infection ($n = 4$; 2.9%). Average pain score reported on a 10-point visual analog scale was 1.6. At 1-year posttreatment, one patient experienced increased leakage, judged by the investigator to be probably related to treatment. Symptoms of urgency or urge incontinence were reported by eight patients; in six, these symptoms resolved by 12 months and one patient reported these symptoms for 25 months. One patient still reported urge and urge incontinence symptoms at 36 months. At 18 months, one patient experienced a myocardial infarction deemed by the investigator to not be related to the procedure [34].

SUMMARY

There are a variety of treatment options for SUI. Initially, conservative measures such as Kegel exercises and behavioral modification can be helpful, but for severe SUI more invasive treatment options are often necessary. Traditional Burch procedures are an option but currently the midurethral sling is considered the standard of care. If a patient does not desire a surgical procedure or is not a good surgical candidate, minimally invasive injection therapy is an option. Urethral bulking agents are currently available and autologous muscle–derived cell injection therapy is in clinical trials.

Nevertheless, clinical evidence indicates that nonsurgical, transurethral radio frequency collagen denaturation is an effective, safe, and cost-effective therapy in the spectrum of treatment options for women with SUI due to bladder neck hypermobility. Since the procedure does not result in gross anatomic changes, it likely would not preclude subsequent surgical procedures if needed, though at 3-year follow-up the efficacy appears durable. Thus, in the properly selected patient, radio frequency collagen denaturation offers SUI patients with an office-based, minimally invasive treatment option, with a nominal disruption of their usual daily activities.

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78 Artificial Urinary Sphincter for Treatment of Stress Urinary Incontinence in Women

David Castro-Diaz, David Staskin, and Roger R. Dmochowski

INTRODUCTION

The artificial urinary sphincter (AUS) remains an alternative to slings or periurethral injection therapy in the management of urinary incontinence, especially when the aforementioned interventions have failed. The AUS has been most often used for treatment of incontinence due to primary urethral sphincter deficiency (type III stress urinary incontinence [SUI], or intrinsic sphincter deficiency [ISD] [1–3]). ISD may be the result of periurethral fibrosis from prior anti-incontinence procedures, neurological disorders (spinal cord injury, peripheral neuropathy), radical pelvic operations, pelvic radiation therapy, or the effects of aging and estrogen deficiency on the urethra and anterior vaginal wall. These conditions affect the ability of the urethra wall elements to coapt, thereby producing a poorly functional sphincteric mechanism. The pubovaginal sling is considered the gold standard for the treatment of ISD, yet some patients will have less than adequate results despite several attempts [4]. The AUS enhances higher intraurethral pressures by increasing pressure circumferentially around the urethra, lessening the transmission of intra-abdominal pressures. Therefore, in some cases, the AUS may benefit women with urethral weakness and good anterior vaginal wall who have sphincteric dysfunction.

The AUS may be inserted either by a transabdominal or a transvaginal approach. The device is composed of three parts: the inflatable cuff, the pressure-regulating balloon, and the pump. The cuff is placed circumferentially around the bladder neck, the pressure-regulating balloon is positioned in the prevesical, and the pump is placed in the labia majora. When the pump is compressed, fluid within the system is transferred from the cuff into the regulating balloon. This decompression opens the bladder neck allowing the patient to void. After a period of time (usually between 1 and 2 minutes), the pressure-regulating balloon initiates cuff refilling by transfer of fluid through a resistor in the pump, re-establishing urethral compression, coaptation, and continence. The American Medical System-800 is the AUS currently available for implantation (Figure 78.1).

PREINSERTION ASSESSMENT

Women with SUI who may be considered candidates for implantation of an AUS should undergo detailed evaluation including a focused urological history and physical examination. Women with SUI from primary urethral sphincter deficiency will experience significant volumetric loss of urine with abdominal straining or other physical exertions. Delineation and characterization of incontinence type as stress, spontaneous, or mixed (associated with some degree of urinary urgency) is important so as to correctly identify those women who may have contributory detrusor overactivity. Bother and amount of urinary loss should be quantified (most commonly with a urinary diary or pad test) to accurately counsel the patient about options. Prior anti-incontinence interventions may have induced bladder neck and periurethral fibrosis and decreased urethral vascularity and integrity of the periurethral tissue and anterior wall of the vagina. Therefore, any history of surgical intervention should be assessed. The history should also assess the patient for any neurological or orthopedic disorders that may affect the patient's manual dexterity and therefore affect her ability to activate the labial pump mechanism.

Physical examination should be performed, directed to the vagina and lower abdomen. Examination may reveal previous surgical procedures by virtue of surgical scarring or other fibrotic changes. Important examination findings include: weakened pelvic floor, associated prolapse defects, or atrophic vaginitis. Urethral hypermobility should be measured by direct examination or the Q-tip test. The lack of hypermobility of the bladder neck or urethra may suggest a better candidate for the AUS. Vaginal vault capacity and ancillary vaginal findings should be noted. Objective demonstration of SUI in the supine or upright position is critical as a correlate to subjective assessment.

Laboratory assessment includes obtaining urine sample for analysis and culture. Urodynamic study (UDS) is critical to assess bladder function and determine bladder storage capabilities. Urine storage at low intravesical pressures is critical for placement of the AUS, given the compressive effect of the device. UDS evaluates bladder filling pressures and bladder capacity. High-pressure urinary storage is a contraindication to AUS placement and critical to determine so as to optimize therapy. UDS also may detect detrusor overactivity, which may require additional medical therapy for optimization of care. Abdominal leak point pressure assists in the assessment of sphincteric function and assists in the delineation of ISD. Urethral pressure profilometry confirming low urethral closure pressures (<25 cm H_2O) has been suggested by some experts [5]. Additional testing modalities may include uroflowmetry and measurement of postvoid residual urine. Intermittent catheterization postoperatively may be a component of therapeutic strategy for some women with poor bladder contractility.

Radiographic evaluations may include a voiding cystourethrogram (VCUG) with resting and straining views and can be combined with UDS. A well-supported urethra with an open bladder neck at rest is consistent with ISD. The VCUG will also confirm any coexistent urinary tract fistula or vesicoureteral reflux.

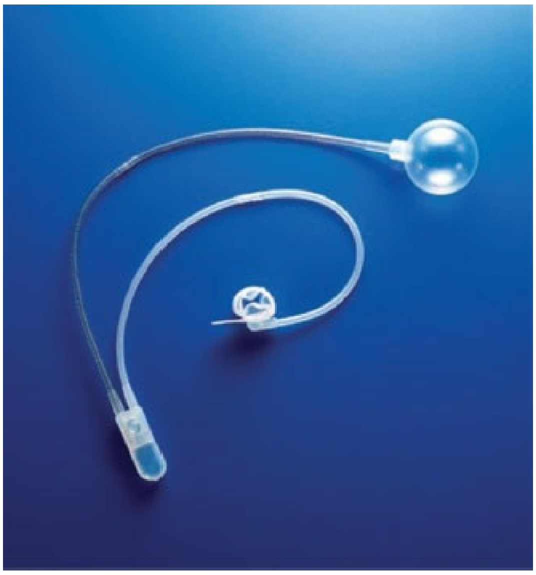


Figure 78.1 Single cuff AMS 800^{TM} urinary control system. (Courtesy of American Medical Systems, Inc., Minnetonka, MN.)

IDEAL CANDIDATES

The AUS is indicated for women who suffer from ISD who demonstrate low-pressure urinary storage. Conservative measures (such as medication therapy, behavioral management, and topical vaginal hormones) should be considered and exhausted prior to operative intervention.

Women who are found to have elevated intravesical storage pressures are at risk for upper tract deterioration with the AUS (hydronephrosis and renal functional impairment). These women should demonstrate a response to antimuscarinic or to alternative therapies on UDS evaluation prior to AUS implantation. Augmentation cystoplasty may be considered in those women who demonstrate persistently high pressures despite maximal medical therapy. Augmentation may be performed either concomitant with or in a staged manner after the AUS implantation.

Women with incomplete emptying and high preoperative postvoid residuals may be considered for AUS implantation; however, intermittent self-catheterization should be considered following the procedure and should be taught preoperatively. If unwilling or unable to perform intermittent catheterization, the woman may still be a candidate but should be aware that elevated residual urine volumes may be problematic in the postoperative period. Manual dexterity should be determined so as to operate the labial pump after AUS implantation. As compared to the pubovaginal sling, the AUS appears less likely to cause permanent urinary retention. The Crede maneuvers may assist voiding for some women after cuff deactivation. However, these women should be meticulously selected, with preoperative demonstration of effective bladder evacuation by the Valsalva effort.

Child-bearing potential is not an exclusion for sphincter implantation. Some authors suggest that when pregnancy occurs, the device should be deactivated in the third trimester to diminish pressure on the cuff and bladder neck. Deactivation during labor and delivery to promote bladder emptying is considered recommended practice. Cesarean section is not contraindicated as AUS components are within the retropubic space [6].

TRANSVAGINAL IMPLANTATION

The transvaginal approach for AUS cuff placement provides the singular advantage of improved urethrovaginal dissection given the immediate access to the periurethral space. Multiple anti-incontinence procedures may make dissection extremely difficult, and direct visualization is promoted by this approach. Inadvertent and unrecognized injury to the vaginal wall and urethra are decreased by the transvaginal approach [7,8].

After admission to the surgical care area, preoperative broad-spectrum antibiotics are administered parenterally at least 1 hour prior to surgery. After the administration of regional or general anesthesia, the patient is placed in the dorsal lithotomy position. The lower abdomen and vagina are clipped and prepared with a 10-minute scrub with a povidone-iodine or Hibiclens solution. A posterior-weighted vaginal retractor is placed for exposure of the anterior vaginal wall. Lateral labial retraction sutures or a self-retaining retraction system may be utilized for retraction of the labia. A 14 F Foley catheter is inserted in sterile fashion for bladder drainage.

A midline incision is made in the anterior vaginal wall. The incision should extend from a point midurethra to the proximal bladder neck (Figure 78.2). With sharp dissection, the vaginal wall is dissected from the underlying urethra on either side. The vaginal flaps should be dissected so as to create thick flaps for purposes of closure of the vagina wall over the AUS cuff. Blunt finger dissection may be used to separate the endopelvic fascia from its lateral attachments to the pubic rim in a woman who has not had prior surgery. The fascia should be swept from lateral to medial, so as to gain access into the retropubic space (Figure 78.3). The retropubic space should be entered sharply in women who have had previous surgery using dissecting scissors positioned against the pubic symphysis angled toward the ipsilateral shoulder. When the retropubic space is dissected bilaterally, final mobilization of the bladder neck and urethra is completed.

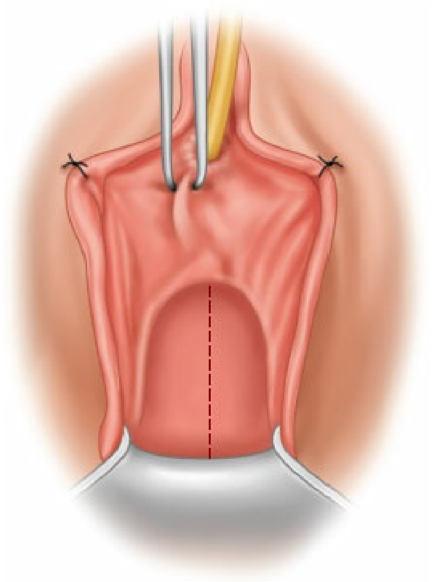


Figure 78.2 With the patient in dorsal lithotomy position, a midline vaginal incision is performed.

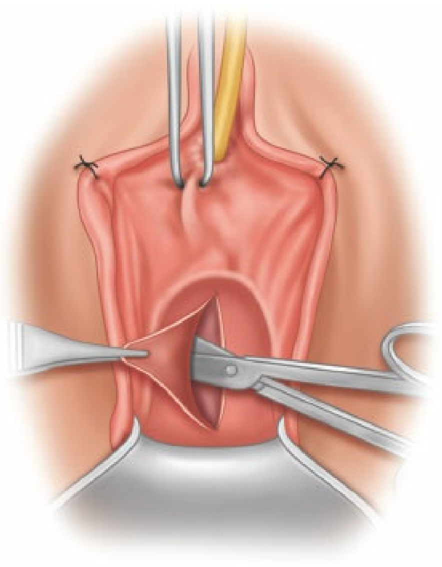


Figure 78.3 Using a combination of sharp and blunt dissection, the vaginal mucosa is dissected off of the underlying tissues and the retropubic space is entered bilaterally.

Next, the anterior aspect of the proximal urethra and bladder neck is separated from the fascial attachments to the pubic symphysis. Blunt finger dissection or sharp dissection may accomplish this component of the procedure. Suprameatal incision (1–2 cm) and dissection may be used (Figure 78.4a) in some women to assist in delineation of the dorsal urethra [9]. The sharp dissection should be performed in the midline immediately inferior to the pubic symphysis (Figure 78.4b). At this stage of the procedure, aggressive dissection may lead to unintentional bladder or urethral tear. Urinary tract injury has conventionally led to abandonment of the procedure. Some authors, however, including Salisz and Diokno have reported successful repair of this type of injury with subsequent successful implantation of the device [10].

After circumferential dissection of the proximal urethra and bladder neck, a right-angle clamp is passed around the urethra from left to right. The cuff measuring tape is passed around the bladder neck and the circumferential dimension of the bladder neck is assessed. Using a larger cuff size is preferred if there is a concern about exact dimension exists. Using a right-angle clamp, the appropriate-sized cuff is placed around the bladder neck (Figure 78.5). If the AUS pump is to be placed into the right labia majora, the cuff should be drawn from right to left. If the pump is to be placed in the left labia, the cuff is placed from left to right. The cuff is then locked in place and rotated 180° so that the locking button of the cuff lies anteriorly, opposite to the anterior vaginal wall (Figure 78.6).

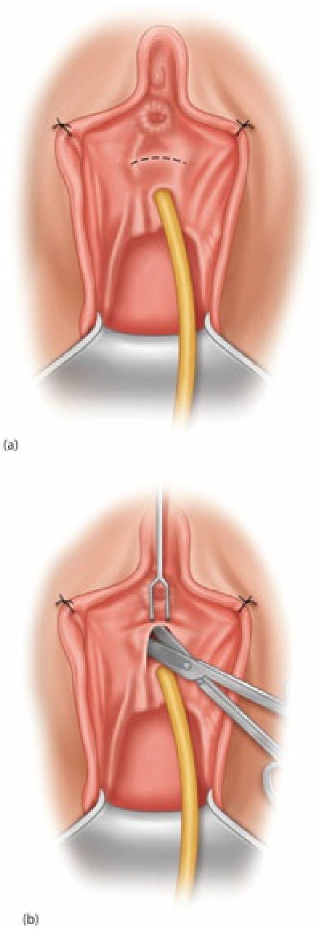


Figure 78.4 (a) If dense scarring is encountered anterior to the urethra, a separate incision can be made above the urethral meatus. (b) The suprameatal dissection is performed in the midline, just below the pubic symphysis.

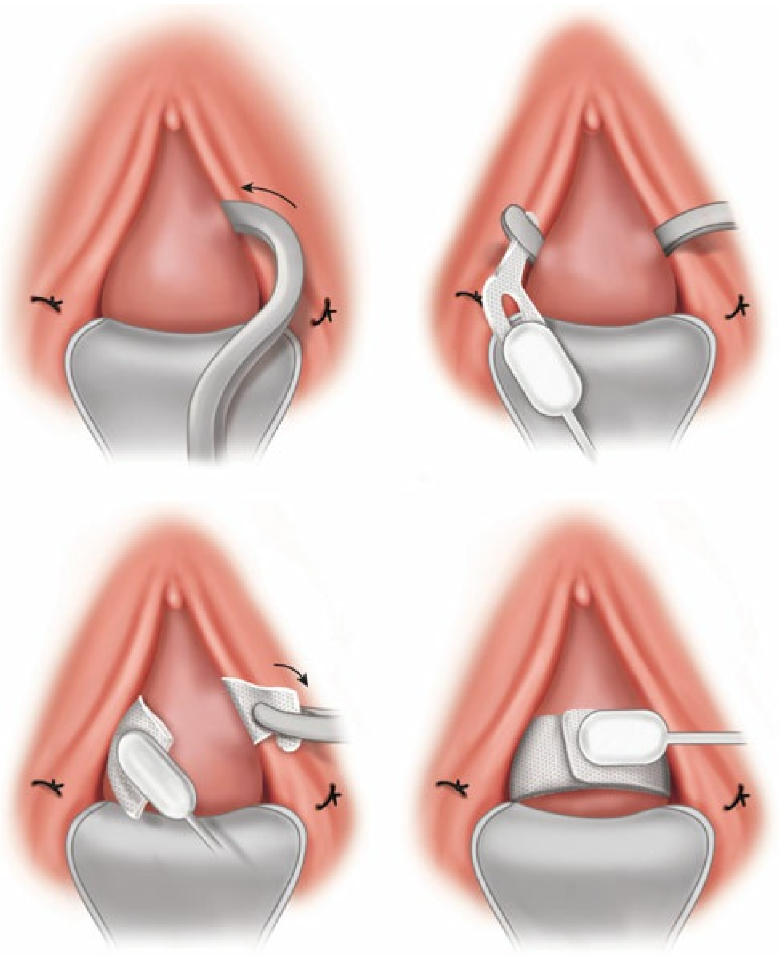


Figure 78.5 The cuff of the artificial urinary sphincter is passed around the bladder neck and locked into place.

On the ipsilateral side to which the pressure-regulating balloon and pump mechanism will be implanted, a transverse suprapubic incision (approx 4 cm) is created. A straight clamp is passed using digital guidance from the suprapubic incision lateral to midline down to the ipsilateral side of the vaginal incision. The cuff tubing is grasped, and the clamp is withdrawn, pulling the tubing up into the suprapubic incision. Rubber-shod clamps should be utilized during this phase of the procedure to ensure that the end of the tubing is not open to the field. The anterior rectus sheath is then incised vertically and the retropubic space is developed adjacent to the bladder. The pressure-regulating reservoir is then inserted into this space. The reservoir is then filled with sterile saline to a volume compatible with reservoir size and requirements for the unique individual (usually 22 mL).

From the suprapubic incision, a subcutaneous tunnel is formed into the labia majora with a combination of blunt and sharp dissection. The pump is passed into the labia majora to reside at the level of the urethral meatus with the deactivation button facing anteriorly (outwardly). During implantation, a Babcock clamp is used to secure the pump in this position. The tubing is trimmed to the appropriate lengths and the ends are irrigated to remove air or debris. The preparation of the cuff and the reservoir is performed according to the instructions specified by the manufacturer. A straight connector is then placed between the pump and the balloon reservoir. A right-angle connector attaches the pump to the cuff. Quick connectors provided in the implantation kits are used to secure these attachments.

The suprapubic and vaginal incisions are irrigated copiously with an antibiotic solution. The wounds are then closed in several layers with absorbable sutures to ensure complete of all implanted materials with host tissue. If the anterior vaginal wall is of suspect quality, interposition of a vascularized flap (e.g., Martius flap) should be considered. Following closure, a vaginal packing is placed. Prior to awakening the patient, the AUS cuff is deactivated.

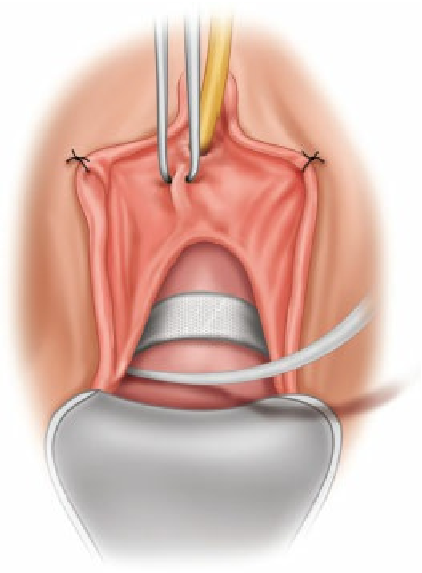


Figure 78.6 The cuff is rotated 180° clockwise so that the locking button lies anterior to the urethra, away from the anterior vaginal wall.

The vaginal packing and Foley catheter can be removed on the first postoperative day. The cuff should be in a deactivated position for a period of 6 weeks.

TRANSABDOMINAL IMPLANTATION

The transabdominal approach allows easy access to the retropubic space and removes the need for of an anterior vaginal wall incision [11]. Similar to the transvaginal approach, after admission to the surgical unit, the woman should receive parenteral broad-spectrum antibiotics 1 hour prior to the start of the operation. After induction of anesthesia, the patient should be placed in the dorsal lithotomy position allowing access to both the abdomen and vagina. The abdominal wall and vagina should be shaved and a 10-minute skin preparatory scrub should be performed. A 14 F Foley catheter is placed and the bladder drained.

A lower midline or Pfannenstiel incision should be made to allow appropriate access to the retropubic space. The retropubic space is developed using a combination of sharp and blunt dissection. If the space does not develop easily, the dissection should follow the posterior aspect of the pubic bone and the periosteum, trying not to injure the anterior bladder wall. This may be assisted by the use of electrocautery. If a cystotomy occurs, this should be performed with absorbable sutures.

At the bladder neck, dissection should proceed laterally and may be facilitated by vagina manipulation with sponge stick or manual assistance (Figure 78.7). The bladder neck is located by palpation of the Foley catheter balloon and the endopelvic fascia is entered approximately 2 cm on either side of the bladder neck. The dissection of the vesicovaginal plane is continued through the endopelvic fascia until the internal aspects of the vaginal fornices are visible. The bladder neck is then dissected from the vagina, taking great care to avoid perforation of the vaginal wall. Intentional anterior cystotomy may be used to assist in mobilization of the bladder neck and facilitate separation of the vesicovaginal plane. Any cystotomy is repaired in multiple layers with absorbable sutures. Any accidental perforations of the vaginal wall are also repaired at this phase of the implantation. If significant injury of the vaginal wall eventuates, the option of a pubovaginal sling should be considered. If an AUS is implanted in this situation, the interposition of a Martius flap is preferred for coverage purposes.

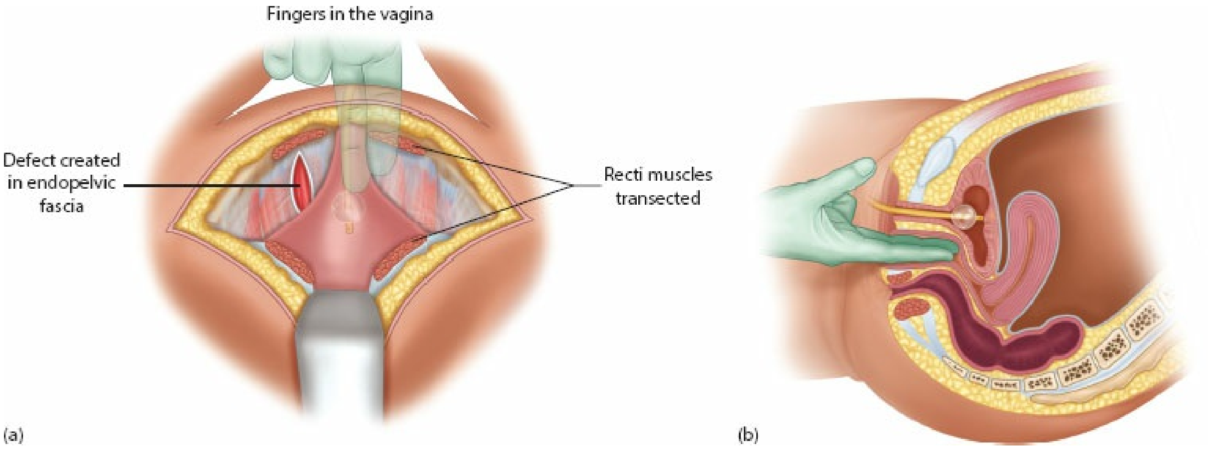


Figure 78.7 Aiding the dissection with an intravaginal finger: (a) frontal view and (b) lateral view.

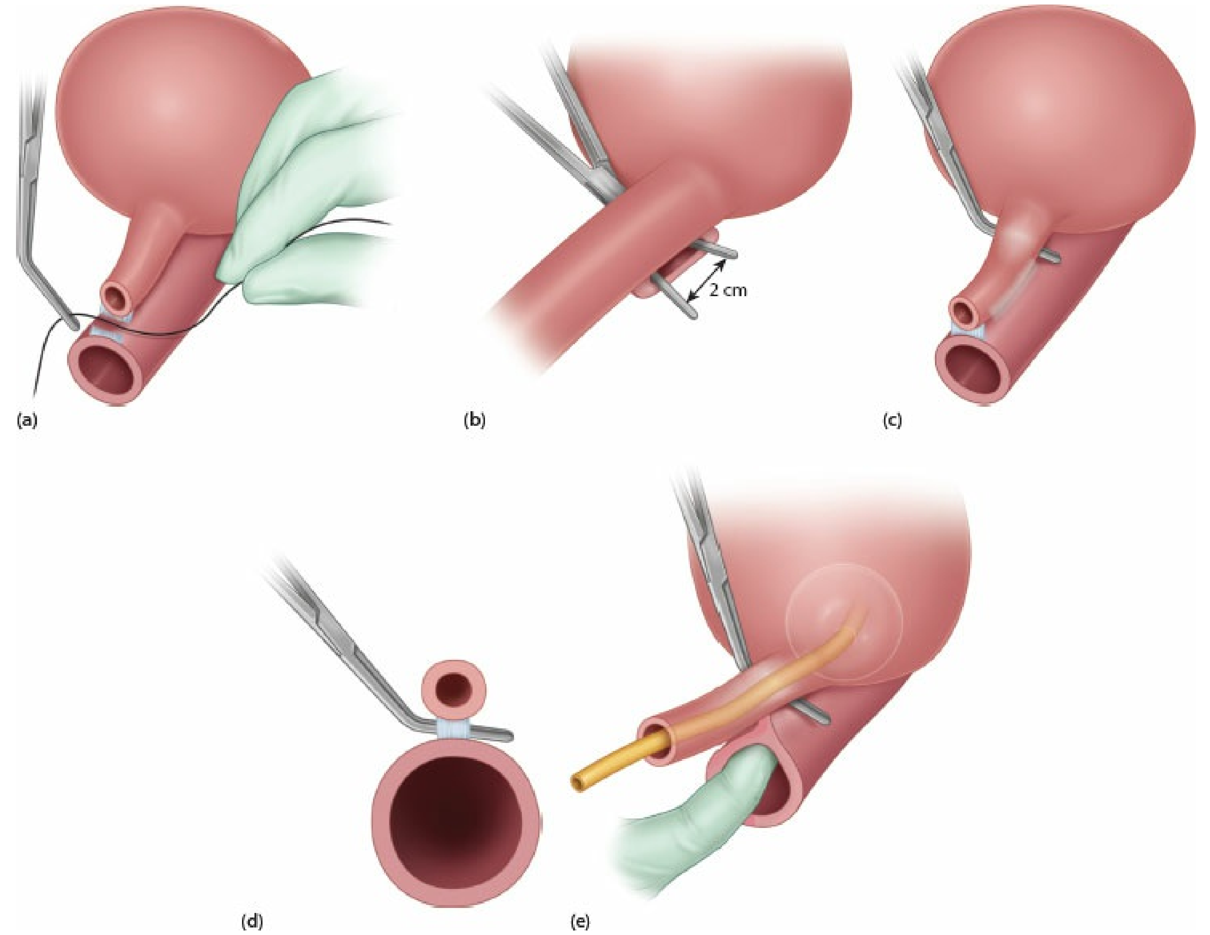


Figure 78.8 (a, b) Insertion of right-angle clamp, (c, d) right-angle clamp in place, and (e) clamp, catheter and finger in position.

After circumferential dissection of the bladder neck has been completed, the cuff sizer is used; the larger size is selected in cases of nonstandard measurement. The appropriate cuff is drawn around the bladder neck with a right-angle clamp and positioned so that the locking button lies on the opposite side from the labia majora in which the pump is to be placed (Figure 78.8).

The appropriate pressure-regulating reservoir is chosen as previously described. The balloon is placed on the same side as the labium majora where the pump will be placed. The system is primed and filled as previously described. A subcutaneous tunnel is created from the suprapubic incision into the labium majora using sharp and blunt dissection. The pump is placed in the labium majora to rest at the level of the urethral meatus with the deactivation button facing anteriorly (outward facing). A Babcock clamp is utilized to fix the pump in place. An absorbable suture can be placed within the tunnel to prevent cephalad migration.

The tubing is then connected as described previously. The cuff is deflated and the device is deactivated. Following hemostasis, the wound is copiously irrigated with antibiotic solution. The abdominal incision is then closed without drainage. The device in place can be seen in Figure 78.9.

The Foley catheter can be withdrawn on the first postoperative day. In cases of accidental or intentional cystotomy, a longer period of catheter drainage is preferred. The device is left in a deactivated position for a period of 6 weeks.

ENDOSCOPIC IMPLANTATION

The AUS in women can also be implanted by either laparoscopic or robot-assisted laparoscopic. The procedure can be performed using either a transperitoneal or an intraperitoneal access depending on patient characteristics and surgeon preferences. The extraperitoneal approach pretends to reproduce the steps of the open procedure, but quite often is difficult because scar tissue of previous pelvic surgery. When using an extraperitoneal approach, the first step consists of approaching the bladder through an incision of the parietal peritoneum from one medial umbilical ligament to other. Anterior and lateral attachments of the bladder have to be incised to expose the bladder neck. When using a transperitoneal approach, an incision of the parietal peritoneum from one medial umbilical ligament to the other is carried out. The endopelvic fascia has to be entered at both sides of the bladder neck, as previously described for the transabdominal implantation. With the help of two surgeon fingers in the vagina, the dissection is performed to visualize the vagina. After releasing the bladder neck, it is important to check the integrity of the bladder. In the case that any accidental injury occurs, management should be the same as to an open implantation. A cuff sizer is used to measure and to select the appropriate cuff size. The balloon and pump are introduced through a mini incision in a similar manner to the transabdominal implantation.

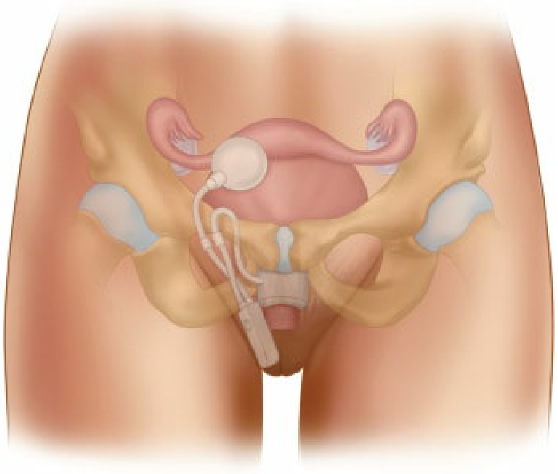


Figure 78.9 Artificial urinary sphincter in place.

COMPLICATIONS

AUS implantation complications include intraoperative injury to the bladder, urethra, or vaginal wall, device failure, erosion, and infection.

When assessing risk factors for explantation including patient age, type and number of prior procedures, time since prior procedure and AUS implantation, and perioperative injury, Costa et al. found only perioperative injury to be contributory. Of 49 patients who had perioperative injuries, 8 explantations resulted, compared with only 4 in the 155 cases that did not have injuries [12]. On a multivariate analysis of a large series of 215 women, Vayleux found that age > 70 years, previous anti-incontinence surgery, and pelvic radiotherapy were risk factors for failure [13]. Surgical technique can minimize major intraoperative complications. Recognized injuries should be repaired primarily under direct visualization with the interposition of well-vascularized tissues if necessary. In many cases, inadvertent injury to the bladder, urethra, or vaginal wall should not preclude implantation of the device. Surgical judgment should be utilized to determine the safety of completing the procedure.

Improvements in the design and manufacture of the device have significantly reduced AUS malfunctions. Device-related issues include fluid loss secondary to tubing fracture at connection sites, cuff leakage at stress points, and kinking of the tubing. Chronic failure may be due to atrophy of the periurethral tissues decreasing the compressive bulk within the cuff, not allowing for pressure to be dispersed evenly around the urethra, resulting in recurrent incontinence. Newly designed cuff backing has addressed this issue; however, it must be considered in cases of failure [14]. Surgical judgment should be used when replacing the malfunctioning portion of the device rather than the whole device. Indications for complete replacement of the device include fluid leakage, which may allow foreign material into the system, or chronic emplacement of the device (more than 3 years) [15].

Device erosion has decreased since the introduction of modified cuff architecture; however, it remains a concern with any foreign body implantation. Significant risk factors for erosions include perioperative injury, incorrect implantation technique, history of prior procedures, and infection [12]. Erosion of the sphincter cuff into the urethra is commonly associated with recurrent incontinence, although urinary tract infection and/or wound surgical site infection may be the first and only symptom. Erosion of the cuff through the vaginal wall is associated with vaginal bleeding and discharge. Erosion of the pressure-regulating reservoir into the bladder is rare, and may present as a urinary tract infection or infection of the device. Pump erosion through the labium majora is diagnosed by direct examination.

Infection or erosion should be treated with explantation of the entire device in the majority of cases. Reimplantation may be considered after 4–6 months. In cases of cuff erosion into the urethra, the placement of an omental flap between the cuff and urethra is recommended at reoperation.

In cases of erosion of the cuff into the urinary tract, salvage of the AUS is not recommended. In the isolated case of erosion of the sphincter tubing through the abdominal skin or erosion of the pump through the labium, aggressive irrigation and debridement of the tissues may make replacement of certain AUS components and wound closure a possibility. When replacement of the pump is necessary, it should be moved to the opposite labium. The device with cuff erosion into the vaginal wall may be salvaged utilizing a Martius flap and vaginal wall closure. Before all salvage attempts, the patient should be counselled as to the high risk of eventual necessity for removal of the complete device.

IMPLANTATION RESULTS

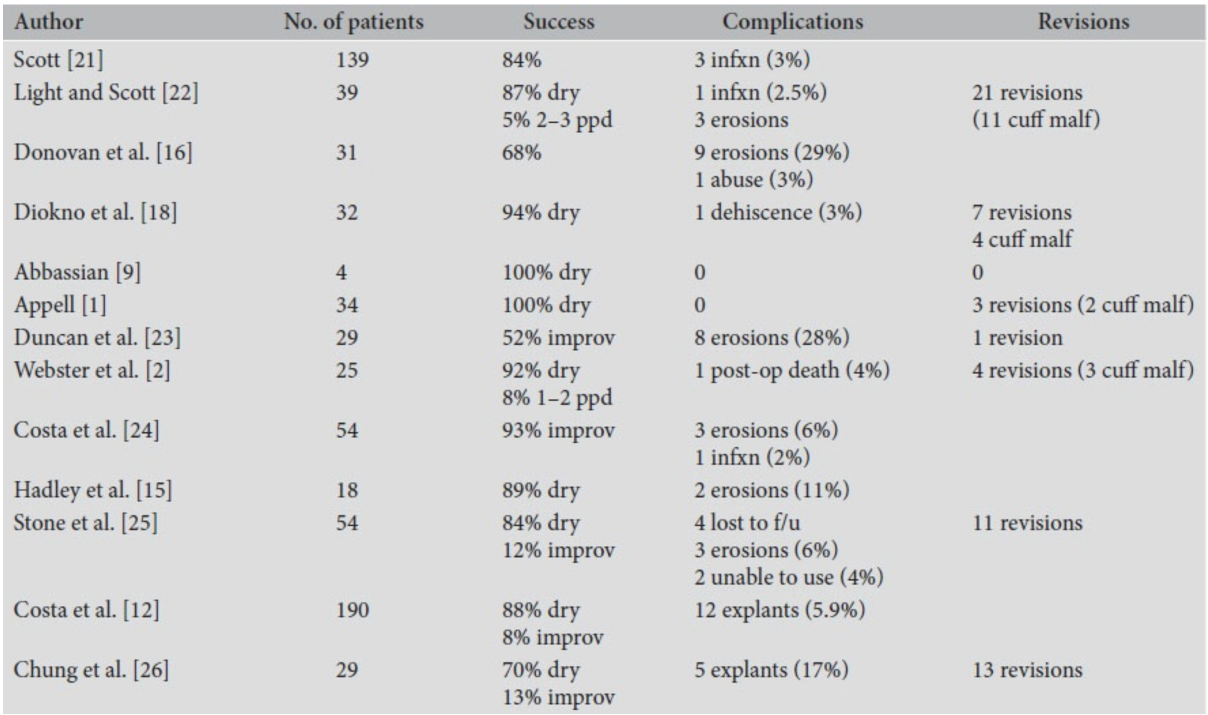
Success rates for implantation of the AUS in female patients are summarized in Table 78.1. The average success rate ranges from 68% in a series of 31 women studied by Donovan et al. [16] to 100% in women studied by Appell [1] and Abbassian [9]. In a large series of 190 patients, Costa et al. reported success rates of 88% and 81.8% in patients with nonneurogenic and neurogenic bladder, respectively [12]. A study comparing AUS and pubovaginal sling in 77 patients with confirmed ISD revealed favorable results for both procedures (84% vs. 91% respectively) [17].

Table 78.1 also includes the published complications from the same series. Infection was seen in 3%–7% of cases. Erosions represented the most common complications, occurring in 7%–29% of cases. Reoperation for cuff malfunction or tubing problems has been as high as 21% in earlier series [18]; however, there is a clear trend toward reduced numbers of device failures due to technological advancements made over the years.

Long-term follow-up data for the AUS in women are sparse. Existing reports indicate mechanical or nonmechanical reasons [3]. In a large series of 344 patients with an average follow-up of 9.6 years, 85.6% of women were continent, 26% had surgical revision of the device, and in 30% the device was explanted [19]. Similar continence rate were found in another series of 55 patients at an average follow-up of 9.3 years [20] (Table 78.2).

Available data on the outcome of the endoscopic implantation suggest a similar outcome, suggesting that laparoscopic or robotic assisted laparoscopic implantation of AUS in women is feasible by surgeons who are very experienced laparoscopically (Table 78.3).

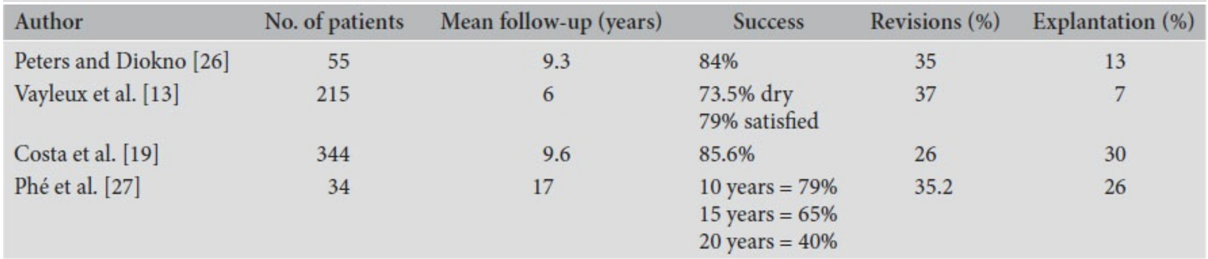
Table 78.1 Success Rates for Implantation of Artificial Urinary Sphincter



Author	No. of patients	Success	Complications	Revisions
Scott [21]	139	84%	3 infxn (3%)	
Light and Scott [22]	39	87% dry 5% 2–3 ppd	1 infxn (2.5%) 3 erosions	21 revisions (11 cuff malf)
Donovan et al. [16]	31	68%	9 erosions (29%) 1 abuse (3%)	
Diokno et al. [18]	32	94% dry	1 dehiscence (3%)	7 revisions 4 cuff malf
Abbassian [9]	4	100% dry	0	0
Appell [1]	34	100% dry	0	3 revisions (2 cuff malf)
Duncan et al. [23]	29	52% improv	8 erosions (28%)	1 revision
Webster et al. [2]	25	92% dry 8% 1–2 ppd	1 post-op death (4%)	4 revisions (3 cuff malf)
Costa et al. [24]	54	93% improv	3 erosions (6%) 1 infxn (2%)	
Hadley et al. [15]	18	89% dry	2 erosions (11%)	
Stone et al. [25]	54	84% dry 12% improv	4 lost to f/u 3 erosions (6%) 2 unable to use (4%)	11 revisions
Costa et al. [12]	190	88% dry 8% improv	12 explants (5.9%)	
Chung et al. [26]	29	70% dry 13% improv	5 explants (17%)	13 revisions

Abbreviations:f/u, follow-up; improv, improvement; infxn, infection; malf, malfunction; post-op, postoperative; ppd, pads per day.

Table 78.2 Long-Term Outcome of Artificial Urinary Sphincter in Women



Author	No. of patients	Mean follow-up (years)	Success	Revisions (%)	Explantation (%)
Peters and Diokno [26]	55	9.3	84%	35	13
Vayleux et al. [13]	215	6	73.5% dry 79% satisfied	37	7
Costa et al. [19]	344	9.6	85.6%	26	30
Phé et al. [27]	34	17	10 years = 79% 15 years = 65% 20 years = 40%	35.2	26

Table 78.3 Success Rates for Endoscopic Implantation of Artificial Urinary Sphincter

Author	**No. of patients**	**Success (%)**	**Complications**	**Revisions**
Ngninkeu et al. [28]	4	75–100	Balloon replacement	1
Hoda et al. [29]	2	100		
Mandron et al. [30]	25	92	1 vaginal perforation 2 vaginal erosions 20% retention	
Rouprêt et al. [31]	12 2 conversions	88	45% urinary retention	
Trolliet et al. [32]	26 3 conversions	61 19 improvement	30% acute retention, 2 pump migration, 1 vaginal injury, 1 vaginal erosion (2 explantation)	
Yates et al. [33]	6 (robot assisted)	100		

CONCLUSION

The AUS provides uniform circumferential compression of the bladder neck, without changing its position. The AUS is indicated for incontinent women with proven ISD and can be particularly useful in those patients who have undergone previous unsuccessful anti-incontinence procedures. In addition, those women with ISD and a poorly contractile bladder, the AUS may be the initial treatment of choice over the sling due to its lower incidence of prolonged postoperative urinary retention.

The AUS may be placed either with a transvaginal or transabdominal approach. The transvaginal approach affords direct visualization of the difficult dissection of the urethrovaginal plane and the option of a suprameatal incision to allow in the anterior dissection of the urethra. Advantages of the transabdominal approach include lack of a vaginal incision and improved exposure to the endopelvic fascia and anterior bladder neck dissection. Additionally, transabdominal exposure allows the opportunity to perform a deliberate cystotomy to assist in a particularly difficult dissection. The endoscopic implantation of the AUS is feasible, seeming to provide similar outcome in the hands of surgeons who are very experienced in laparoscopy. Regardless of operative approach, emphasis should be placed on meticulous surgical approach as intraoperative complication places the patient at risk for postoperative problems such as infection and erosion with eventual device explantation. The AUS compares well to the success of more traditional procedures for urinary incontinence. The data suggest that placement of the AUS is a safe and effective treatment option for the carefully selected patient with ISD.

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Diagnosis and Treatment of Obstruction Following Incontinence Surgery: Urethrolysis and Other Techniques

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INTRODUCTION

Stress urinary incontinence (SUI) is a common condition among women. This, in combination with an increase in public awareness, has more and more women actively seeking treatment. Although there are many available treatment options for SUI, the introduction of less morbid anti-incontinence procedures has led to a rise in the utilization of surgery to combat this problem. In particular, the synthetic midurethral sling (MUS) has become popular over the last decade, owing to high efficacy, minimal patient morbidity, and technical simplicity [1]. This in turn has led to an increase in the number of patients having postoperative voiding issues. Postsurgical voiding dysfunction (VD) can be transient and is generally lower than historically reported, but obstruction requiring intervention will still unavoidably occur.

INCIDENCE OF OBSTRUCTION AND VD AFTER STRESS INCONTINENCE SURGERY

The incidence of iatrogenic obstruction and VD varies widely in the literature, ranging from 2.5% to 24%, with the true incidence unknown and likely underestimated for a multitude of potential reasons [2] (Table 79.1). The American Urological Association panel cited a 1%–10% risk of either retention lasting greater than 1 month or requiring intervention after incontinence surgery [3]. In a large review of 1175 TVT (transvaginal tape) procedures, Rardin et al. found 23 (1.9%) women with persistent VD that required sling release. Twenty women had urinary retention or incomplete emptying while three had refractory urgency/urge urinary incontinence (UUI) [4]. In the Finnish nationwide TVT database of 9040 patients, 50 cases (0.6%) of sling release for urinary retention were reported [5].

ETIOLOGY

The risk of iatrogenic obstruction is usually related to technical factors. In a retropubic urethropexy, sutures elevating the bladder neck may be too tight and can cause overcorrection of the urethrovesical angle or “hypersuspension.” Sutures placed too close to the urethra can cause urethral deviation. Excessive periurethral scarring can occur anteriorly between the urethra and the pubis and lead to urethral compression. Sutures placed too distally can cause kinking with obstruction and an inadequately supported bladder neck/proximal urethra with potentially continued stress incontinence. A similar mechanism may occur with transvaginal bladder neck suspension. With suburethral sling procedures, excessive tension on the sling around or under the urethra is usually responsible for obstruction. Sling tensioning, be it fascial or polypropylene, is highly arbitrary with considerable variability between surgeons as to what constitutes an appropriate amount of tension. For a pubovaginal sling (PVS), tensioning may be performed under cystoscopic guidance to determine adequate coaptation of the proximal urethra. This approximately corresponds to a two fingerbreadth width between the rectus fascia and the sutures once tied down. For synthetic MUS, sling tension should be minimal and should easily accommodate a surgical instrument or metallic sound between the sling and the urethra. As a result, small nuances in tension may explain the difference in outcomes and complications reported by different groups [1].

Less commonly, displacement of the sling from its intended position may result in obstruction. Sarnelli et al. showed that patients with obstruction after their surgery had a shorter distance between the pubic symphysis and their sling on ultrasonography. This shorter distance may indicate a more proximal sling or may indicate a tighter sling (one that elevates the urethra more toward the symphysis), either of which may be responsible for the subsequent obstruction [6]. Similarly, based on anecdotal experience on post–sling obstruction, the authors have found that obstructive slings are most likely to be found close to the bladder neck. In addition, the authors have found that progression of anterior and apical pelvic organ prolapse (POP) can cause a nonobstructive sling to become obstructive 10 years or more after placement of the sling. Also, in theory, patients with an altered wound healing cascade, as in the case for keloid formers or those suffering from scleroderma, can result in excessive scarring and lead to obstruction, even in cases where the sling appears to be loosely tied.

Occasionally, postoperative VD is caused by a learned VD or failure of relaxation of the striated urethral sphincter [7]. In these cases, patient education and sometimes biofeedback can be helpful. When the problem persists, botulinum A toxin injection into the urethral sphincter has been reported to be successful [8]. Finally, impaired detrusor contractility may be responsible for a “relative obstruction” after incontinence surgery. Sometimes, this can be diagnosed preoperatively and the patient may be warned of the possibility of VD after surgery.

The pathophysiology of obstructive symptoms is fairly easy to explain, but that of de novo storage symptoms is more complex. However, it is important to remember that a portion of patients who preoperatively have mixed symptoms will have their urge symptoms assume a more prominent and bothersome role once the stress incontinence has been cured postoperatively [9]. Static changes in bladder outlet resistance can occur as a result of a tensioned sling or a “tension-free” MUS with documented increased void times, decreased maximum flow rates (Q_{max}), increased mean detrusor pressure, increased detrusor pressure at maximal flow, increased mean urethral resistance, and elevated postvoid residual (PVR) volumes [1]. Several authors have demonstrated detrusor instability in association with obstruction [10,11]. Chaikin et al. reported an increasing incidence of urge incontinence over time after PVS. They postulated that it was suggestive of the deleterious effects of chronic insidious obstruction as the sling tightens due to the increasing shrinkage over time [12]. It is believed by some that increased detrusor overactivity secondary to obstruction develops due to the acquired parasympathetic denervation sensitivity, while others believe that damage inflicted on the autonomic innervation of the bladder by surgical dissection leads to this without obstruction [13,14]. Others have suggested alterations in cholinergic and purinergic afferent pathways due to obstruction playing an integral role in the development of storage symptoms [15]. Although the exact pathophysiological mechanisms may not be agreed upon, it is clear that de novo storage symptoms do develop in a large number of patients with urethral obstruction.

Table 79.1 Potential Factors for Varying Incidence of Obstruction and Voiding Dysfunction after Stress Urinary Incontinence Surgery

No standardized definition of obstruction in this setting.
Symptoms can range from storage to obstructive.
Patient loss to follow-up.
Patient loss to seeking second opinion.
Patient may elect to remain obstructed rather than undergo further surgery or risk recurrence of incontinence.
Diagnosis during early postoperative period when symptoms can be transient.

IDENTIFYING RISK FOR POSTOPERATIVE VD

Ideally, for both patient selection and informed counseling, risk factors for postoperative VD would be informative, but no definitive conclusions are available. Risk factors cited include prior anti-incontinence surgery [16], concomitant POP surgery [17,18], age [19], elevated PVR volume [20], and $Q_{max} < 20$ mL/s [20]. Wheeler et al. found the only patient characteristic or parameter predictive of voiding trial passage and lack of urinary retention or incomplete emptying following MUS was Q_{max}. A $Q_{max} > 30$ cc/s had a 100% positive predictive value for voiding trial passage. Other characteristics such as prior incontinence procedure, concurrent anterior repair, PVR volume, and other potential predictors were not found to be significantly predictive of voiding trial passage using multivariate analysis in their study [21]. While evidence exists that women who void with no/minimal detrusor pressure or who void primarily with Valsalva maneuvers were more likely to require prolonged catheterization [22,23]; there are conflicting reports [24,25]. In a secondary analysis of the ValUE

(value of urodynamics evaluation) trial, Sirls et al. evaluated the effect of urodynamic testing on clinical diagnosis, treatment plan, and outcomes in women undergoing SUI surgery. Of those who were diagnosed with voiding phase dysfunction preoperatively, there was no change in the odds of self-voiding at discharge or developing postoperative VD [26]. However, these results are confounded by the fact that surgical modification was allowed based on preoperative results, with nearly all modifications making surgery less obstructive, likely undertaken due to the theoretically higher risk of retention in those with detrusor underactivity or acontractility. Additionally, in the SISTEr (stress incontinence surgical treatment efficacy) trial, Lemack et al. found no urodynamic variables were predictive of postoperative VD (defined as need for catheter greater than 6 weeks or surgical intervention to improve voiding) following Burch colposuspension or PVS [27]. Sling approach is another factor possibly associated with sling obstruction. In the TOMUS (trial of MUSs), Richter et al. demonstrated a significantly higher rate of VD requiring surgery (or permanent catheter) after a retropubic sling compared with a transobturator sling (2.7% vs. 0%, $p = 0.002$) [28].

DIAGNOSTIC EVALUATION

No consensus has been reached on the optimal timing of evaluation of a patient with suspected obstruction or VD after a sling procedure, but the single most important piece of clinical information used to determine if urethrolysis is indicated is a clear temporal relationship of VD following incontinence surgery [2]. While transient VD and urinary retention are frequent and expected after many types of anti-incontinence surgery, most cases will resolve within 4 weeks postoperatively. In a study evaluating early postoperative VD in patients after TVT, Burch, and vaginal sling procedures, the return to normal voiding occurred at a mean of 9 (0–90) days after TVT, 5 (2–42) days after Burch and 21 (2–210) after sling procedures [29]. PVS result in less rapid tissue ingrowth and have a high likelihood of resolution of VD by within 3 months [30]. Thereafter, there is a very low probability that any persistent retention will resolve without intervention. As a result, it had been common practice to delay evaluation of the patient with urinary retention or severe storage symptoms for approximately 3 months postoperatively to allow adequate time for obstruction/retention to resolve. Additionally, this time frame is thought to allow for adequate retropubic scarification and fibrosis, which may help minimize the risk of recurrent SUI.

The waiting period advocated for obstruction and retention for more traditional anti-incontinence procedures has been largely abandoned for MUS. In these cases, earlier intervention is suggested when obstruction is suspected [4,16,31]. After MUS, temporary VD has been reported to resolve in 25%–66% of patient in 1–2 weeks [32,33], but due to the tremendous ingrowth of fibroblastic tissue and subsequent immobility of the sling, patients with severe symptoms or urinary retention are less likely to improve after this time period. Considering these facts, early intervention may be warranted but which some believe carry a higher likelihood of resulting in recurrent SUI, though no formal studies or guidelines have been issued [16]. At the other end of the spectrum is the delayed intervention, which may risk success as long-standing symptoms would intuitively seem less likely to respond to relief of obstruction the longer one is obstructed, but this has not been proven conclusively, with some groups showing favorable results with earlier intervention [34,35] while others do not [36]. However, the decision to proceed with workup and possible intervention must be considered early and discussed with the patient as their symptomatology, level of dissatisfaction, and willingness to risk possible recurrence of SUI should guide when it’s done and what is done.

History and Physical Examination

Key points in the history are the patient’s preoperative voiding status and symptoms and the temporal relationship of the lower urinary tract symptoms to the surgery. The type of procedure performed and the number and the type of other procedures done should be elicited. Urodynamic data from before incontinence surgery are useful if available. Finally, it is important to determine if the symptom of stress incontinence persists.

Symptoms related to obstruction lie along a continuum that includes storage and emptying symptoms. The most obvious sign of obstruction is the complete or partial urinary retention, the inability to void continuously, the presence of a slow stream with or without intermittency, or the need to strain to void. Some patients may have more subtle symptoms, including the need to bend forward/change positions to void or recurrent urinary tract infections (rUTI) that are associated with an elevated PVR volume. However, many women will present with predominate storage symptoms of frequency, urgency, and urge incontinence, with or without obstructive symptoms. Carr and Webster reviewed the presenting symptoms in 51 women subsequently undergoing urethrolysis and are as follows: storage (irritative) symptoms (75%), voiding (obstructive) symptoms (61%), de novo urge incontinence (55%), need for intermittent catheterization (40%), rUTI (8%), and painful voiding (8%). Urinary retention as the sole symptom occurred in 24% [37]. More recently, Clifton et al. reported on 93 cases of sling release of which the indication for intervention was retention in 54%, obstructive or urge symptoms in 42%, and rUTI in 4% [38].

A full genitourinary examination should be performed to assess urethral angulation, urethral mobility, vaginal estrogen status, POP, and evidence of mesh extrusion in the vagina. The examination may reveal overcorrection or hypersuspension where the angle of the urethra and urethral becomes more vertical than is normal. When severe, this is usually quite obvious, but can be confirmed by a negative (downward) angle on Q-tip test. A ridge at the point of obstruction may be seen or felt as the Q-tip or cystoscope passes through it. Other findings on physical exam can include nonpliable vagina, foreshortened urethra, or periurethral dimpling. While these signs may help solidify the diagnosis, their absence does not rule it out. Conversely, not all obstructed patients will appear to be overcorrected. Goldman reported seeing a negative angle on cotton swab test in most patients that had PVS but not in those with synthetic MUS [39].

Urodynamics

The inclusion of urodynamics (UDS) as a standard component in the workup of postoperative VD is controversial. This partly stems from the lack of a standardized criterion that reliably characterizes obstruction in women with a high level of sensitivity or specificity. However, a number of investigators have attempted to address this, and several definitions have been proposed and are listed in Table 79.2. We feel UDS is helpful and can provide information on the presence of involuntary detrusor contractions, impaired compliance, or the presence of VD, even in cases of obvious urinary retention. UDS can confirm the diagnosis of obstruction with the classic findings of high-pressure, low-flow voiding dynamics (Table 79.2) but should not exclude a patient from surgical intervention, even if contractility is impaired or absent as many women do not generate a significant contraction on UDS but are obstructed nevertheless. Surface pad electromyography may help identify a lack of pelvic floor relaxation during voiding and diagnose VD. For a patient with mainly storage symptoms but normal emptying, UDS may provide a specific diagnosis that can be helpful in directing therapy, especially if obstruction can be ruled out. On the other hand, Aponte et al. demonstrated that UDS did not change outcomes in those whose primary indication for surgery was urinary retention or increased PVR volume and thus reserve UDS for those who present with mainly storage symptoms [40]. Additionally, patients with nondiagnostic UDS or who failed to produce a detrusor contraction have the same outcome as those with classic high-pressure and low-flow voiding [41], which highlights the critical importance of the temporal relationship between surgery and the onset of VD as an indicator of obstruction.

Table 79.2 Carious Female Bladder Outlet Obstruction Criteria

Author	Year	Parameter
Chassagne et al. [42]	1998	Q_{max} of <15 mL/s and p_{det} Q_{max} of >20 cm H_2O
Nitti et al. [43]	1999	Radiographic evidence of an obstruction between the bladder neck and distal urethra in the presence of a sustained detrusor contraction of any magnitude during voiding
Blaivas et al. [44]	2000	Q_{max} of <12 mL/s and p_{det} Q_{max} of >20 cm H_2O
Lemack et al. [45]	2000	Q_{max} of <11 mL/s and p_{det} Q_{max} of >21 cm H_2O
Defrietas et al. [46]	2004	Q_{max} of <10 mL/s and p_{det} Q_{max} of >25 cm H_2O
Gravina et al. [47]	2007	Q_{max} of <15 mL/s and bladder outlet obstruction index ≥−8

Nitti et al. reported on the utility of adding fluoroscopy to UDS to aid in the diagnosis of female bladder outlet obstruction. In this study, patients were classified as obstructed if there was radiographic evidence of obstruction between the bladder neck and distal urethra in the presence of a sustained detrusor contraction of any magnitude. Fluoroscopy helps localize the site of obstruction and allows for the diagnosis of obstruction even in cases where contractility is impaired as long as the site can be localized. Using this definition, the authors were able to demonstrate significant differences between obstructed and unobstructed cases for the parameters of Q_{max}, p_{det} at Q_{max}, and PVR volume [43]. A wide range of values were seen, which makes assigning specific cutoff values to define obstruction restrictive. More recently, Akikwala et al. compared the contemporary definitions of obstruction and how well they correlated with a clinical suspicion of obstruction and found the fluoroscopic definition to have the highest concordance [48].

There does not appear to be any consistent preoperative parameters that predict success or failure of urethrolysis. For example, Foster and McGuire found that patients with detrusor overactivity had a higher rate of failure [49]. Others have reported similar findings [36,40]. Nitti and Raz found that as the PVR volume increased, so did the rate of failure, but others have not confirmed this correlation [41]. Carr and Webster found that the only parameter predictive of success was no prior urethrolysis [37]. McCrery and Appell reported that no urodynamic parameter was predictive of success or failure of urethrolysis [50]. Neither the presence nor the strength of the detrusor contraction preoperatively, nor pressure flow analysis predicted postoperative outcomes [41].

Endoscopy and Imaging

Cystoscopy may show scarring, narrowing, occlusion, kinking, or deviation of the urethra. As discussed prior, a hypersuspensed urethra that is fixed with poor mobility in the sagittal axis due to the pronounced vertical angulation of the urethra against the pubis is highly suggestive of obstruction, but its absence does not rule it out. The urethra and bladder should be carefully inspected for eroded sutures or sling material and the presence of a fistula that could be other sources of their symptoms. Secondary signs of obstruction, such as bladder trabeculations or diverticula may be seen. In cases where intervention is anticipated, endoscopy should be done routinely, either before surgery or at the time of surgery prior to incision.

Radiographic imaging may be done independent of videourodynamics. A standing cystogram in the anteroposterior, oblique, and lateral positions, with and without straining, assesses the degree of bladder and urethral prolapse and displacement or distortion of the bladder. A voiding cystourethrogram can assess the bladder, bladder neck, and urethra during voiding to determine the narrowing, kinking, or deviation. The lack of midurethral dilation and funneling of the bladder neck would be suggestive. While not mandatory, imaging can be useful in equivocal cases.

In summary, the diagnosis of obstruction is made on the basis of clinical presentation and diagnostic evaluation, depending on the circumstances. A temporal relationship between surgery and the onset of symptoms is the most critical factor in diagnosis. Patients with normal emptying before incontinence surgery who have significant retention or obstructive voiding symptoms after incontinence surgery need little in the way of a diagnostic workup.

MANAGEMENT OF IATROGENIC OBSTRUCTION

Conservative Treatment

Treatment of obstruction and its timing are usually dictated by the degree of bother of symptoms. It is important to remember, in the early postoperative period, VD is common and usually transient. After this time period, conservative measures can be tried. A selective α blocker is a safe and low-risk alternative that can provide some symptomatic relief by augmenting relaxation of the bladder neck with resulting improved voiding and urinary storage in some patients [1]. Patients who are emptying well but have significant storage symptoms may be treated initially with behavioral modification or pharmacotherapy. Besides cholinergic blockade, anticholinergic medications may have local anesthetic properties that may lessen irritation from suture or inflammation. In our experience, these measures are not usually successful when obstruction exists, but can be considered before surgery. CIC is a reasonable option in women who are not very bothered by catheterization and who rather not undergo surgery or fear the risk of recurrent SUI.

The role for urethral dilation in cases of postsurgical obstruction is not clear. There are conflicting reports as seen in Table 79.3. There are also concerns about the potentially traumatic nature of dilation, which could induce scarring of the urethra or predispose to mesh erosion [1]. The cutting of suspension or sling sutures above the rectus has been described anecdotally with variable success.

In those patients that void with Valsalva, physical therapy may aid to help them learn how to relax pelvic floor and avoid straining to void, which may be compounding their problem. In patients with learned VD, some authors have suggested the use of diazepam 2–10 mg orally two to three times per day or baclofen 5–10 mg orally twice per day to aid in relieving urethral or pelvic floor spasm in lieu of or in conjunction with physical therapy [58].

When conservative measures fail, definitive surgical therapy may be required.

Table 79.3 Summary of Series on Treatment of Obstruction after Incontinence Surgery

	n	Time to intervention	Resolution of obstruction (%)	Resolution of irritative voiding symptoms (%)	Overall success[a] (%)	Recurrent SUI[b] (%)	Notes
Urethral dilation							
Karram et al. [16]	28	<6 weeks			82		
Mishra et al. [33]	3				67	0	
Klutke et al. [31]	5				0		
Sling loosening							
Klutke et al. [31]	17	2.13 months	100	100	100	6	Includes sling incision
Nguyen et al. [62]	10	4.8 days	100			0	
Lord et al. [63]	10				80		
Sling incision							
Lavrikainen et al. [5]	48		88			51	
Clifton et al. [38]	93	5 months				14	
Thiel et al. [64]	13	2.3 months	100		100	36	
Goldman et al. [39]	14	8.6 months	86	57	93	21	
Nitti et al. [46]	19	10.6 months	81	88	84	17	
Segal et al. [65]	14	4.25 months	69.2	0		61.5	
Amundsen et al. [66]	32	10 months	94	67	84	11	Includes transvaginal urethrolysis
Rardin et al. [4]	23	4.3 months	100	30		39	
Transvaginal urethrolysis							
Foster et al. [42]	48	26 months			85	18	
Nitti et al. [41]	41	54 months	66	83	71	0	
Starkman et al. [36]	19			52.6			
Segal et al. [65]	20	43.6 months	72.2	18.8		13.3	
McCrery et al. [43]	31		79.1	36		16	
Carr et al. [37]	15				73		
Suprameatal							
Petrou et al. [51]	32		65	67	66	3	
McCrery et al. [43]	23		83	58		9	
Carr et al. [37]	4				25		
Retropubic urethrolysis							
Petrou et al. [67]	12	19.2 months	83	60	83	8	
Segal et al. [65]	10	32.5 months	80	0		20	
Webster et al. [68]	15	8 months	86	100	93		
Carr et al. [37]	35				86		
Anger et al. [49]	9	13 months	100	60	78	11	

[a] Success is usually defined as cure or significant improvement in presenting symptoms (resumption of normal bladder emptying for patients in retention, and resolution of symptoms for patients with obstructive symptoms or frequency, urgency, or urge incontinence).

[b] Recurrent SUI is defined as percentage of patients without SUI before urethrolysis who experienced SUI after urethrolysis.

Surgical Intervention

There are numerous ways to free up the obstructed urethra, which vary based on many factors including the type and number of anti-incontinence surgery, prior attempts at urethrolysis, and surgeon and patient preferences. Success rates for various procedures range from 25% to 100% dependent on whether success is defined as the return to normal voiding or resolution of all symptoms (Table 79.3) and appear to be independent of the particular procedure chosen, though no randomized head-to-head surgical trial has ever been performed. The specific risks of surgery, including bladder or urethral injury, persistence of storage symptoms, recurrent SUI, and persistence of obstruction, need to be outlined, and each patient should carefully weigh these risks against the success rates of intervention. In this section, we will describe surgical techniques for the treatment of iatrogenic obstruction in order of invasiveness.

Midurethral Sling Loosening

In women with postoperative urinary retention after PVS, intervention is reserved after a waiting period of at least 3 months since there is a very high likelihood of VD resolution [30]. In contrast, the vast majority of patients are able to empty fairly normally within 72 hours after MUS, but for those who are remain in retention, early intervention prior to tissue ingrowth is recommended. This allows one to perform a minimally invasive procedure, under local anesthesia in an office setting [59] or in the operating room, if greater adjustment is needed or due to patient intolerance. The anterior vaginal wall is infiltrated with local anesthetic and the prior vaginal incision is opened. The MUS is usually easily visualized. The sling is hooked with a right-angle clamp (or a similar instrument). Spreading of the right-angle clamp or downward traction on the sling will usually loosen it (1–2 cm) [31]. This is usually possible if intervention is done by 10 days. The incision is suture closed, and the patient is allowed to attempt to void. The longer one waits, the more scarring occurs and anesthesia and a wider exposure may be necessary.

Transvaginal Sling Incision

The transvaginal incision of a sling has similar results compared with urethrolysis but with decreased morbidity (Table 79.3). Cystoscopy is performed firstly to assess the urethra and rule out erosion or urethral injury, followed by an inverted U or midline incision to expose the area of the bladder neck and proximal urethra [60]. As the vaginal flap is dissected off, the sling should be identified above the periurethral fascia. The sling may be encased in scar tissue and thus require careful dissection to identify the sling. If the sling has significant tension on it, it may be especially difficult to identify. Insertion of a cystoscope or sound into the urethra with gentle upward torque improves visualization of the bladder neck and places tension on the sling, allowing for its identification. Once the sling is isolated, it should be separated from the underlying periurethral fascia with sharp or blunt dissection. The dissection may be facilitated by grasping the sling with an Allis clamp on either side of the midline and exerting downward pressure. Care should be taken to avoid injury to the bladder and urethra by beginning the dissection distally, identifying normal urethra then proceeding more proximally until the plane between the sling and urethra is identified. A right-angle clamp can be placed between the urethra and periurethral fascia and the sling. The sling is lifted and cut in the midline (Figure 79.1a). Alternatively, if scarring is dense and the plane between the sling and periurethral fascia cannot be developed easily, the sling can be isolated lateral to the midline, off of the urethra. For practitioners who do not routinely perform this procedure, this lateral approach followed by lateral incision provides a margin of safety in minimizing inadvertent urethral injury. The edges of the sling are then mobilized off the periurethral fascia to, but not through, the endopelvic fascia (Figure 79.1b). Lateral support is preserved because the retropubic space is not entered, and the urethra is not freed from the undersurface of the pubic bone. Typically, synthetic material is excised and autografts/allografts are left in place. Cystourethroscopy should be carried out to rule out urethral or bladder injury. In cases of autologous or biological materials, if the sling cannot be clearly identified, then formal transvaginal urethrolysis (see in the following text) should be performed.

MUS can be isolated and incised in a similar manner. Unlike autologous and biological slings, it is imperative to identify the sling and cut it. Conversion to urethrolysis without specifically cutting the sling may fail to relieve obstruction. Usually, the sling is easily found, and identification can be aided by palpation of the sling. However, sometimes this can be quite difficult, especially in cases where the sling has migrated proximally or has rolled onto itself and created a tight narrow band. In many cases, after the MUS is cut, it retracts away from the urethra. The cut ends can be grasped with clamps and dissection proceeds hugging the sling to minimize injury to underlying tissue. The extent of excision largely depends on the primary indication for MUS removal with some suggesting dissecting to the level of the endopelvic fascia and excising the sling ends [60] while others do not [61]. If sling incision is not successful in relieving obstruction, formal urethrolysis may be carried out.

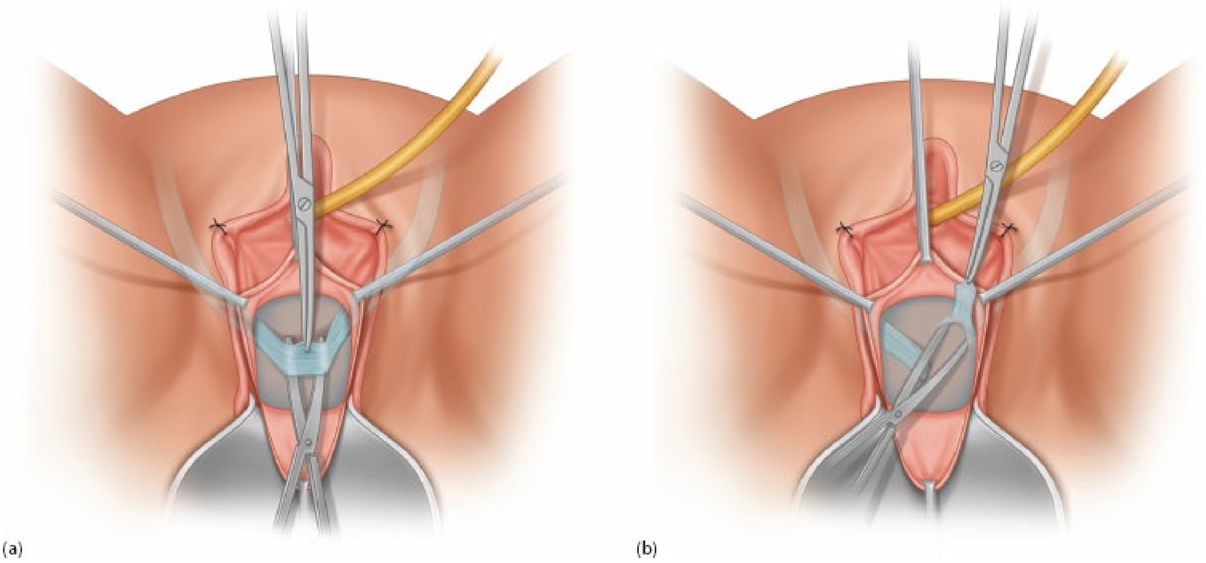

Figure 79.1 (a) After an inverted U or midline incision, the sling is isolated in the midline and incised. A right-angle clamp may be placed between the sling and the periurethral fascia to avoid injury to the urethra. (b) The sling is freed from the undersurface of the urethra toward the endopelvic fascia. Ends may be excised or left in situ. (Reproduced from Nitti VW et al., *Urology*, 59, 47, 2002; discussion 51–52. With permission.)

Urethrolysis

The ultimate goal of urethrolysis is to restore mobility and can be accomplished through a retropubic or a transvaginal approach. The approach chosen depends on several factors that include patient presentation, type of initial anti-incontinence surgery, history of prior urethrolysis, and surgeon and patient preference. In general, proceeding from the less morbid transvaginal approach and reserving the retropubic approach for failures is prudent. However, exceptions exist that would favor a retropubic approach as the primary initial procedure such as inadequate vaginal access precluding a transvaginal approach, in cases where the original anti-incontinence surgery was performed transabdominally or associated with bladder perforation, fistula, or other operative complication, after a Burch resuspension, or associated with intravesical mesh exposure, which must be removed. Indeed, Anger et al. did report a higher rate of success with retropubic urethrolysis compared to transvaginal approach for the treatment of obstruction after Burch procedures [62]. This was felt secondary to the inability to reach proximal most sutures transvaginally.

Transvaginal Urethrolysis

In 1984, Leach and Raz described the transvaginal technique of urethrolysis, and though variations have been published since, it is still the most commonly used today [63]. A midline or inverted U incision approximately 3 cm long is made in the anterior vaginal wall extending from the level of the midurethra to 1–2 cm proximal to the bladder neck. Dissection proceeds laterally along the glistening surface of the periurethral fascia to the pubic bone. The retropubic space is entered sharply by perforating the attachment of the endopelvic fascia to the obturator fascia (Figure 79.2a). The urethra is dissected bluntly and sharply off the undersurface of the pubic bone and completely freed proximally to the bladder neck. Some separation of the urethra from the pubis is done blindly with the Metzenbaum scissors (Figure 79.2b). Care should be taken to stay as close to the underside of the pubis as possible, and manual palpation of this plane along with an awareness of the location of the urethral catheter provides a proprioceptive map in this hard-to-visualize space. If an inadvertent injury to the urethra or anterior bladder wall near the bladder neck is caused, primary repair should be attempted and completion of the procedure should be entertained as further bladder or urethral wall damage can occur.

A Foley catheter is left for 2–3 weeks. Fistula formation is minor as the area of perforation is well away from the vaginal incision. Once sufficient space is developed in this plane, the remaining adhesions and scar can be swept down bluntly with an index finger. If suspension sutures are felt, a clamp can be used to bring it into view so it can be cut safely. After this initial mobilization, a right-angle clamp can be placed between the pubic bone and the urethra, and a Penrose drain is placed around the urethra. Downward traction is applied on the Penrose drain to aid visualization and all remaining retropubic attachments are dissected free (Figure 79.3). At this point, the urethra should be freely mobile in all planes, and this can be tested with movement of an intraurethral sound or cystoscope. Cystoscopy should be performed to rule out urethral and/or bladder injury prior to vaginal closure. If injury is noted, a catheter is left in place. If all is intact, the catheter can be removed at the end of the procedure. It is also good practice to assess ureteral integrity by giving intravenous indigo carmine or methylene blue to assure efflux.

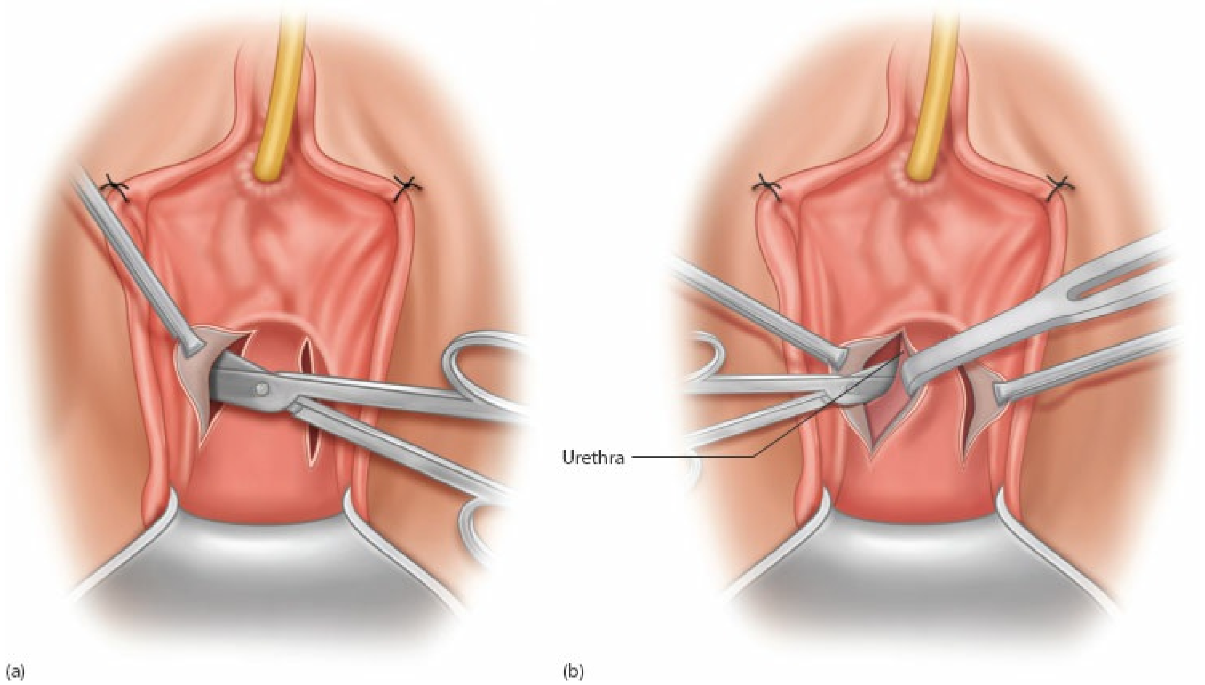

Figure 79.2 Transvaginal urethrolysis. (a) An inverted U incision in the anterior vaginal wall and entrance into the retropubic space. (b) The urethra is sharply dissected off the undersurface of the pubic bone. The endopelvic fascia, periurethral fascia, and vaginal wall are retracted medially to expose the urethra in the retropubic space. (Reproduced from Nitti VW and Raz S, *J Urol*, 152, 93, 1994. With permission.)

If it is difficult to incise the scar tissue or if urethral mobility is still limited, a suprameatal technique has been described, either as part of the traditional transvaginal approach or by itself. In their description, Petrou et al. make an inverted U incision with the apex of the U at the 12 o’clock position and about 1 cm above the urethral meatus. Allis clamps are used to retract both edges of the incision. With tension on the upper edge, the perineal membrane is perforated and all attachments, scar, and sutures between the pubic bone and urethra are incised sharply with scissors. An index finger can be followed along the underside of the pubis into the retropubic space. With a sweeping motion directed laterally and posteriorly, obstructing bands can be identified and either bluntly or sharply freed. The arms of the sling or suspending sutures are encountered with lateral dissection and should be divided sharply. Once done, urethral mobility is assessed and if adequate, cystoscopy is performed to rule out inadvertent injury prior to vaginal incision closure [64]. Because lateral dissection is limited, potential advantages of this approach include preservation of the lateral endopelvic fascia and urethropelvic ligament, which allows for continued urethral support, thus theoretically decreasing the risk of recurrent SUI. Clitoral denervation is a potential complication limiting its wider application.

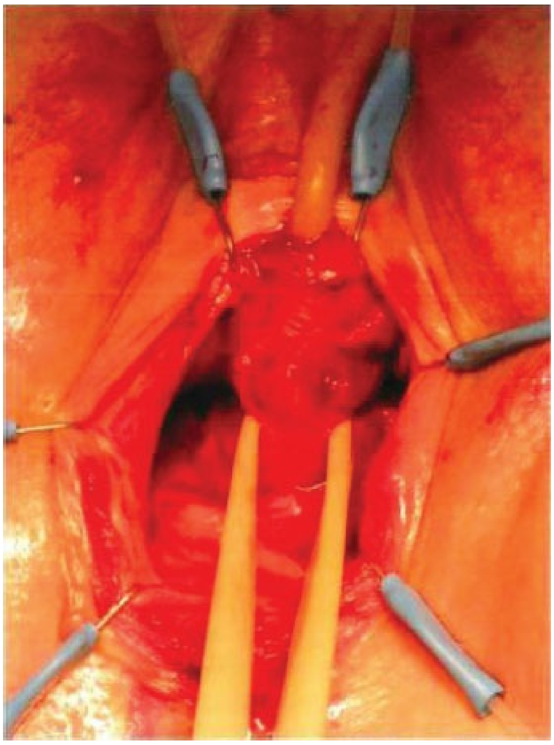

Figure 79.3 Intraoperative photo after completed urethrolysis. A Penrose drain has been placed around the urethra, isolating it from the pubic bone.

In cases of extensive urethrolysis or coexistence of SUI with obstruction, resupporting the urethra at the time of urethrolysis has been introduced, though this remains controversial. In many of the original descriptions of urethrolysis, patients underwent resuspension irrespective of the presence of preoperative SUI. Resuspension poses the risk of persistent obstruction and if symptoms do not resolve, it is difficult to determine whether this situation resulted from inadequate urethrolysis or resulted from the secondary resuspension. Additionally, outcome studies have demonstrated a similar risk of recurrent SUI [2]. There is also evidence that patients can be salvaged with transurethral collagen injections should SUI recurs [65]. As a result, it is our practice to attend to the presenting complaint of obstruction and address recurrent SUI at a later date should it occur.

Retropubic Urethrolysis

The patient is placed supine on the operating table with the legs slightly spread apart to allow for manual vaginal access. Either a Pfannenstiel or low midline incision is made. The rectus fascia and muscle are opened in the midline to the level of the pubic symphysis. The retropubic space is developed and exposed. Any visible and palpable suspension sutures are cut and all attachments and scar between the urethra and pubis are incised sharply. Complications can be minimized by keeping the tips of the scissors up against the pubic symphysis during sharp dissection. Careful attention is paid to the location of the Foley catheter to avoid inadvertent bladder or urethral injury. If bladder injury occurs, prior to repairing it, it may be helpful to leave the bladder open until the dissection is complete to give a constant sense of where the bladder is, with respect to the scar tissue. The index finger of the surgeon’s nondominant hand placed into the vagina helps identify the boundaries of the vagina in relation to the urethra and urethrovesical junction. At the end of the dissection, the urethra, bladder neck, and anterior vaginal wall should be mobile and free from the overlying pubic bone. It should be possible to pass fingers through the abdominal wound, under the pubis, and see your fingers pushing the vaginal skin out in the distal vagina.

In cases of severe scarring, it may be necessary to mobilize laterally as far as the ischial tuberosities, creating a paravaginal defect. This defect should be repaired by reapproximating the paravaginal fascia to the fascia of the obturator internus along the arcus tendineus. The paravaginal repair sutures are left untied. An omental flap can be brought down and fixed between the pubis and urethra so that recurrent scarring is minimized [37]. The paravaginal repair sutures are then tied and the abdomen is closed. Cystoscopy is performed to rule out urethral injury and confirm efflux of indigo carmine from the ureteral orifices.

Failed Urethrolysis

Failure of urethrolysis may be due to persistent or recurrent obstruction, inadequate initial lysis, detrusor overactivity, impaired detrusor contractility, or learned VD. Recurrent obstruction may result from periurethral fibrosis and scarring, or intrinsic damage to the urethra that has occurred as a consequence of the urethrolysis surgery. When obstruction persists, it is reasonable to attempt a repeat urethrolysis. Scarpero et al. reported on the efficacy of repeat urethrolysis in 24 women who failed initial urethrolysis and remained in urinary retention. Both transvaginal and retropubic approaches were chosen depending on the clinical situation. Obstruction was cured in 96%, but storage symptoms completely resolved in only 12% and were improved and required medication in 69%. SUI recurred in 18% [66]. In another series, repeat urethrolysis resulted in cure of obstructive symptoms in 72% and storage symptoms in 59% [50]. These data clearly support aggressive repeat urethrolysis in the face of initial failure, at least for retention and incomplete emptying. In general, if an aggressive transvaginal urethrolysis fails, then a retropubic approach may be considered. In cases where the aggressiveness of the initial transvaginal procedure is unknown, or if only a sling incision was performed, then a repeat transvaginal approach may be appropriate. Consideration should also be given to the use of a Martius labial fat pad flap as an interposition layer to decrease recurrent fibrosis and provide some urethral support. The flap is divided midway along its longitudinal axis to allow for circumferential coverage of the urethra, effectively supporting the undersurface and retropubic surface of the urethra [67].

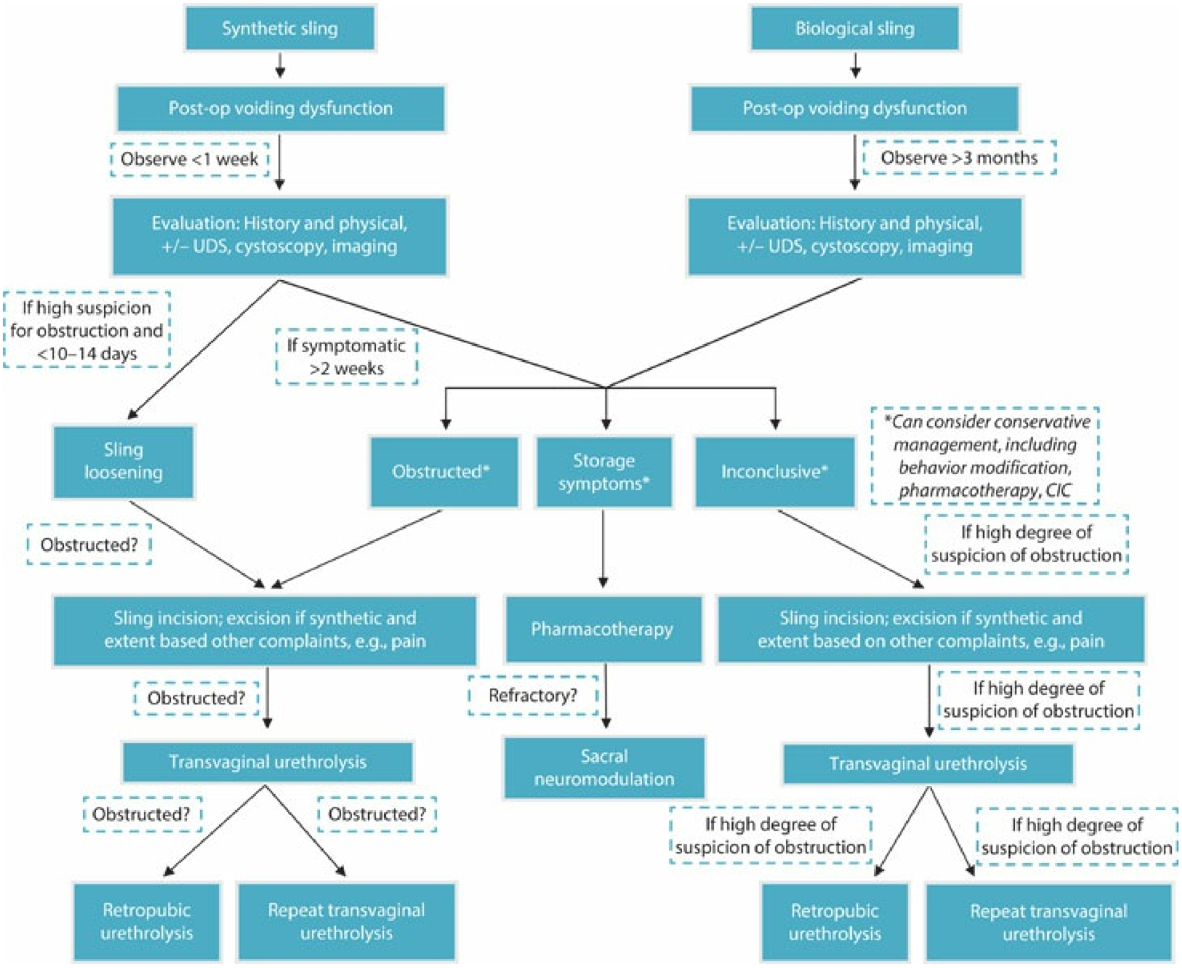
Synthetic sling
Biological sling
Post-op voiding dysfunction
Post-op voiding dysfunction
Observe <1 week
Observe >3 months
Evaluation: History and physical, +/– UDS, cystoscopy, imaging
Evaluation: History and physical, +/– UDS, cystoscopy, imaging
If high suspicion for obstruction and <10–14 days
If symptomatic >2 weeks
Sling loosening
Obstructed*
Storage symptoms*
Inconclusive*
*Can consider conservative management, including behavior modification, pharmacotherapy, CIC
Obstructed?
If high degree of suspicion of obstruction
Sling incision; excision if synthetic and extent based other complaints, e.g., pain
Pharmacotherapy
Sling incision; excision if synthetic and extent based on other complaints, e.g., pain
Obstructed?
Refractory?
If high degree of suspicion of obstruction
Transvaginal urethrolysis
Sacral neuromodulation
Transvaginal urethrolysis
Obstructed?
Obstructed?
If high degree of suspicion of obstruction
If high degree of suspicion of obstruction
Retropubic urethrolysis
Repeat transvaginal urethrolysis
Retropubic urethrolysis
Repeat transvaginal urethrolysis

Figure 79.4 Treatment algorithm.

Residual and refractory storage symptoms after urethrolysis may be treated with sacral neuromodulation after obstruction has been ruled out, and the treating physician feels that the likelihood of residual/recurrent obstruction is low. Starkman et al. found a >50% reduction in symptoms in 75% of patients they treated with this modality. In the 75% of patients that responded, 100% were able to stop all antimuscarinics [68]. However, if there is any concern for residual obstruction or inadequate initial urethrolysis, then a repeat urethrolysis should be considered. The treatment algorithm flowchart summarizes the diagnosis and treatment approach (Figure 79.4).

CONCLUSION

It is indeed a challenging prospect to treat the patient with significant irritative and obstructive features after performing an operation for incontinence. While keeping in mind the patient’s symptoms and goals, the physician must use careful decision making when assessing, diagnosing, and treating obstruction. Fortunately, the various urethrolysis techniques are highly successful for restoring efficient voiding. Though progress has been made, improved methods of identifying those at risk for obstruction, diagnosing obstruction, and treating troublesome irritative voiding symptoms are warranted.

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80 Complications of Stress Urinary Incontinence Surgery

Véronique Phé and Emmanuel Chartier-Kastler

INTRODUCTION

According to the International Continence Society, stress urinary incontinence (SUI) is defined as “the complaint of involuntary leakage on effort or exertion, or on sneezing or coughing” [1]. SUI is responsible for major disability in many women. The prevalence of SUI is difficult to estimate, but possibly as high as 50% [2] depending on the definition of urinary incontinence adopted and the age group studied. This prevalence is probably underestimated. According to the 2012 update of the International Consultation on Incontinence guidelines, the surgical treatments of SUI may include the use of pubovaginal slings, suburethral slings, colposuspension, and artificial urinary sphincters. Recently, adjustable continence therapy (ACT®) balloons have been introduced as a minimally invasive option. The guidelines do not define a clear priority among these options. However, various efforts have been made to reduce the morbidity associated with these procedures.

SUI surgery is a functional surgery, which requires a careful patient selection and evaluation to improve surgical outcomes and decrease failure and complications rate. Before undergoing an SUI surgery, the risk of potential complications should be carefully assessed and addressed with the patients. Complications may occur during and after the procedure, and it is essential to identify high-risk patients and minimize risk from surgery before the procedure. Thus, it is necessary to inform and counsel the patients concerning the operative risks commonly attributed to general anesthesia including intubation, myocardial infarction, cerebrovascular accident, and deep vein thrombosis. As may be anticipated, mortality increases with advancing age and the presence of medical comorbidities.

Increased awareness regarding the numerous management options for SUI has produced heightened interest in determining standards for outcomes measures, including the reporting of surgical complications [1,3,4]. Recent attention to the potential complications of mesh implantation from the Food and Drug Administration has certainly heightened awareness in the urologic community to reporting of complications (http://www.fda.gov/cdrh/safety/102008-surgicalmesh.html).

This chapter will focus on the complications of the surgical modalities used for SUI, namely, not only midsuburethral sling procedures, colposuspension, and pubovaginal slings but also artificial urinary sphincter, ACT, and periurethral injections.

COMPLICATIONS OF MIDSUBURETHRAL SLINGS

Due to minimal invasiveness, retropubic tension-free vaginal tape (TVT) is widely used in the treatment of SUI associated with urethral hypermobility, with a high success and low complication rates since it has been described by Petros and Ulmsten [5]. This procedure has been recently challenged by transobturator tapes (TOT) and mini-slings (regardless if they are retropubic or transobturator) [10–12]. Long-term data about midsuburethral slings are only now becoming available. Comparison between transobturator slings (TVT-O or TOT) show equal effectiveness with slightly lower cure rates than TVT [12]. Recent randomized controlled studies and meta-analysis studies did not support routine use of mini-slings in clinical practice [10,11].

The significant reported complications of midsuburethral sling procedures include bladder and urethral injuries, bleeding, de novo urgency, voiding dysfunction, bladder and urethral erosion, vaginal extrusion, urinary tract infections, pain, and dyspareunia. There is some difficulty in summarizing the published complications of midsuburethral slings data due to the lack of standardization of definitions and differences in reporting methods between studies. The reported complication rates ranged from 4.3% to 75.1% for TVT and 10.5% to 31.3% for TOT [4]. The incidence of complications varies with operative experience, procedure, and center reporting, and there is a learning curve that requires further delineation [6].

Intraoperative Complications

Bladder and Urethral Injuries

Bladder perforation during needle passage of TVT is not uncommon, with reported rates of 0.7%–24% [7,8]. Previous anti-incontinence surgery and surgeon experience were reported as potential risk factors for perforation [9]. In an update meta-analysis, the risk of bladder perforation during TOT approach is lower than TVT procedure [10]. The outside-in techniques seem to be more risky than the inside-out technique although the difference is not statistically significant [11].

In case of bladder perforation when recognized intraoperatively, repositioning the tape is mandatory and without any short- or long-term consequence. Most of the authors recommend a 2- or 3-day bladder catheterization with a Foley catheter [12]. But the benefit of an extended bladder catheterization in case of bladder perforation has not been demonstrated as opposed to a 24-hour bladder drainage. Failure to recognize intravesical needle passage of sling can lead to hematuria, irritative bladder symptoms, pelvic and urethral pain, fistulas, recurrent urinary tract infections, and a return to the operating room. Given the ease, speed and availability of cystoscopy, and the potential for serious complications if perforation is overlooked, cystoscopy could be recommended in all midsuburethral sling procedures [13]. Technique (use of a 70° lense) and training to it is of major interest in the case of TVT practice.

Urethral injuries are uncommon during midsuburethral sling procedures [14]. If urethral injury is noted at midsuburethral sling placement, the procedure should be aborted and the urethra closed with multiple layers.

Vaginal Perforation

Vaginal perforation has been reported to be less frequent in a TVT procedure (0%–1.5%) than in TOT (0%–10.9%) [4,13]. This complication occurs significantly more often in outside-in procedure than in inside-out procedure [15]. This complication is likely due to an insufficient vaginal dissection for outside-in TOT procedure and to a wrong needle trajectory in inside-out TOT procedure. In case of perforation, the vagina has to be closed immediately and the sling can be placed.

Finally, two types of vaginal perforation may be described:

- Laterally in the culs-de-sac during a TOT procedure
- Medially as a mid- to long-term complication at the incision level (TOT and TVT)

This last condition may be more described as a vaginal extrusion than a vaginal perforation (see the “Vaginal Extrusion” section).

Hemorrhage

The occurrence of hemorrhage ranges from 0.7% to 8% [3,7] without any statistical difference between TVT and TOT [13]. Intraoperative bleeding from the vaginal dissection can usually be controlled with direct pressure on the paraurethral and retropubic areas and then followed by vaginal packing. Greatly increased bleeding that results in a retropubic hematoma usually arises from a blinded venous injury during needle passage, and up to 2.8% may require transfusion [16]. Vascular injuries involving large arteries such as the external iliac, femoral, obturator, epigastric, and inferior vesical have been reported and have been responsible for at least one mortality [17]. Accordingly, arterial injuries must be managed immediately by laparotomy or angioembolization. Arterial perforation during TVT procedure may be avoided by a good patient’s installation (legs down) and a retropubic introduction of the ancillary, always close to the midline and parallel to it, avoiding any lateral movement.

Bowel Perforation

The literature reported few bowel perforations during TVT procedure (less than 1%) [16]. To our knowledge, there are no published cases of bowel perforation with TOT techniques. A review of the Food and Drug Administration Manufacturer and User Facility Device Experience database revealed seven deaths that occurred after TVT placement as of 2004, of which six were associated with bowel injury [17]. Patients with a history of abdominal or pelvic surgery are at a greater risk for bowel injury because of adhesions in the retropubic space and pubic symphysis.

Postoperative Complications

Vaginal Extrusion

Reported rates of vaginal extrusion ranged from 0% to 1.6% [18,19]. A meta-analysis of polypropylene midsuburethral slings revealed a possible trend toward increased extrusion after the transobturator approach (OR 1.5, 95% CI 0.51–4.4) [20]. Several reasons may account for this finding including atrophic, scarred, or compromised vaginal mucosa. Potential risk factors for extrusion related to surgery include inadequate closure of vaginal tissue, infection, mesh rejection, and unrecognized vaginal injury during needle passage. Patients with vaginal extrusion may present with vaginal discharge, vaginal pain, dyspareunia, or sling palpable. However, patients may also be asymptomatic [21]. Most cases occur in the first few months after surgery but they can also occur later. In the case of small vaginal extrusion, spontaneous healing can be expected in 6–12 weeks [22]. If conservative management fails or the erosion is greater than 1 cm (Figure 80.1), the sling may be excised with vaginal closure.

Bladder Erosion

Bladder erosion occurs 4–11 months after surgery and can lead to recurrent urinary tract infections, overactive bladder symptoms, pelvic pain, and hematuria [14,21]. Then a cystoscopy should be performed. The resection of the sling by cystoscopy is not recommended [14,21,23]. A resection of the sling combining an abdominal and a vaginal approach is generally performed [14,24] (Figure 80.2).

Prevention of this complication may be done with a good training to the technique, checking during cystoscopy that the ancillary has not been inserted inside the detrusor muscle (moving it, the detrusor must not move with). In case of any doubt, the surgery must be repeated after removal of the ancillary and/or mesh.

Urethral Erosion and Injury

Urethral erosions are rare (0.3%). They may be caused by a poor surgical technique that could damage the integrity of the urethral tissue, excessive tension placed on the sling or local infection. Poorly estrogenized tissue, previous vaginal surgery, or a history of pelvic radiation may also contribute. Postoperative symptoms of erosion include overactive bladder symptoms, urethral or pelvic pain, recurrent urinary tract infections, urinary retention, and hematuria. Management of these symptoms includes complete excision of the eroded part of the synthetic sling and urethroplasty.

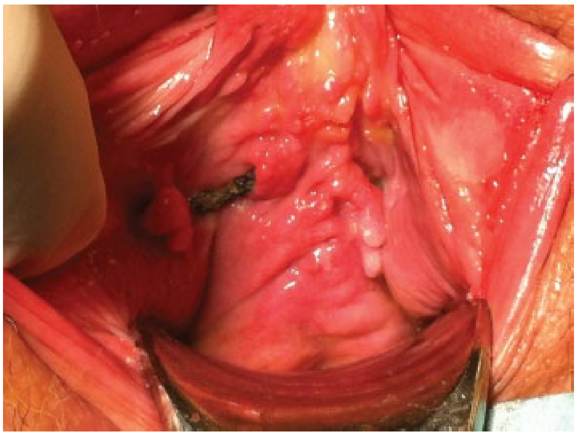

Figure 80.1 Vaginal extrusion caused by a midsuburethral tape.

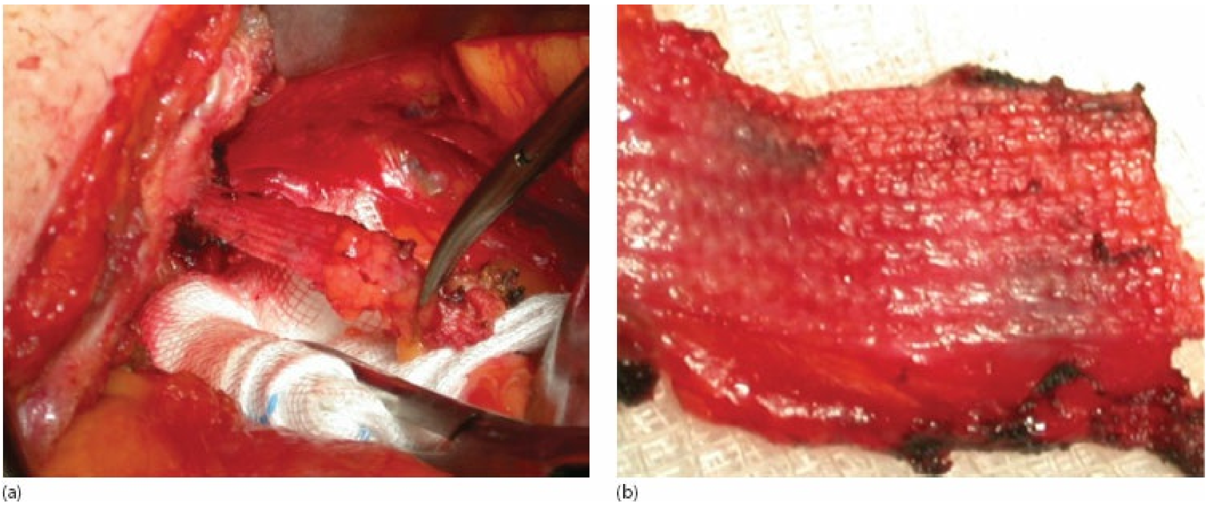

Figure 80.2 (a, b) Resection of tension-free vaginal tape by an abdominal approach.

De Novo Urgency

The onset of de novo urgency and its possible treatment is one of the most clinically relevant and largely debatable postoperative complications of midsuburethral slings. Previous studies reported de novo urgency rates ranging from 4% to 33% after TVT [12,19]. Discrepancies can be related to the different definitions and questionnaires used to collect overactive bladder symptoms, different demographic characteristics of the women included, and different concomitant surgical procedures associated with TVT. Furthermore, the prevalence of urgency symptoms is known to increase with age. This phenomenon is thought to result from a combination of mild obstruction and urethral irritation caused by the sling. Bladder irritability caused by undiagnosed pelvic hematoma has been proposed as well. Elevation of the bladder neck may also be a contributing factor and has been demonstrated on transperitoneal ultrasound after TVT [25]. There is no significant difference in de novo urgency between TVT and TOT [10]. After excluding reversible causes such as extrusion and obstruction, anticholinergic medications are the mainstay of current therapeutic interventions. In the case of urgency refractory to medical therapy and in the absence of any clinically significant obstruction, alternative therapy such as sacral neuromodulation and botulinum toxin A injections may be considered.

Voiding Dysfunction

TVT may lead to bladder outlet obstruction [20]. Consequently, patients can complain of a slow or intermittent urine stream with a significant post-voiding residual volume and recurrent lower urinary tract infections. The reported rates of postoperative obstruction range from 1.9% to 19.7% [9,26]. Postoperative maximum stream flow is significantly decreased [27]. There are no significant differences in postoperative urinary retention between retropubic and transobturator approaches [10]. Moreover, urinary tract infections in case of chronic obstruction can increase from 8% during the first year after surgery to 44% during the fifth year [28]. In a patient with immediate postoperative retention or incomplete bladder emptying, indwelling or intermittent self-catheterization should be tried because resolution is commonly spontaneous [18]. If improvement is not seen within 4 weeks, early sling lysis should be considered. Studies revealed that this was required in 0.1%–7% of cases [26,29]. Some authors recommended total resection of the TVT as first-line treatment by an abdominal approach in order to obtain more satisfying results [30].

Urinary Tract Infections

Urinary tract infection is less commonly reported than some other postoperative complications. Moreover, the definition of urinary tract infections and how it is diagnosed is often not clear. In comparative prospective studies, urinary tract infections were reported in 7.4%–13% of women undergoing TVT or TOT procedures, without any statistically significant differences [7,26]. In the case of recurrent urinary tract infections, voiding dysfunction and urethral or bladder erosions should be investigated.

Groin and Thigh Pain

A meta-analysis revealed that groin and thigh pain was more common in patients who underwent a transobturator (inside-out) approach (OR 8.8, 95% CI 2.6–29.5) [20]. A randomized controlled study revealed that 16% of women in the transobturator (inside-out) arm had groin pain compared to 1.5% of those in the TVT arm, which led to an increased need for analgesia in the transobturator group [7]. Both of these findings were statistically and clinically significant. Groin pain after TVT-O tended to persist longer than that after TVT. The etiology of this pain is not yet clear but may be of neurological origin. Injuries to nerves such as the obturator have been reported but are rare (less than 1%) [26,31,32]. In the case of persistent pain, some authors recommended resection of the sling [33].

Dyspareunia

Postoperative dyspareunia has not routinely been prospective reported. In a prospective observational study of 300 women who underwent a TVT-O procedure, 1.3% reported new onset dyspareunia [34]. The authors attributed this finding to posterior migration of the tape, which could be palpated close to the anterior vaginal fornix. Then all women were treated successfully by cutting the tape in the midline. Further prospective studies should be conducted to address this end point because many women with SUI are sexually active.

COMPLICATIONS OF COLPOSUSPENSION

Open abdominal retropubic procedures for urinary incontinence were widely performed till the turn of the century when the use of synthetic midsuburethral slings gained in popularity. In Novara's meta-analysis, midsuburethral slings were followed by significantly higher cure rates than Burch colposuspension, considering success rates evaluated according to any definition of continence. With regard to complication rates, bladder perforation was significantly more common after midsuburethral slings, whereas the risk of pelvic hematoma, urinary tract infections, storage lower urinary tract symptoms, voiding lower urinary tract symptoms, and reoperation were similar between the two surgical treatments. A randomized controlled study on 344 patients with SUI who were randomized to TVT or Burch colposuspension [35] reported, at a 24-month follow-up, that TVT was followed by higher rates of intraoperative complications (mainly bladder and vaginal perforations), whereas operation times, blood loss, analgesic requirements, postoperative complications, and catheterization were greater in the colposuspension group. Reoperation rates for urinary incontinence were similar in both arms (1.8% after TVT vs. 3.4% after colposuspension, $p = 0.48$), but surgical procedures for pelvic organ prolapse were more common after colposuspension (0% vs. 4.8%, $p = 0.0042$).

COMPLICATIONS OF PUBOVAGINAL SLINGS

The pubovaginal sling is an efficient procedure in the long run. Indeed, the 10-year range of success rates of this surgery has been reported to be between 55% and 70% [36]. However, the technique is invasive and followed by significant risks of de novo storage symptoms (3%–23%) and voiding dysfunction (up to 11% with 1.5%–7.8% long-term self-catheterization) [36]. Although currently considered the gold standard for transvaginal sling procedures, recent studies have revealed some of these materials may encapsulate rather than integrate [37,38]. In a comparative analysis (Stress Incontinence Surgical Treatment Efficacy Trial [SISTEr]), 655 women with SUI were randomized to undergo either Burch colposuspension or autologous fascia pubovaginal sling with success defined as no self-reported SUI, a negative stress test, and lack of retreatment [38]. Although the pubovaginal sling group performed significantly better than the Burch colposuspension (66% vs. 49% success), the pubovaginal sling group experienced a substantially increased number of postoperative issues including urinary tract infections, voiding dysfunction, urge incontinence, and a need for surgical revision.

Randomized controlled trials comparing midsuburethral tapes and pubovaginal slings had similar efficacy in terms of both overall and subjective continence rate [10]. With regard to complication, the risk of intraoperative bladder perforation were significantly lower in the pubovaginal sling group; pelvic hematoma was similar in the two procedures. However, midsuburethral tapes were followed by a significantly lower risk of storage symptoms and reoperation. The prevalence of voiding dysfunction was similar in the two procedures.

COMPLICATIONS OF ARTIFICIAL URINARY SPHINCTER (AMS 800®, AMERICAN MEDICAL SYSTEM, MINNEAPOLIS, UNITED STATES)

Artificial urinary sphincter is the treatment of female severe SUI with intrinsic sphincter deficiency, most often after failure of other surgical treatments and as a “last treatment.” This surgery is only performed by experienced and trained teams [39,40] due to the technical difficulties related to the short female urethra or a history of local surgery responsible for the morbidity of this operation [41].

Intraoperative Complications

In case of bladder injury, localizing precisely the injuries by opening the bladder dome allows to repair and does not prevent from implanting the device if correctly repaired [40,42]. It is of trained center expert opinion that any injury at the level of the bladder neck or posterior urethral portion indicates not to implant the device. Any bladder injury far away from the bladder neck, either involuntary or voluntary done as an eye control of dissection, do not contraindicate implantation of the cuff.

Vaginal injury is rare and leads to stop the procedure when it is located posteriorly to the bladder neck and/or urethra, in front of cuff placement. Any vaginal injury (lateral on cul-de-sac) may not stop the surgery and must be carefully repaired. The cuff may be inserted except in any other intraoperative complication.

Postoperative Period

Postoperative acute urinary retention can occur and leads to a new indwelling catheter insertion for at least 48 hours [40]. Usually, it is of interest to let a catheter until day 5 or 6 to decrease recatheterization rate. The overall early postoperative morbidity is 6% [43].

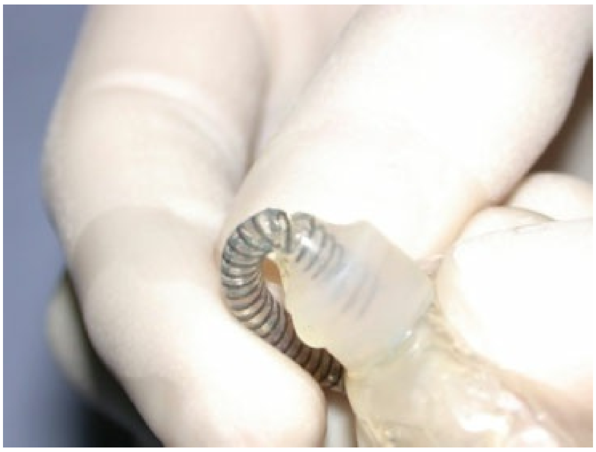

Figure 80.3 Artificial urinary sphincter tube perforation.

The main long-term complications of an artificial urinary sphincter is explantation of the device in 3%–50% of cases due to infection and/or erosion [43–45] and the need for revision of the device in 13%–63% of cases [43].

The major reported risk factors for explantation are aging, previous anti-incontinence procedures, a delay between the previous procedure and sphincter implantation, perioperative complications, and pelvic irradiation [43,46–48].

Few studies have focused on the survival of the device [39,40,49–51]. The revision rates after 5 years reported in the literature range from 13% to 63%. Most of revisions were due to the mechanical failure of the pump, balloon, cuff, or connections (Figure 80.3). Discrepancies between series may also be related to the medical histories of irradiation among the women [44], the number of previous anti-incontinence procedures before the insertion of the artificial urinary sphincter [39], or learning curves and the surgeon’s experience. The artificial urinary sphincter is supposed to have an average life span of 10 years. After 15 years, the survival rates are significantly lower [40]. According to the American and European Guidelines, the exact indication and the optimum timing for artificial urinary sphincter implantation in women are not clear [52,53]. A group of experts attempted to clarify and optimize indication and technique [41].

COMPLICATIONS OF ADJUSTABLE CONTINENCE THERAPY BALLOONS

The balloons named ACT (Uromedica, United States) are a recent treatment modality of female UI and are indicated in a specific population of patients: difficult situations of primary or secondary failure of treatment for urethral hypermobility by midsuburethral sling or patients unsuitable for artificial urinary sphincter placement (e.g., women over the age of 80 with cognitive impairments and motor disabilities) [54]. But the place of this therapy in the decision tree for female urinary incontinence management has not been clearly defined at this moment in international guidelines [52]. The main reason is related to the paucity of long-term prospective data.

Only eight studies were published between 2007 and 2013, evaluating the efficacy and complications of treatment for female UI by ACT balloon [55–61]. During the procedures, no major complications were reported. Most intraoperative complications are urethral or bladder perforations, observed in 3%–17% of cases. It is worth noting that the 17% perforation rate was reported in the study by Chartier-Kastler published in 2007 [55], which was the first nationwide, multicentered, prospective, controlled study evaluating treatment for female SUI by ACT balloon and therefore corresponded to the early experience with this type of management in France. The most recent studies have reported intraoperative perforation rates between 3.7% and 4.5%. Perforation does not necessarily lead to cancel the procedure.

Postoperative complications, during the first year, includes urethral erosion (2%–15%), cutaneous erosion of the port (3%–7.5%), balloon migration (6.5%–17.5%), device infection (0.6%–8.9%), balloon dysfunction (0.6%–6%) (Figure 80.4), inefficacy of treatment or even worsening of incontinence (2.5%–11.7%), dysuria or acute urinary retention (1.5%–6.8%), and de novo urgency (10.5%) [58]. Migration can lead to explantation ± reimplantation. The explantation rate ranged between 18.7% and 30.8% [57,61]. The risk factors for explantation of ACT balloons have not been clearly identified in women. Other reported complications are less frequent: labial hematoma, labial infection, urinary infection, de novo urgency, dyspareunia, dysuria, pain, and discomfort. They are not always reported in the different studies. ACT balloons appear to be a minimally invasive treatment of female SUI. The balloons are easily adjusted percutaneously to enhance efficacy. Complications are usually mild and can be easily managed. The need for explantation does not preclude repeat implantation. Additional follow-up will determine the long-term durability of this device.

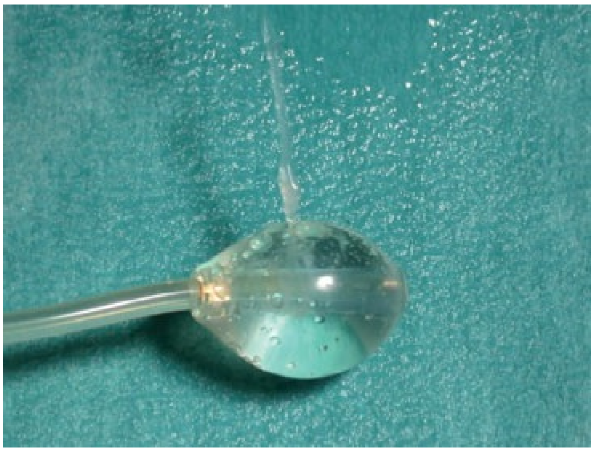

Figure 80.4 Adjustable continence therapy balloon perforation.

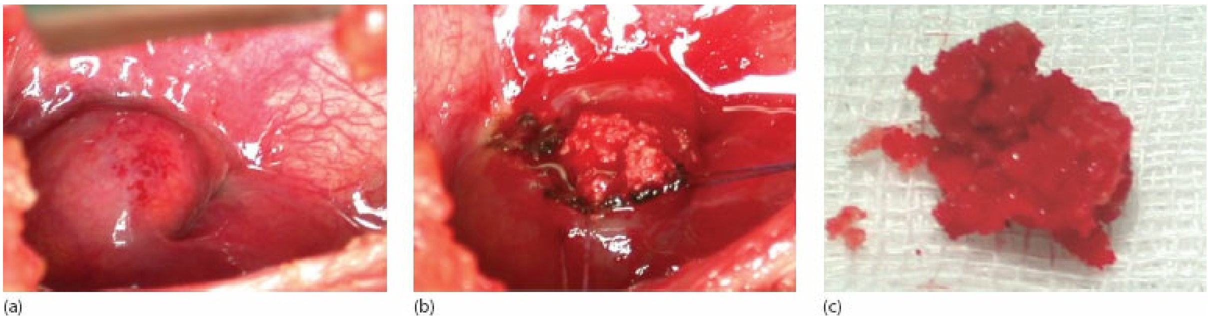

Figure 80.5 (a–c) Bulking agent protrusion in the bladder.

COMPLICATIONS OF PERIURETHRAL INJECTIONS

Bulking agents have historically demonstrated disappointing long-term success rates [62,63]. There are currently no data in the literature in support of the use of periurethral injections as first-line treatment for SUI. Only limited data are available concerning comparison of the various techniques. Periurethral injections can sometimes have lasting effects, but repeated injections may be necessary [64,65]. Periurethral injection is associated with few complications and adverse effects. Potential local side effects include urinary tract infection, urinary retention, local pain, pseudo-abscess formation, and urethral erosion. Distant effects as a result of particle migration are generally site specific and include pulmonary embolism. The incidence of urinary retention following the procedure ranges from 15% to 25% [66–68]. This usually resolves within 24–48 hours.

De novo urgency has been reported as high as 39% [66,69]. In case of persistent obstruction, resection of the implanted material may be performed [70] (Figure 80.5). In conclusion, this technique can be used because of its good benefit/risk balance in frail patients, previously operated patients, and patients refusing surgery. But the results are considerably inferior to other techniques.

STANDARDIZED CLASSIFICATION OF COMPLICATIONS

All complications listed earlier were reported by authors without any standardization, leading to probable underestimated rates of complications. To adequately assess results of a specific SUI surgery and counsel patients regarding the options, outcomes must be measured and quantified in a standard and consistent manner to permit purposeful conclusions. The International Urogynecological Association and the International Continence Society recognized the increasing use of prostheses (meshes) and grafts in female pelvic floor surgery [71]. They proposed a standardized terminology and classification. The classification was developed to be sensitive to all possible physical complications involving the use of a prosthesis or graft in a female pelvic floor surgical procedure. Complications were classified according to three aspects: category, time, and site. Indeed, complications involving the use of meshes, tapes, and grafts in female pelvic floor surgery need to involve the following viewpoints of (1) local complications, (2) complications to surrounding organs, and (3) systemic complications. A key advantage of a standardized classification is that all parties involved in female pelvic floor surgery including surgeons, physicians, nurses, allied health professionals, and industry will be referring to the same clinical issue. The standardized classification may certainly be helpful to report complications in long-term studies evaluating long-term follow-up of SUI surgeries.

CONCLUSIONS

Surgical interventions for SUI are widely employed with substantial success and low morbidity and mortality. Careful counseling allowing realistic patient expectations with regard to complications will set a benchmark from the perspective of the most important outcome, namely, patient satisfaction.

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Section VIII

Surgery for Urogenital Prolapse

81 Classification and Epidemiology of Pelvic Organ Prolapse

Steven E. Swift

INTRODUCTION

The study of pelvic organ prolapse (POP) is one area of medicine that seems so intuitive but in actuality is replete with anecdotal evidence, case series, and very little hard science. Most of this stems from the lack of a scientifically validated and universally agreed upon definition of the disease state of "pelvic organ prolapse." A classification system to codify pelvic organ support has been defined and has gained international recognition. However, while it accurately describes the degree or stage of pelvic organ support, it does not classify it into normal versus abnormal or "prolapse." This is akin to having a blood pressure cuff to measure blood pressure but no definition as to what represents normal versus hypertension. Until we can define the disease, we cannot properly identify its etiology or make any statements regarding therapy, prognosis, or natural history. Therefore, all of the scientific literature regarding POP should be viewed with caution, paying particular attention to how POP is described and defined. Despite the current state of affairs, studies into the classification and epidemiology of POP are moving forward as the scientific community has recognized the problems and is addressing them via research protocols.

CLASSIFICATION OF PELVIC ORGAN SUPPORT

The aforementioned title specifically does not use the term "prolapse" but instead uses "support" as none of the current POP classification systems attempts to define "prolapse." Instead, they only address where the vaginal walls or structures extend anatomically without making any reference as to what is normal versus abnormal or "prolapsed."

The history of classification systems for pelvic organ support extends back into the nineteenth century, with a new system appearing every generation or so, but with no system ever attaining widespread acceptance as the "gold standard" [1–7]. Several of these systems are diagramed in Figure 81.1. Over the last decade, the POP quantification (POPQ) system has gained international recognition as the "gold standard" for classifying pelvic organ support, and it is the first and only system to gain recognition by most of the major societies that study pelvic organ support defects: the International Continence Society (ICS), the American Urogynecologic Society (AUGS), and the Society of Gynecologic Surgeons [8]. It is also one of the few systems to be extensively studied with several reports in the literature documenting excellent inter- and intraexaminer reliability [9–11]. Two other classification systems that have been studied include the Baden and Walker "half-way" system and a simplified POP classification (S-POP) system. The Baden and Walker "half-way" system has been around for decades and has gained some widespread notoriety. In a recent survey of the literature on POP, it was the second most commonly employed classification system behind the more popular POPQ system [10,12]. The S-POP system is a simplified version of the POPQ that has been studied in a large international multicentered trial [13]. It was shown to have very good intra- and interexaminer reliability and had good intersystem association with the POPQ [14].

Currently, there is only one internationally recognized classification system for codifying pelvic organ support—the POPQ. It has proven itself to be a reliable system, and it is the system that should be employed in research regarding pelvic organ support. The Baden and Walker "half-way" system remains a common system in clinical practice, and this may stem from its ease of use; however, it should not continue to supplant the POPQ in research studies and the scientific literature [10].

PELVIC ORGAN PROLAPSE QUANTIFICATION SYSTEM

While the POPQ system is recognized as the standard for describing pelvic organ support, it has not resolved all of the questions regarding POP. First, while it is a good system for codifying pelvic organ support, like its predecessors, it does not establish any diagnostic criteria for POP. In addition, while it is the only universally recognized system, it has yet to gain universal acceptance in research or clinical practice. Despite being initially described and published in 1996, as of 2003, it still only appeared in about 30% of the literature regarding pelvic organ support defects and, as of 2006, is only used clinically by about 40% of the members of the societies (ICS, AUGS) that acknowledge it as the recognized scientific standard for describing pelvic organ support [12,15].

There are many reasons why the POPQ system has not gained widespread clinical use, but the most commonly cited reasons are the following: (1) not used by colleagues, (2) too time-consuming, and (3) too confusing [15]. There is some validity to these concerns, but there are also some misconceptions. If only 40% of the members of the ICS and AUGS use it in their clinical practice, it would be surprising to find that other health-care providers outside of these societies had embraced the POPQ in their clinical practice. While there is no literature on how the system is used outside of the field of urogynecology, there is a study of 54 obstetrics and gynecology house officers and students who were trained to use the system. When specifically queried, only 1 of 54 reported seeing or using the system outside of their urogynecology rotation [16]. Concerns about taking too much time to complete are unwarranted as it only takes 2–3 minutes to complete the examination, even in neophytes [9].

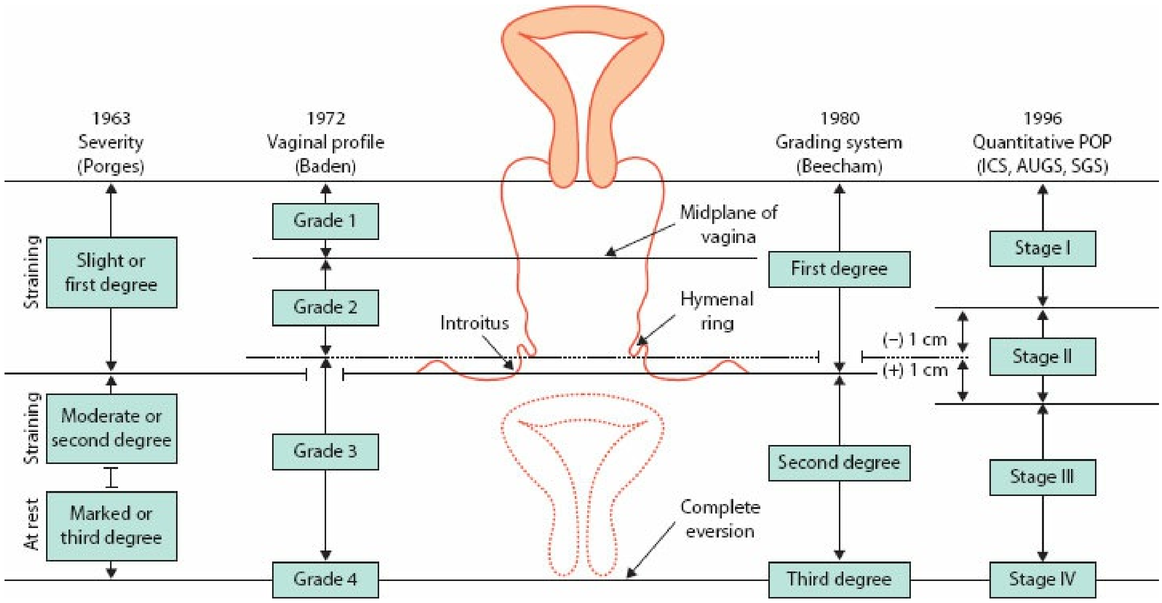


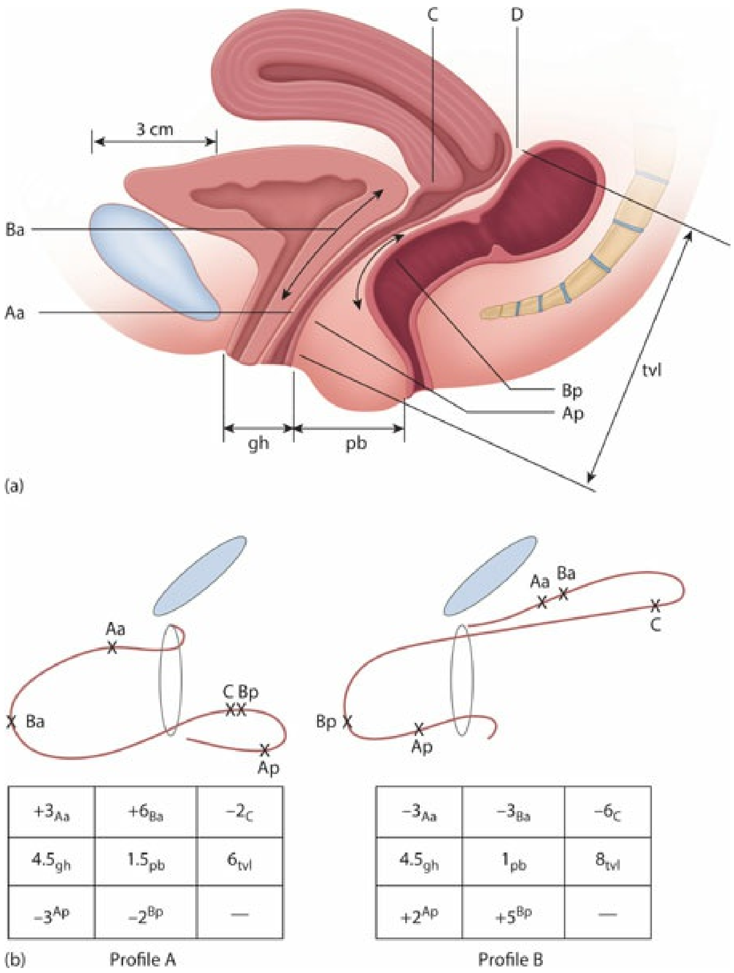
Figure 81.1 Comparison of the four most commonly used pelvic organ prolapse grading systems. AUGS, American Urogynecologic Society; ICS, International Continence Society; SGS, Society of Gynecologic Surgeons.

Performing the Pelvic Organ Prolapse Quantification Examination

The POPQ examination takes nine measures of the position of midline vaginal structures (Table 81.1). All of the measurements are in centimeters relative to the hymeneal ring. The remnant of the hymeneal ring is used as the reference point because it is a fixed and easily identified landmark, as opposed to the introitus, which is a nonstandardized anatomic structure (it is defined as the “entrance into the vagina”). All of the points recorded during the examination, with the exception of total vaginal length, are measured with the subject performing a Valsalva or a deep cough. Structures that lie above the hymeneal ring are recorded as negative, whereas structures that prolapse beyond the hymeneal ring are recorded as positive (both recordings in half centimeters) (Figure 81.2). Any structure that descends to the level of the hymeneal ring is recorded as 0 cm. Nine measurements are taken during the examination: two from the anterior vaginal wall, two from the apex of the vagina, two from the posterior vaginal wall, and one each recording the genital hiatus, perineal body, and the total vaginal length at rest (see Table 81.1). These points are depicted diagrammatically in Figure 81.2; note also the two diagrams representing a large anterior segment defect with some apical descent (Profile A) and a large posterior defect (Profile B). The nine points may be recorded in a convenient manner using a three-by-three grid as noted in the figure. Any rigid measuring device—such as a marked wooden Pap smear spatula, ruler, or engraved instrument—may be used.

Table 81.1 Sites Measure in the Quantitative Pelvic Organ Prolapse Examination

Point	**Description**
A anterior (Aa)	A point on the anterior vaginal wall 3 cm above the hymeneal ring
B anterior (Ba)	Most dependent or distal point on the anterior vaginal wall segment between A anterior and point C or the cuff if subject is status posthysterectomy
C	Anterior lip of the cervix or the cuff if subject is status posthysterectomy
A posterior (Ap)	A point on the posterior vaginal wall 3 cm above the hymeneal ring
B posterior (Bp)	Most dependent or distal point on the posterior vaginal wall segment between A posterior and point D or the cuff if subject is status posthysterectomy
D	Posterior fornix (this space is left blank in the subject who is status posthysterectomy)
Genital hiatus (gh)	Middle of external urethral meatus to posterior hymeneal remnant
Perineal body (pb)	Posterior hymen to middle of anal opening
Total vaginal length (tvl)	Hymeneal ring to vaginal apex



Profile A

$+3_{Aa}$	$+6_{Ba}$	-2_{C}
4.5_{gh}	1.5_{pb}	6_{tvl}
-3^{Ap}	-2^{Bp}	—

Profile B

-3_{Aa}	-3_{Ba}	-6_{C}
4.5_{gh}	1_{pb}	8_{tvl}
$+2^{Ap}$	$+5^{Bp}$	—

Figure 81.2 (a) The nine points recorded for the pelvic organ prolapse classification system. Terms are defined in Table 81.1. (b) Profile A represents a large anterior wall defect with some apical descent; Profile B represents a large posterior defect. Note the grid system used for recording the nine points.

For descriptive purposes, an ordinal staging system is used whereby the prolapse stage is defined by the vaginal structure that demonstrates the greatest degree of prolapse (Table 81.2). An easy method of remembering this staging system involves understanding stage II. Any vaginal structure that descends such that the leading edge is at or between 1 cm above and 1 cm past the hymeneal ring is stage II. If the vaginal structure or leading edge has some movement but remains above –1 cm, it is stage I, and any structure or leading edge that descends beyond +1 cm is stage III up to complete eversion, which is stage IV. Stage 0 is no descent of any vaginal segment.

At a practical level, an efficient method of performing the examination consists of placing a bivalve speculum in the vagina and measuring apical descent using the posterior blade of the speculum to measure anterior and then posterior structures, and then measuring the perineal structures. Further information regarding the performance of the POPQ examination, including a videotape, is available at the AUGS website (www.augs.org).

Table 81.2 Staging of Pelvic Organ Prolapse

Stage	**Description**
0	No descensus of pelvic structures during straining.
I	The leading surface of the prolapse does not descend below 1 cm above the hymeneal ring.
II	The leading edge of the prolapse does not extend from 1 cm above the hymen to 1 cm through the hymeneal ring.
III	The prolapse extends more than 1 cm beyond the hymeneal ring, but there is not complete vaginal eversion.
IV	The vagina is completely everted.

One aspect of this system that may be awkward, or even an anathema, to adherents of prior systems is the strict avoidance of terms such as cystocele, rectocele, or enterocele. The rationale behind this seemingly dogmatic practice is to avoid erroneous assumptions regarding the prolapsing organs. Since the vagina is relatively opaque, it is not possible to identify which organ is on the other side of the epithelium. It is often difficult even for experienced observers to discriminate between a high rectocele and a pulsion enterocele. Furthermore, patients who have had prior reconstructive pelvic surgery may have gross alterations in their vaginal axis, which result in unusual patterns of prolapse (e.g., anterior enterocele after sacrospinous ligament suspension). Another change from previous systems is the avoidance of staging the individual vaginal segments, i.e., a patient having a stage II cystocele and stage III rectocele. Instead, the patient is given one overall stage; for example, the previously noted patient would be described as having a POPQ stage III examination.

Simplified Pelvic Organ Prolapse Quantification System

In response to concerns regarding the clinical utility of the POPQ, the International Urogynecological Association sets up a task force to develop a more user-friendly system for classifying pelvic organ support. They also wanted a system that would demonstrate good association with the POPQ such that clinicians could use the user-friendly version in their clinical practice but take advantage of scientific literature using the standard POPQ. Out of this task force was developed the S-POP. The S-POP is basically the ordinal staging of the POPQ applied to each segment of the vaginal wall (anterior, posterior, apex, and cervix) without the need for nine separate measures. This idea stemmed from observations that several investigators were already reporting on simple ordinal staging for pelvic organ support without taking the nine measurements [11]. The S-POP is just a codification of applying what many investigators were already proposing.

Performing the Simplified Pelvic Organ Prolapse Quantification Exam

The technique for performing the simplified POPQ exam is as follows. Patients are asked to empty their bladder prior to the exam. The subject is then placed in the dorsal lithotomy position. Once the subject is positioned for examination, they are instructed to forcefully perform Valsalva or to cough—if the clinician feels the Valsalva is inadequate.

The four areas to be examined and staged include the anterior and posterior vaginal walls, the apex/cuff, and the cervix. If a subject was status posthysterectomy, then only three measurements are taken: the anterior and posterior vaginal walls and the cuff scar/apex. For the exam of the anterior and posterior vaginal wall segments, a disarticulated Graves speculum or two fingers of the examiner are employed as a retractor. For examination of the anterior vaginal segment, the speculum or fingers are placed into the vagina and the posterior vaginal wall is retracted to allow for full visualization of the anterior vaginal wall. A point or rugal fold approximately 3 cm proximal to the urethral meatus on the anterior vaginal wall is identified. The patient is then instructed to perform Valsalva or cough in a forceful fashion and where that point or rugal fold previously identified descends in relation to the hymenal remnants is noted and recorded as the stage of the anterior vaginal wall (noted in the following under staging). The posterior segment is examined in a similar fashion. The point chosen to represent the posterior vaginal segment is identified in a similar fashion retracting the anterior vaginal wall. The only difference is the point is approximately 3 cm proximal to the hymenal remnants instead of the urethral meatus. The cervix is evaluated by placing a speculum in the vagina and directly observing its descent during a Valsalva or cough to determine its stage in relation to the hymenal remnants. Care should be taken to make certain that the cervix is not inadvertently supported by the speculum during the exam. The vaginal apex or cuff scar is visualized in a similar fashion. If the cervix, apex, or cuff scar descends beyond the hymenal remnants with Valsalva or cough, then a speculum is not necessary. If the subject has a cervix, then the vaginal apex or posterior fornix is described separately from the cervix.

The staging system for each segment is as follows:

Stage I: Prolapse where the given point remains at least 1 cm above of the hymenal remnants during Valsalva or forceful cough

Stage II: Prolapse where the given point descends an area extending from 1 cm above to 1 cm below the hymenal remnants (Figure 81.3)

Stage III: Prolapse where the given point descends greater than 1 cm past the hymenal remnants but does not represent complete vaginal vault eversion or complete procidentia uteri (Figure 81.4)

Stage IV: Complete vaginal vault eversion or complete procidentia uteri

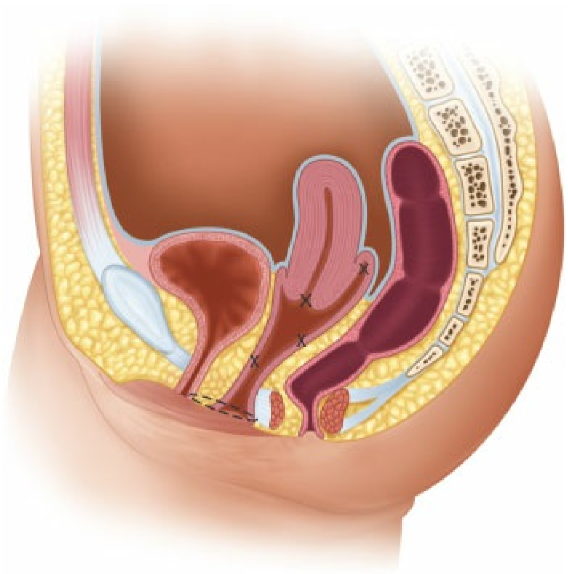


Figure 81.3 The four points measured for the simplified pelvic organ prolapse classification exam. Note the dotted line representing the hymenal remnants.

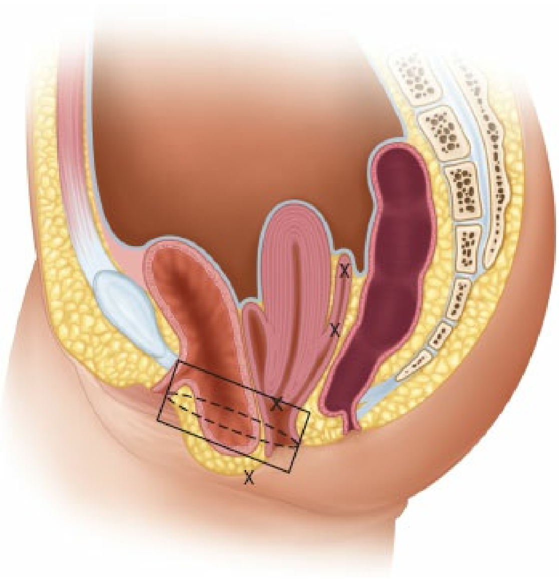


Figure 81.4 Simplified pelvic organ prolapse classification (S-POP) stage III anterior vaginal wall prolapse, stage II cervical support, and stage I apex and posterior vaginal wall support. Note the dotted line representing the hymenal remnants and the box representing S-POP stage II.

No specific measuring devices need to be used. The examining clinician can approximate the 1 cm above or below the hymenal remnants defining stage II. The subjects are assigned an overall stage as the highest value among the four segments, and each segment is assigned an individual stage.

Assigning individual stages to the various vaginal segments while not part of the POPQ is a standard clinical practice. In addition, the task force that developed the simplified POPQ felt that a stage 0 was not necessary since it is asymptomatic and not different enough from stage I to warrant a separate classification stage.

EPIDEMIOLOGY OF PELVIC ORGAN PROLAPSE

The National Institutes of Health (NIH) consensus conference recognized that without a standard validated definition of POP there could be little progress in studying the disease and its treatment. They noted that currently there are no clinically or scientifically validated definitions and felt that any proposed definition should take into account both a subject's anatomy and their symptoms [17]. Despite the lack of knowledge on which to base a rational definition for POP, the NIH defined POP as ≥POPQ stage II exam.

Subsequent to the NIH consensus conference, there have been several published studies examining the distribution of pelvic organ support in various general female populations [18–25]. However, only four studies have looked at general populations of a significant age range employing the POPQ system [18–20,26]. From the distribution of these four studies as plotted in Figure 81.5, it can be seen that POPQ stage II support represents between 30% and 50% of the populations studied. However, it is doubtful that POP is this prevalent; therefore, the NIH definition may be too broad. Only 2%–11% of the subjects in these studies have stage III and IV examinations, which is more consistent with current estimates on the percent of subjects undergoing surgical treatment for this condition. There is an 11% lifetime risk of undergoing surgical correction of POP, and the incidence of surgery for POP/incontinence is 22.7 per 10,000 [27,28].

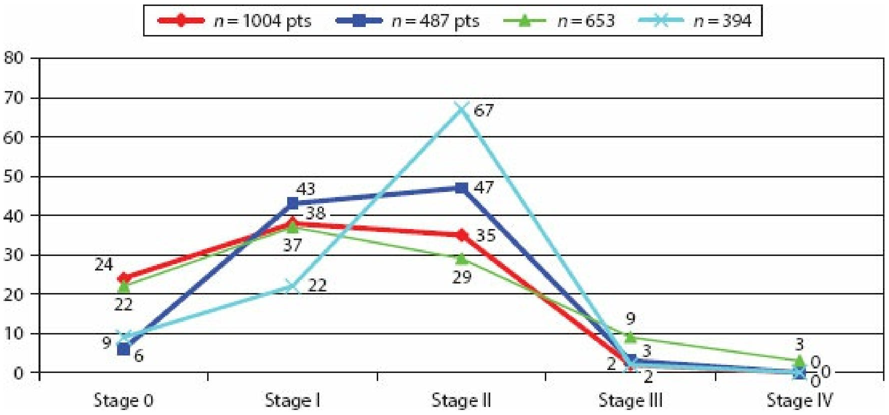


Figure 81.5 Percent of subjects in each pelvic organ prolapse quantification stage in three studies of general female populations. *n* is the number of subjects examined in each study. (*n* = 487: From Swift SE, *Am J Obstet Gynecol*, 183, 277, 2000; *n* = 1004: From Swift SE et al., *Am J Obstet Gynecol*, 192, 795, 2005; *n* = 653: From Slieker-ten HMCP et al., Distribution of pelvic organ prolapse in a general population: Prevalence, severity, etiology and relation with the function of pelvic floor muscles, Abstract Presented at the *Joint Meeting of the ICS and IUGA*, August 25–27, 2004, Paris, France; *n* = 394: From Trowbridge ER et al., *Am J Obstet Gynecol*, 198, 548.e1, 2008.)

POP is a disease with essentially no mortality and only minimal morbidity; however, it is a condition that greatly impacts the quality of life. Therefore, symptoms play a central role in defining at what point a patient goes from “normal” pelvic organ support to “abnormal” POP. Most studies demonstrate that there is a very weak (if any) correlation between symptoms and advancing degrees of POP with the exception of the symptom of a bothersome vaginal bulge [29–33]. In the few studies that correlated POPQ stage with symptoms, it appears that symptoms begin to significantly increase once the leading edge of the vaginal wall extends to or just beyond the hymen [19,28]. Therefore, a reasonable definition of POP may be protrusion of any vaginal segment to or beyond the hymen in symptomatic patients. If one carefully reads the literature, this definition, while not recognized, is slowly becoming the standard. A recent review article has suggested that we should define the disease and outcomes regarding management strategies using composite scores based on objective and subjective findings [34].

ETIOLOGY OF PELVIC ORGAN PROLAPSE

As previously noted, there is no currently accepted definition of POP; therefore, each study into its pathophysiology is left to employ its own definition. Generally, the literature defines prolapse in one of two ways—either anatomically by examination or by surgical admission for corrective surgery. The concern regarding surgical admissions is that they miss those patients that manage their prolapse conservatively; the concern regarding anatomic descriptions is that no two studies use the same anatomic cutoffs [19,21,23,25,27,35–39]. A list of epidemiological studies and their definitions is provided in Table 81.3. This plethora of definitions makes it difficult to evaluate trends in the literature into the various etiologies and can lead to conflicting results. This portion of the chapter will examine the various proposed etiologies of POP, bearing in mind that the frequently conflicting results stem from the various definitions employed in each study.

The only universally accepted risk factor for POP is the increasing age. Regardless of the definition used, this factor is always identified as a risk for prolapse, and most estimates suggest that there is roughly a doubling in the risk of prolapse with every completed decade of life [18,19,25,35]. The other proposed pathophysiologies for POP are many but for the most part involve two types of insult: either the acute damage that occurs with pregnancy or the chronic insults from conditions that lead to continuous intermittent increases in intra-abdominal pressure. In addition, other areas that have been investigated include prior pelvic surgery and genetic factors.

Effect of Pregnancy

The relationship between pregnancy and POP has been extensively studied and is mentioned in almost every treatise on this subject. It is assumed that as the fetal vertex passes through the birth canal, there is direct damage to the nerves, fascia, and muscle that leads to eventual relaxation of the pelvic floor musculature and POP. While it is generally recognized that any parity is associated with an increased risk of prolapse, what role the delivery mode plays is more controversial [18–21,23,33–36,38]. Specifically, can one delivery mode (i.e., cesarean section) provide protection against prolapse? The majority of the literature supports the notion that increasing parity increases the risk of POP [18,19,21,33,36]. Studies suggest that anywhere from a 4- to an 11-fold increase in the risk of prolapse is dependent on parity, with increasing parity imparting greater risk [19,21,35].

However, the literature on the mode of delivery is mixed. When women who delivered only by cesarean section were compared to women who had any vaginal delivery, the data are inconclusive and do not suggest a protective effect [19]. The data on instrumented vaginal delivery are sparse, and in one study forceps delivery was not identified as a risk factor for the development of prolapse [36]. In addition, there is one study suggesting that episiotomy protects against prolapse [37].

The data regarding infant weight are more consistent, with most studies demonstrating an increase in prolapse with increasing fetal weight; delivery of a macrosomic infant carries the greatest risk [19,23,35,36].

Table 81.3 Definitions of Pelvic Organ Prolapse from the Various Epidemiological Studies

Author	**Definition**
Jorgensen et al. [39]	Surgical admission for surgery to correct prolapse
Olsen et al. [27]	Surgical admission for surgery to correct prolapse
Mant et al. [21]	Surgical admission for surgery to correct prolapse
Chiaffarino et al. [36]	Baden and Walker stage II and greater
Marchionni et al. [37]	Baden and Walker stage II and greater
Samuelsson et al. [23]	Presence of any cystocele, rectocele, uterine descent, or absence of the urethrovesical crease
Gruel and Gruel [38]	Any vaginal relaxation to the introitus (roughly equivalent to Baden and Walker stage II and greater)
Swift et al. [35]	POPQ stage III prolapse
Hendrix et al. [25]	Stage I or greater prolapse by a unique system defined for this study (stage I is defined as in the vagina)
Swift et al. [19]	Leading edge at –0.5 cm above the introitus or greater (some POPQ stage II and all stage III and IV)

Pregnancy and macrosomia are consistently identified as risk factors for POP, but whether cesarean delivery or avoidance of an operative vaginal delivery can protect against POP remains a topic of debate with no clear evidence to support or refute this supposition.

Modifiable Lifestyle Risk Factors

There are several opinions regarding how to counsel patients in ways to prevent POP. Factors such as occupations that require a lot of lifting, together with obesity and smoking, all contribute to POP, and modifying or removing these insults will reduce the risk.

The data on occupation, as a risk for prolapse, stem from an article published in 1994 on nursing assistants in Denmark. The investigators noted a 60% increased risk of surgery to correct POP and herniated lumbar disks in nursing assistants over the general population [39] and felt this was due to the excess heavy lifting of patients inherent in their job description. Since then, two large studies have incorporated job description into their data collection [19,36]. Both found that manual workers and housewives had a slightly increased risk of prolapse over women who classified themselves as professionals.

Obesity is another risk factor commonly quoted for POP. It is felt that the increasing weight from abdominal adipose tissue increases the pressure on the intra-abdominal organs, leading to pelvic floor weakness and prolapse. Here, the literature is divided, with several studies suggesting it as a risk factor [19,21,25,27,37] and several studies finding no association [23,35,37].

Smoking is the final modifiable risk factor often associated with POP. Again, the data are mixed, with several studies suggesting that current smokers are at risk [21,25,27], two showing no relationship

[23,36], and one study suggesting smoking has some protection against POP [19].

Among the lifestyle or modifiable etiologies, the only factor that demonstrates a consistent relationship with an increased risk of POP is job description, with those individuals engaged in more manual labor having a greater risk of prolapse.

Medical Illnesses

Other areas that are commonly discussed and implicated as being etiologies of POP are chronic medical or congenital illnesses that result either in increased intra-abdominal pressure or in microvascular disease and poor-quality collagen. The relationship between chronic illness and prolapse has been investigated in large epidemiological studies with mixed results. It would seem intuitive that those illnesses associated with chronic recurrent increases in intra-abdominal pressure, constipation, and chronic obstructive pulmonary disease (COPD) would increase the risk of POP. Constipation is an illness that can be difficult to define; however—when evaluated—it appears consistently related to an increase in prolapse [25,40].

Two studies evaluated COPD and neither noted it as a risk for prolapse [27,35]. In one of these studies, the number of subjects with COPD was very small, and in the other the pelvic organ, prolapse was defined by surgical admission so the data could be questioned. However, when taken with data on smoking, there does not appear to be a strong relationship between pulmonary disease and prolapse.

Medical illnesses that lead to long-term damage to the microvasculature and peripheral neuropathies, such as hypertension and diabetes mellitus, have been suggested as a potential cause of POP. However, as with many etiological studies, the results are mixed. In one large study, the presence of any chronic illness was not associated with an increased incidence of prolapse [19]; in another study, only hypertension was identified as a risk factor [35].

There are also a few studies in women with collagen vascular diseases, such as Marfan and Ehlers–Danlos syndrome, which suggest that these patients are at an increased risk of prolapse [41,42]. However, again the data are somewhat conflicting, and this may stem from the lack of any definition of prolapse in these studies.

Race

There is a long history of observational data to suggest that women of certain racial groups are at a greater or lesser risk of POP. There are early anecdotal reports of African-American and “Chinese” women having a very low risk of POP in comparison to Caucasian women [43–45]. While it can be difficult to classify women into race (with the Tiger Woods phenomenon), it appears that African-American women having a slightly decreased risk of prolapse when compared to their Caucasian counterparts and Hispanic women have an increased risk over Caucasian women [19,25,35]. The data on Asian women in these trials are too sparse to draw any conclusions.

Menopausal Status and Hormone Replacement Therapy

The association between menopausal status, hormonal therapy, and POP is a very complicated issue. First, women who are menopausal tend to be older than their premenopausal counterparts, and, as pointed out earlier, increasing age is probably the greatest risk factor for POP. In addition, women who take hormone replacement therapy (HRT) may not have taken it consistently since menopause and can be on any of a myriad of dosing schedules, further complicating any comparative studies. The majority of the studies suggest that postmenopausal women are at greater risk; however, when a multiple logistic regression analysis takes age into account, menopausal status becomes nonsignificant, suggesting that it may be the age factor more than the decreased estrogen levels that places the woman at risk for prolapse [19,25,35,36].

In these same studies, when the role of HRT was evaluated in menopausal women, the results are even less clear. One study suggested that past use decreases risk but not current use, another suggested no difference between ever and never using HRT, and one suggested that postmenopausal women with current use had a risk equal to that of premenopausal women. It should be noted that, while HRT may not protect menopausal women from developing prolapse, it has never demonstrated a negative effect.

Prior Pelvic Surgery

This is another area where it is difficult to determine if there are any significant relationships. First, it is known that up to 30% of women who undergo surgery for POP will require a second procedure to correct recurrent prolapse [27]. Therefore, subjects who have had prior prolapse surgery have many of the underlying conditions that put them at risk for prolapse, and using this as a risk factor is similar to noting the increased risk of cancer in patients undergoing treatment for cancer. Conversely, many patients who have undergone a hysterectomy had it done to correct POP, as pelvic relaxation is the third most common indication for hysterectomy in the United States [46]. Therefore, many of these patients have already been treated for prolapse and many will have been treated successfully. However, when hysterectomy is evaluated, most studies suggest that it does expose patients to an increased risk of POP [21,23,35,37]. When the hysterectomy was done specifically for prolapse, it increases the risk even more [37]. The mechanism behind this phenomenon may be the disruption of the normal apical supports of the vagina in subjects with otherwise good support. This emphasizes the need to be ever mindful of providing strong attachment of the cardinal and uterosacral ligament complex to the vaginal cuff at the time of hysterectomy. In subjects who have undergone prior prolapse surgery, there appears to be upwards of a fivefold increase in their risk of developing POP [35].

Family History

This is one area where we have almost no data; however, this may be of central importance when we counsel patients about other modifiable risk factors. There is one study where subjects who had undergone surgery for prolapse were asked about any family history of other relatives undergoing similar surgery [36]. The authors noted that there was an increased risk of POP surgery if a patient’s mother or sister had undergone prolapse surgery.

Natural History of Pelvic Organ Prolapse

This is an area of study with almost no data. There is one good study that evaluated the effect of no treatment on subjects with minimally symptomatic POP followed over time. The 64 women who were followed had minimally symptomatic prolapse (95% had POPQ stage II and stage III) and declined pessary or surgical management. They were followed on average for 16 months and in approximately 80% there were no changes in their POPQ examinations. Of the 64 women, 20% eventually elected an intervention, but this study demonstrated that no intervention is an acceptable therapeutic option in minimally symptomatic subjects and that patients generally do not experience rapid progression of prolapse [47].

SUMMARY

While we are still in the infancy of understanding POP, we are moving forward. There is now a growing body of literature regarding the classification and epidemiology of POP incorporating the POPQ and well-described definitions of POP that are beginning to help us understand this complex disease.

Currently, it is difficult to evaluate the pathophysiology of POP because of the lack of a standard definition. This makes the plethora of emerging data difficult to interpret because often we are comparing apples and oranges. There are a few consistencies, with age and pregnancy being acknowledged risk factors for POP. Other factors that probably play a role include obesity, a job with a greater proportion of manual labor and lifting, lack of HRT, hysterectomy, and family history. However, before recommendations can be made regarding preventive strategies, more studies using a consistent definition are required.

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82 Anterior Vaginal Wall Prolapse

Mark D. Walters and Matthew D. Barber

INTRODUCTION

Anterior vaginal prolapse occurs commonly and may coexist with disorders of micturition. Mild anterior vaginal prolapse often occurs in parous women but usually presents few problems. As the prolapse progresses, symptoms may develop and worsen, and treatment becomes indicated. The anterior vaginal wall is the most common segment of the vagina to prolapse and the segment that is most likely to fail in the long term after surgical correction. This chapter reviews the anatomy and pathology of anterior vaginal prolapse, with and without stress incontinence, and describes methods of surgical repair.

ANATOMY AND PATHOLOGY

Anterior vaginal prolapse (cystocele) is defined as pathological descent of the anterior vaginal wall and overlying bladder base. According to the International Continence Society (ICS) standardized terminology for prolapse grading [1], the term “anterior vaginal prolapse” is preferred as “cystocele.” This is because the information obtained at the physical examination does not allow the exact identification of structures behind the anterior vaginal wall, although it usually is, in fact, the bladder. The ICS grading system for prolapse is discussed in detail in Chapter 81.

The etiology of anterior vaginal prolapse is not completely understood, but it is probably multifactorial, with different factors implicated in prolapse in individual patients. Normal support for the vagina and adjacent pelvic organs is provided by the interaction of the pelvic muscles and connective tissue [2]. The upper vagina rests on the levator plate and is stabilized by superior and lateral connective tissue attachments; the midvagina is attached to the arcus tendineus fasciae pelvis (ATFP) (white lines) on each side [3]. Pathological loss of that support may occur with damage to or impairment of the pelvic muscles, connective tissue attachments, or both.

Nichols and Randall described two types of anterior vaginal prolapse: distension and displacement [4]. Distension was thought to result from overstretching and attenuation of the anterior vaginal wall, caused by overdistension of the vagina associated with vaginal delivery or atrophic changes associated with aging and menopause. The distinguishing physical feature of this type was described as diminished or absent rugal folds of the anterior vaginal epithelium caused by thinning or loss of midline vaginal fascia. The other type of anterior vaginal prolapse—displacement—was attributed to pathological detachment or elongation of the anterolateral vaginal supports to the ATFP. It may occur unilaterally or bilaterally and often coexists with some degree of distension cystocele, with urethral hypermobility or with apical prolapse. Rugal folds may or may not be preserved.

Another theory ascribes most cases of anterior vaginal prolapse to disruption or detachment of the lateral connective tissue attachments at the ATFP, resulting in a paravaginal defect and corresponding to the displacement type discussed earlier. This was first described by White in 1909 [5] and 1912 [6] but disregarded until reported by Richardson et al. in 1976 [7]. Richardson described transverse defects, midline defects, and defects involving isolated loss of integrity of the pubourethral ligaments. Transverse defects were said to occur when the “pubocervical” fascia separated from its insertion around the cervix, whereas midline defects represented an anteroposterior separation of the fascia between the bladder and vagina. A contemporary conceptual representation of vaginal and paravaginal defects is shown in Figure 82.1 [8].

There have been few systematic or comprehensive descriptions of anterior vaginal prolapse based on physical findings and correlated with findings at surgery to provide objective evidence for any of these theories of pathological anatomy. In a study of 71 women with anterior vaginal wall prolapse and stress incontinence who underwent retropubic operations, DeLancey [9] described paravaginal defects in 87%

on the left and 89% on the right. The ATFP were usually attached to the pubic bone but detached from the ischial spine for a variable distance. The pubococcygeal muscle was visibly abnormal with localized or generalized atrophy in over half of the women.

Improvements in pelvic imaging are leading to a greater understanding of normal pelvic anatomy and the structural and functional abnormalities associated with prolapse. Magnetic resonance imaging (MRI) holds great promise, with its excellent ability to differentiate soft tissues and its capacity for multiplanar imaging. The pelvic organs, pelvic muscles, and connective tissues can be identified easily with MRI. Various measurements can be made that may be associated with anterior vaginal prolapse or urinary incontinence, such as the urethrovesical angle, descent of the bladder base, the quality of the levator muscles, and the relationship between the vagina and its lateral and apical connective tissue attachments. Aronson et al. [10] used an endoluminal surface coil placed in the vagina to image pelvic anatomy with MRI and compared four continent nulliparous women with four incontinent women with anterior vaginal prolapse. Lateral vaginal attachments were identified in all continent women. In Figure 82.2, the “posterior pubourethral ligaments” (bilateral attachment of ATFP to posterior aspect of the pubic symphyses) are clearly seen. In the two subjects with clinically apparent paravaginal defects, lateral detachments were evident (Figure 82.3). More recent studies based on MRI analysis and computer modeling suggest that apical support abnormalities are at least as important as, if not more important than, paravaginal defects; the degree of apical decent can explain about half of anterior wall descent [11]. This supports studies that used clinical examination with pelvic organ prolapse quantification (POPQ) that also demonstrates a strong correlation between anterior and apical vaginal support ($r = 0.89$) [12]. Other factors, such as levator ani muscle impairment, levator avulsion, greater anterior wall length, and widened urogenital hiatus, also contribute to anterior vaginal prolapse [13–15].

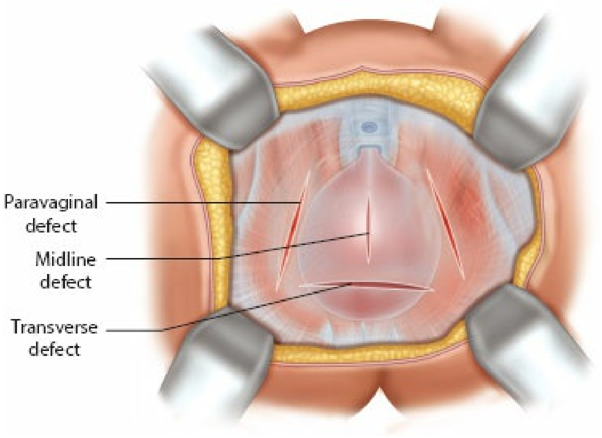

Figure 82.1 Three different defects can result in anterior vaginal wall prolapse. Lateral or paravaginal defects occur when there is a separation of the pubocervical fascia from the arcus tendineus fasciae pelvis, midline defects occur secondary to attenuation of fascia supporting the bladder base, and transverse defects occur when the pubocervical fascia separates from the vaginal cuff or uterosacral ligaments. (Reproduced from Karram MM, Vaginal operations for prolapsed, in Baggish MS and Karram MM, eds., *Atlas of Pelvic Anatomy and Gynecologic Surgery*, Saunders, Philadelphia, PA, 2001. With permission.)

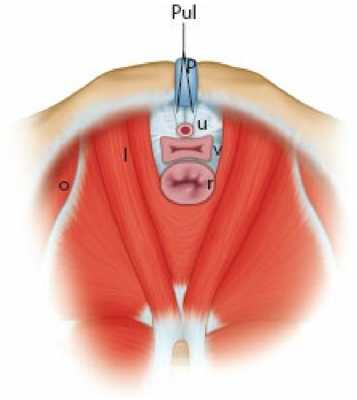

Figure 82.2 Axial T1-weighted image from a continent 38-year-old nulliparous woman, showing the connection of the anterior vaginal wall (v) to the posterior pubic symphysis (p) by the pubourethral ligaments (pul). The anterior vaginal wall and endopelvic fascia function as a sling or hammock for support of the urethra (u). o, obturator internus muscle; r, rectum; l, levator ani musculature. (Reproduced from Aronson MP et al., *Am J Obstet Gynecol*, 173, 1702, 1995. With permission.)

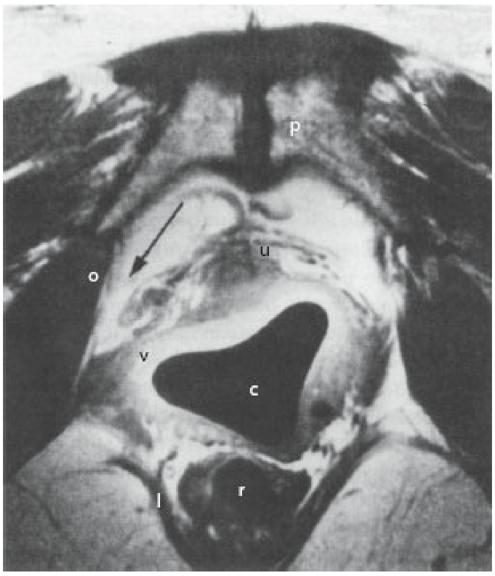

Figure 82.3 Axial T1-weighted image from a 57-year-old woman, para 5, with stress urinary incontinence. The paravaginal detachment (arrow) is seen at the level of the urethrovesical junction. v, anterior vaginal wall; p, posterior pubic symphysis; u, urethra; o, obturator internus muscle; c, endovaginal coil; r, rectum; l, levator ani musculature. (Reproduced from Aronson MP et al., *Am J Obstet Gynecol*, 173, 1702, 1995. With permission.)

Anterior vaginal prolapse commonly coexists with stress urinary incontinence. Some features of pathophysiology may overlap, such as loss of anterior vaginal support with bladder-base descent and urethral hypermobility; other features, such as sphincteric dysfunction, may occur independent of vaginal and urethral support. The pathophysiology of stress incontinence is covered more fully in Chapter __.

EVALUATION

History

When evaluating women with pelvic organ prolapse or urinary or fecal incontinence, attention should be paid to all aspects of pelvic organ support. The reconstructive surgeon must determine the specific sites of damage for each patient, with the ultimate goal of restoring both anatomy and function.

Patients with anterior vaginal prolapse complain of symptoms directly related to vaginal protrusion or of associated symptoms such as urinary incontinence or voiding difficulty. Symptoms related to prolapse may include the sensation of a vaginal mass or bulge, pelvic pressure, low back pain, and sexual difficulty. Stress urinary incontinence commonly occurs in association with anterior vaginal prolapse. Voiding difficulty may result from advanced prolapse. Women may require vaginal pressure or manual replacement of the prolapse in order to accomplish voiding, or they may relate a history of urinary incontinence that has since resolved with worsening of their prolapse. This can occur with urethral kinking and obstruction to urinary flow; women in this situation are at risk for incomplete bladder emptying and recurrent or persistent urinary tract infections and for the development of de novo stress incontinence after the prolapse is repaired.

Physical Examination

The physical examination should be conducted with the patient in the lithotomy position as for a routine pelvic examination. The examination is first performed with the patient supine. If physical findings do not correspond to symptoms or if the maximum extent of the prolapse cannot be confirmed, the woman is reexamined in the standing position.

The genitalia are inspected, and if no displacement is apparent, the labia are gently spread to expose the vestibule and hymen. The integrity of the perineal body is evaluated, and the approximate size of all prolapsed parts is assessed. A retractor or Sims speculum can be used to depress the posterior vagina to aid in visualizing the anterior vagina. After the resting examination, the patient is instructed to strain down forcefully or to cough vigorously. During this maneuver, the order of descent of the pelvic organs is noted, as is the relationship of the pelvic organs at the peak of straining.

It may be possible to differentiate lateral defects, identified as detachment or effacement of the lateral vaginal sulci, from central defects, seen as midline protrusion but with preservation of the lateral sulci, by using a curved forceps placed in the anterolateral vaginal sulci directed toward the ischial spine. Bulging of the anterior vaginal wall in the midline between the forceps blades implies a midline defect; blunting or descent of the vaginal fornices on either side with straining suggests lateral paravaginal defects. Studies have shown that the physical examination technique to detect paravaginal defects is not particularly reliable or accurate. In a study by Barber et al. [16] of 117 women with prolapse, the sensitivity of clinical examination to detect paravaginal defects was good (92%), yet the specificity was poor (52%) and, despite an unexpectedly high prevalence of paravaginal defects, the positive predictive value was poor (61%). Less than two-thirds of women believed to have a paravaginal defect on physical examination were confirmed to possess the same at surgery. Another study by Whiteside et al. [17] demonstrated poor reproducibility of clinical examination in detecting specific anterior vaginal wall defects. Thus, the clinical value of determining the location of midline, apical, and lateral paravaginal defects remains unknown. Although valuable for research, the value of MRI for the clinical evaluation of anterior vaginal prolapse has yet to be demonstrated.

Anterior vaginal wall descent usually represents bladder descent with or without concomitant urethral hypermobility. In 1.6% of women with anterior vaginal prolapse, an anterior enterocele mimics a cystocele on physical examination [18]. Other uncommon conditions, such as large suburethral diverticulum or anterior vaginal cysts or myomas, can also mimic anterior vaginal prolapse.

Diagnostic Tests

After a careful history and physical examination, few diagnostic tests are needed to evaluate patients with anterior vaginal prolapse. A urinalysis should be performed to evaluate for urinary tract infection if the patient complains of any lower urinary tract dysfunction. Hydronephrosis occurs in a small proportion of women with prolapse; however, even if identified, it usually does not change management in women for whom surgical repair is planned [19]. Therefore, routine imaging of the kidneys and ureters is not necessary.

If urinary incontinence is present, further diagnostic testing is indicated to determine the cause of the incontinence. Urodynamic (simple or complex), endoscopic, or radiologic assessments of filling and voiding function are generally indicated only when symptoms of mixed incontinence, pain, or voiding dysfunction are present. Even if no urologic symptoms are noted, a full-bladder cough stress test should be done with the prolapse reduced, and voiding function should be assessed to evaluate for completeness of the bladder emptying. This usually involves a timed, measured void, followed by urethral catheterization or bladder ultrasound to measure postvoid residual urine volume.

If surgery to repair the prolapse is planned, it is important to check urethral function after the prolapse is repositioned. Women with severe prolapse may be paradoxically continent because of urethral kinking; when the prolapse is reduced, urethral dysfunction may be unmasked with occurrence of incontinence (occult stress incontinence) [20]. A pessary, vaginal retractor, or vaginal packing can be used to reduce the prolapse before office bladder filling or electronic urodynamic testing. If urinary leaking occurs with coughing or Valsalva maneuvers after reduction of the prolapse, the urethral sphincter is probably incompetent, even if the patient is normally continent. This is reported to occur up to two-thirds of women with stage III or IV prolapse. In this situation, the surgeon should consider adding an anti-incontinence procedure in conjunction with anterior vaginal prolapse repair [21]. If stress incontinence is not present even after reduction of the prolapse, an anti-incontinence procedure probably still decreases the rate of postoperative urinary incontinence but results in more complications, voiding dysfunction, and higher cost [21,22]. A validated, individualized computer prediction model for de novo stress incontinence after prolapse surgery is available [23].

SURGICAL REPAIR TECHNIQUES

Anterior Colporrhaphy

The objective of anterior colporrhaphy is to plicate the layers of vaginal muscularis and adventitia overlying the bladder (“pubocervical fascia”) or to plicate and reattach the paravaginal tissue in such a way as to reduce the protrusion of the bladder and vagina. Modifications of the technique depend on how lateral the dissection is carried, where the plicating sutures are placed, whether apical support is added, and whether additional layers (natural or synthetic grafts) are placed in the anterior vagina for extra support.

The operative procedure begins with the patient supine, with the legs elevated and abducted and the buttocks placed just past the edge of the operating table. Antibiotics should be given within 60 minutes of incision to achieve minimal inhibitory concentrations in the skin and tissues by the time the incision is made. This typically means a first-generation cephalosporin (cefazolin) or combination regimens (500 mg metronidazole and 400 mg ciprofloxacin) if the patient has an allergy to penicillin [24]. In general, all patients undergoing vaginal prolapse surgery are at moderate risk for thromboembolic events and require a prevention strategy [25]. Low-dose unfractionated heparin (5000 units every 12 hours), low-molecular-weight heparins (e.g., 40 mg enoxaparin or 2500 units of dalteparin), an intermittent pneumatic compression device, or a combination of these are recommended. Either form of heparin should be started 2 hours before surgery and the compression stockings placed on the patient in the operating room before incision. These treatment approaches should be continued until the patient is ambulatory.

The abdomen, vagina, and perineum are sterilely prepped and draped, and a 16 Fr Foley catheter with a 10 mL balloon is inserted for easy identification of the bladder neck. A weighted speculum is placed into the vagina. Hemostatic solutions (such as 0.5% lidocaine with 1:200,000 epinephrine) or saline may be injected below the epithelium along the midline of the anterior vaginal wall, to decrease bleeding and to aid in dissection. If a vaginal hysterectomy has been performed, the incised apex of the anterior vaginal wall is grasped transversely with two Allis clamps and elevated. Otherwise, a transverse or diamond-shaped incision is made in the vaginal epithelium near the apex. A third Allis clamp is placed about 2 cm below the posterior margin of the urethral meatus and pulled up. If a midurethral sling is to be done, then the incision is only made to the bladder neck; a separate incision is made for the sling. Additional Allis clamps may be placed in the midline between the urethra and apex. A scalpel is used to open the anterior wall in the midline. Alternatively, the points of a pair of curved Mayo scissors are inserted between the vaginal epithelium and the vaginal muscularis, or between the layers of the vaginal muscularis, and gently forced upward while being kept half opened/half closed (Figure 82.4a and b). Countertraction during this maneuver is important to minimize the likelihood of perforation of the bladder. The vagina is incised in the midline, and the incision is continued to the level of the midurethra (or bladder neck if a sling is being done). As the vagina is incised, the edges are grasped with Allis or T-clamps and drawn laterally for further mobilization. Dissection of the vaginal flaps is then accomplished by turning the clamps back across the forefinger and incising the vaginal muscularis with a scalpel or Metzenbaum scissors, as shown in Figure 82.4c. An assistant maintains constant traction medially on the remaining vaginal muscularis and underlying vesicovaginal adventitia. This procedure is performed bilaterally until the entire extent of the anterior vaginal prolapse has been dissected; in general, the dissection should be carried further laterally with more advanced prolapse. The spaces lateral to the urethrovesical junction are sharply dissected toward the ischiopubic rami. It is also important to use sharp dissection to mobilize the bladder base from the vaginal apex as shown in Figure 82.5.

If the patient does not suffer from stress urinary incontinence, plicating sutures at the urethrovesical junction could be placed to augment posterior urethral support and to help ensure that stress incontinence, if not present at the time of operation, does not develop postoperatively. Although it may help to prevent de novo stress incontinence, it can also lead to voiding difficulty after surgery. Vesical neck plication was used to treat mild stress urinary incontinence in the past but is no longer done for that indication. Once the vaginal flaps have been completely developed, the urethrovesical junction can be identified visually or by pulling the Foley catheter downward until the bulb obstructs the vesical neck. Repair should begin at the urethrovesical junction, using No. 0 delayed absorbable suture. The first plicating stitch is placed into the periurethral endopelvic fascia and tied (Figure 82.6a). One or two additional stitches are placed to support the length of the urethra and urethrovesical junction.

In a standard anterior colporrhaphy, stitches using No. 2-0 or 0 delayed absorbable sutures are placed in the vaginal tissue (muscularis and adventitia) medial to the vaginal flaps and plicated in the midline without excessive tension. Depending on the severity of the prolapse, one or two rows of plication sutures or a purse-string suture followed by plication sutures are placed (Figure 82.6b). The vaginal epithelium is then trimmed from the flaps bilaterally, and the remaining anterior vaginal wall is closed with a running No. 2-0 subcuticular or locking suture.

Anti-incontinence operations are often performed at the same time as anterior vaginal prolapse repair to treat coexistent stress incontinence, although this practice is somewhat controversial and varies in different geographic regions. Suburethral bladder neck sling placement may also improve the cure rate of the prolapse [26]. Bladder neck suspension procedures (pubovaginal sling procedures or retropubic colposuspension) effectively treat mild anterior vaginal prolapse associated with urethral hypermobility and stress incontinence. More advanced anterior vaginal prolapse will not be treated adequately and, in these cases, anterior colporrhaphy or anterior vaginal mesh repair should be performed, often in conjunction with a colpopexy procedure and a midurethral sling. Surgical judgment is required to perform the bladder plication tightly enough to reduce the anterior vaginal prolapse sufficiently, yet preserve some mobility of the anterior vagina. If anterior colporrhaphy is combined with a sling procedure (midurethral or bladder neck), the cystocele should be repaired before the final tension is set for the sling. Randomized trials support concurrent placement of a midurethral sling at the time anterior vaginal prolapse surgery even in continent women in order to prevent de novo stress urinary incontinence after surgery [22]. A midurethral sling, such as a tension-free vaginal tape or transobturator sling, is best done through a separate midurethral incision after the cystocele repair is complete.

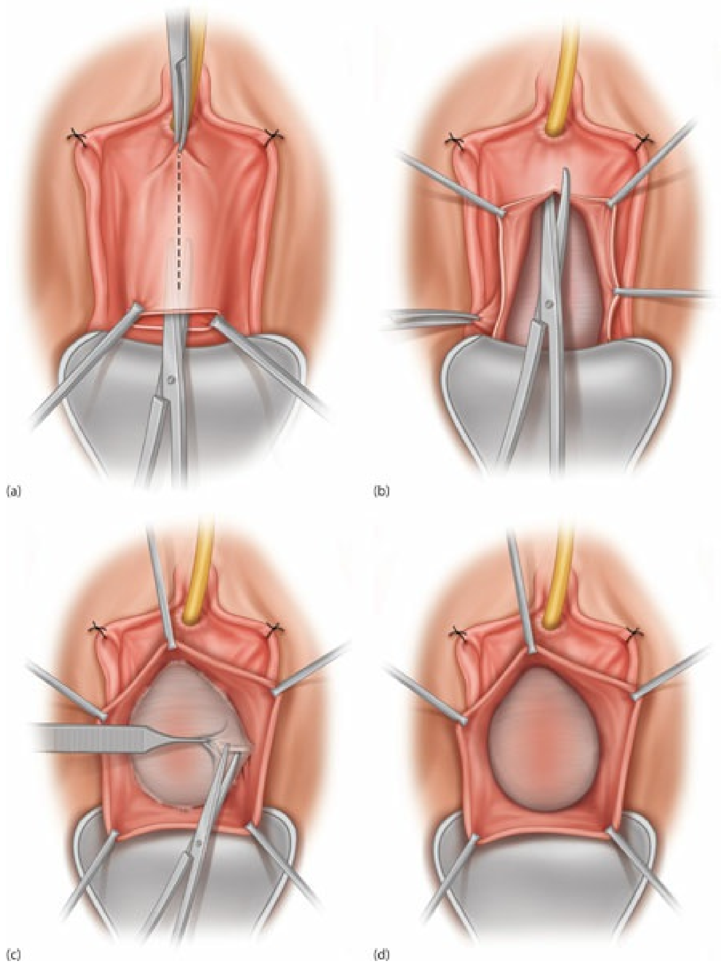

Figure 82.4 Cystocele repair: (a) initial anterior vaginal wall incision is at midline, (b) the incision is extended to the level of the proximal urethra, (c) sharp dissection and traction on the bladder facilitate dissection of the bladder off the vaginal wall, and (d) mobilization of the cystocele off the vaginal wall is completed. (Reproduced from Karram MM, Vaginal operations for prolapsed, in Baggish MS and Karram MM, eds., *Atlas of Pelvic Anatomy and Gynecologic Surgery*, 2nd edn., Saunders, Philadelphia, PA, 2001. With permission.)

Anterior Prolapse Repair with Grafts

A prosthetic material can be used to provide support in the anterior vagina. This can be done in a number of ways and the surgical techniques continue to evolve. Graft materials may include synthetic absorbable grafts (e.g., polyglactin 910 mesh), synthetic permanent meshes (e.g., polypropylene), and biological materials. Biological materials that have been used include autografts of harvested rectus fascia and fascia lata, human allografts including fascia lata and dura mater, and xenografts such as porcine dermis, porcine small intestinal submucosa, and bovine pericardium. In 2010, approximately 25% of surgeries for pelvic organ prolapse in the United States included transvaginal placement of biologic or synthetic mesh. Many surgeons use transvaginal graft placement in an attempt to increase the efficacy and durability of their surgical repair. For anterior prolapse, studies have demonstrated improved anatomic outcomes after transvaginal placement of permanent synthetic mesh when compared to anterior colporrhaphy without mesh (“native-tissue repair”) [27]. However, this comes at the expense of an increased rate of complications unique to synthetic mesh placement including longer operating time and higher blood loss, vaginal mesh exposure or extrusion, mesh erosion or perforation into an adjacent organ (bladder, urethra, or rectum), and vaginal mesh contraction with associated pain and dyspareunia [27]. Concerns over increased adverse events from transvaginal mesh placement led to two separate FDA notifications. In October 2008, the FDA issued a Public Health Notification (PHN) to inform clinicians and patients of adverse events related to urogynecological use of surgical mesh and to provide recommendations on how to mitigate risks and counsel patients. In July 2011, the FDA provided an updated PHN on urogynecological surgical mesh and reported that the complications of mesh used transvaginally are not rare.

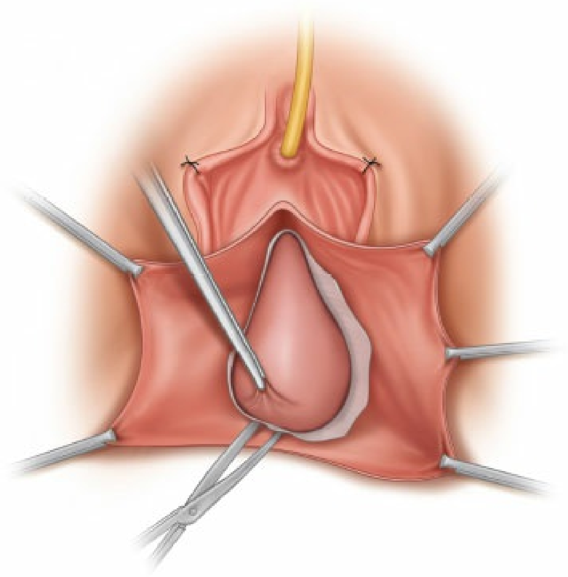

Figure 82.5 Cystocele repair. Sharp dissection is used to mobilize the bladder base from the vaginal apex during anterior colporrhaphy.

When considering the use of transvaginal mesh for anterior prolapse, surgeons and patients must balance improved anatomic support of the anterior vaginal wall against the cost of the devices and increased complications such as mesh erosion, exposure, or extrusion, pelvic pain, groin pain, and dyspareunia. In a joint Committee Opinion published in December 2011, the American Urogynecologic Society and the American College of Obstetrics and Gynecology recommended that pelvic organ prolapse vaginal mesh repair should be reserved for high-risk individuals in whom the benefit of mesh placement may justify the risk, such as individuals with recurrent anterior prolapse or with medical comorbidities that preclude more invasive and lengthier open and endoscopic procedures [28]. They also noted that surgeons placing vaginal mesh should undergo training specific to each device and have experience with reconstructive surgical procedures and a thorough understanding of pelvic anatomy.

Prior to considering treating the anterior vaginal prolapse with graft or mesh, patients should undergo a thorough informed consent process including discussion of risks, benefits, and both surgical and nonsurgical alternative treatments. Surgeons considering mesh use are encouraged to review the FDA's recommendations to health-care providers for pelvic organ prolapse (http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/UroGynS

There are several situations where mesh use is contraindicated. Many surgeons would not consider the use of mesh in a patient who has had a previous mesh complication. Mesh augmentations should not be used in pregnant women or women who are contemplating future pregnancy, as the vaginal mesh does not stretch significantly. In patients who have had pelvic radiation, mesh placement is not recommended because of the risk of poor wound healing. Similarly, preexisting local or systemic infection is a contraindication for vaginal mesh placement, particularly nonabsorbable synthetic mesh. Many surgeons would not recommend the use of nonabsorbable synthetic mesh if colorectal surgery is being performed concurrently. Chronic steroid use, smoking, uncontrolled diabetes mellitus, or other causes of a compromised immune system can impair wound healing, and many would consider these conditions to be relative contraindications to vaginal mesh placement. Pelvic pain syndromes such as endometriosis, vulvodynia, interstitial cystitis, fibromyalgia, and dyspareunia should be evaluated preoperatively to allow for comprehensive counseling as to the best surgical and nonsurgical form of treatment.

Currently, there are three general categories of transvaginal mesh or graft placement options for the management of anterior vaginal prolapse: (1) self-tailored mesh, (2) commercially available trocar-guided mesh kits that use a transobturator approach, and (3) commercially available mesh kits that use a transvaginal fixation method rather than a trocar (nontrocar kits). No matter what placement option is used, the general surgical approach to treat anterior vaginal wall prolapse is fixation of mesh to the ATFP or the coccygeus muscle. The initial incision for anterior vaginal mesh placement usually involves significant hydrodissection and a deeper colpotomy incision than usually performed for a traditional native-tissue anterior colporrhaphy so that the perivesical space is entered. The mesh is spread laterally toward the ATFP proximally and distally and, in many of the newer nontrocar kits, attached apically to the sacrospinous ligament. Despite the lack of evidence that any one placement technique is best in managing a patient’s symptoms, most experts would agree on some basic perioperative tenets:

- The bladder should be drained with a transurethral catheter.
- A well-estrogenized vaginal wall is preferred prior to surgery. (We use intravaginal estrogen cream daily [0.5–1.0 g/day] for at least 2–3 weeks preoperatively.) A vaginal pessary should be removed 1–2 weeks prior to surgery to limit vaginal epithelium irritation.

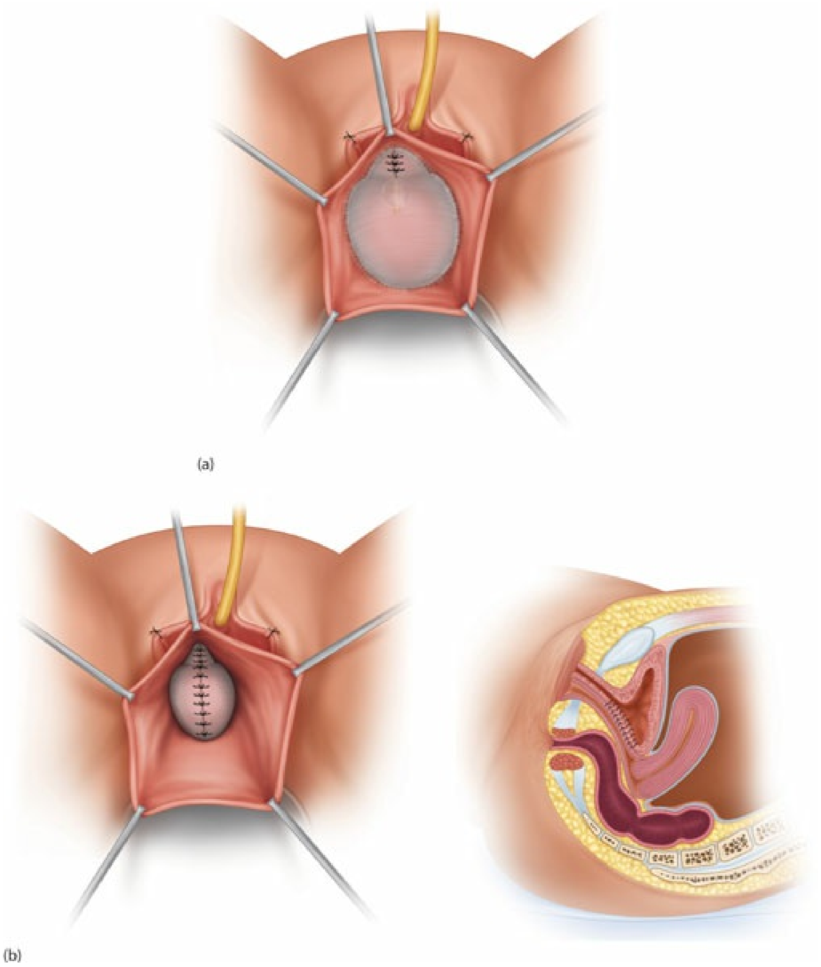

Figure 82.6 Cystocele repair. (a) Kelly plication sutures have been placed and tied, plicating the pubocervical fascia across the midline at the level of the bladder neck. (b) The bladder base has been plicated. Inset: preferential support of the bladder neck when compared to the bladder base. (Reproduced from Karram MM, Vaginal operations for prolapsed, in Baggish MS and Karram MM, eds., *Atlas of Pelvic Anatomy and Gynecologic Surgery*, 2nd edn., Saunders, Philadelphia, PA, 2001. With permission.)

- All patients require perioperative prophylactic antibiotics and efforts to prevent venous thromboembolic events, as noted earlier.
- Avoid making inverted “T-shaped” incisions from a concurrent hysterectomy and colporrhaphy, if possible.

- Exposure of the correct vesicovaginal space is performed with hydrodissection of 20–80 mL of 0.5% lidocaine with 1:200,000 epinephrine, dilute Pitressin (20 units in 60–100 mL of saline), or normal saline. The correct space for dissection is found using a “loss of resistance” technique similar to that used by an anesthesiologist placing an epidural. A wheal or blanching illustrates incorrect intraepithelial placement of the fluid. Hydrodissection in the correct plane will create a fluid bubble in the avascular vesicovaginal and rectovaginal spaces.
- As opposed to an anterior colporrhaphy where the vaginal epithelium and muscularis are split for plication, the mesh should be placed underneath the vaginal muscularis. It is vital that the surgeon perform a full-thickness dissection deep into the vesicovaginal and rectovaginal spaces to avoid erosion of the mesh postoperatively. Proper hydrodissection, as described earlier, facilitates the identification of the proper dissection plane.
- It is unknown whether or not the bladder wall should be plicated in the midline below the graft.
- Loosely place the graft because the mesh can contract by up to 20% following placement, compromising vaginal length and caliber. Allow enough room for Mayo scissors to be easily placed between the mesh and the vagina. Also, ensuring that the mesh is placed flat and with minimal tension will improve fibroblast growth and minimize complications of pain or erosion.
- The vaginal epithelium should not be trimmed. The colpotomy incision is closed utilizing a nonlocking continuous absorbable suture.
- Cystourethroscopy with assessment of urine flow from both ureters should be performed routinely after anterior mesh placement to identify potential urethral, bladder, or ureteral injury.

Self-Tailored Mesh Placement

Self-tailored mesh can be customized by the surgeon to match the size and shape of each patient’s individual pelvic anatomy. Mesh is cut into a trapezoid multiarmed shape for compartment augmentation and fixed to sacrospinous ligaments, obturator fascia, ATFP, and/or the distal bladder neck (Figure 82.7). This type of surgery requires a strong set of vaginal surgical skills as it involves dissections similar to sacrospinous ligament fixation, iliococcygeus suspension, uterosacral suspension, and vaginal paravaginal defect repair. No studies have compared standard repair techniques using self-tailored mesh with other mesh placement techniques.

Trocar-Based Mesh Kits

Trocar-guided devices can be used to suspend mesh by passing needles through the transobturator and/or ischiorectal fossa. Trocar-based mesh kits were the first commercially available transvaginal mesh products and included Anterior Prolift® (Ethicon, Somerville, NJ), Perigee® (American Medical Systems, Minnetonka, MN), and Avaulta® (CR Bard, Murray Hill, NJ). While these three products are no longer marketed by their respective companies in the United States, some trocar-based kits are still available in the United States and worldwide. In general, the technique for placement of these products is similar. First, a weighted speculum, self-retaining retractor, or Deaver retractors are placed in the vagina. Allis clamps are positioned at the urethrovesical junction for traction and 1 cm distal to the vaginal apex. The bladder can be palpated between the two Allis clamps. As opposed to an anterior colporrhaphy in which the vaginal epithelium and muscularis are split for plication, the mesh is placed underneath the muscularis to maintain a thickened vascularized epithelium in order to minimize mesh exposure or erosion. To enter this potential space, the surgeon injects a dilute vasopressin solution or 0.5% lidocaine with 1:200,000 epinephrine underneath the vaginal muscularis as noted earlier to facilitate dissection and minimize blood loss. Irrigation may help during the dissection, as the defect is a glistening white line. A sagittal colpotomy incision is made between the Allis clamps long enough to admit two fingers comfortably. Next, countertraction along the entire incision line is achieved with either the serial Allis clamps or a self-retaining retractor. The vaginal epithelium and full-thickness muscularis are dissected away from the bladder defect. Sharp and blunt dissection of the bladder is then performed while keeping the muscularis and epithelium on the vaginal flaps. As this dissection plane is advanced superiorly, loose areolar tissue is encountered until the ischial spine, ATFP, and, depending upon the kit, the sacrospinous ligaments are exposed. A number of different trocar types are available including helical-shaped trocars similar to those for transobturator slings and flexible straight trocars. Cutaneous incisions that are 4–7 mm in length are made over the appropriate locations for the obturator foramen and/or gluteus trocars. When placing multiple mesh arms through the transobturator space, the superior and inferior puncture sites should be at least 3 cm apart so the mesh can lay flat. Two fingers placed into the vagina can retract the colon, elevate the bladder, and minimize deviation of the trocar tip with direct palpation. For anterior compartment mesh, the surgeon immediately identifies the incoming trocar passing through the ATFP. The prosthesis is loosely placed in a "tension-free" manner. A finger should be kept inside the vagina whenever tensioning the graft. This provides countertraction and splints the tissue at the points of fixation. Stay sutures can be used to help the mesh lay flat against the vagina. If the surgeon conserves the uterus, then permanent sutures can be placed into the cervical stroma to stabilize the mesh. Cystoscopic and rectal examinations before, during, and after each portion of the surgery can be helpful. Once adequate hemostasis is obtained, the vaginal epithelium is closed with a continuous nonlocking stitch of delayed absorbable suture. Placing a lubricated vaginal pack may minimize bleeding and keep the mesh flat during healing. After desired tensioning, all ends of the mesh arms should be trimmed below the surface of the skin and the incisions closed. Concurrent procedures, such as a midurethral sling, should be done through a separate vaginal incision at this time.

Nontrocar Mesh Kits

The nontrocar or "single-incision" mesh kits have become increasingly popular and largely replaced trocar-based kits. The products avoid the potential complications associated with blind trocar passage through the transobturator space and ischiorectal fossa and allow mesh fixation via direct visualization. Additionally, most currently available nontrocar kits provide apical fixation to the sacrospinous ligaments bilaterally as well as anterior vaginal support. The technique for the nontrocar kits begins similarly to the technique for trocar-guided kit placement. After the vesicovaginal space is dissected, pertinent fixation points are identified including the ischial spines, ATFP, and sacrospinous ligaments. For apical fixation, the surgeon palpates the location of interest then identifies the sacrospinous ligament at least 2 cm medial to the ischial spine. The ligament is penetrated using the surgeon's device of choice. The Uphold kit uses the Capio transvaginal suture-capturing device (Boston Scientific®, Marborough, MA) to secure the mesh arms to the sacrospinous ligaments. Alternatively, the Elevate system (American Medical Systems, Minnetonka, MN) uses self-fixating appendage tips delivered by vaginal trocars to the same site (Figure 82.8). The ATFP mesh arms provide lateral fixation. An index finger placed into the vagina palpates the ATFP from the ischial spine to the posterior pubis. The mesh can be passed through the upper third of the ATFP using the same fixation methods. With the Uphold device, there are no ATFP arms to implant, and a sutured anterior colporrhaphy is often performed prior to mesh placement. The mesh arms are slowly and individually adjusted to a loose tension, and then the mesh is sutured flat. Cystoscopy with visualization of ureteral flow is performed to ensure integrity of the bladder and ureters. The colpotomy is closed and the vagina packed as described earlier.

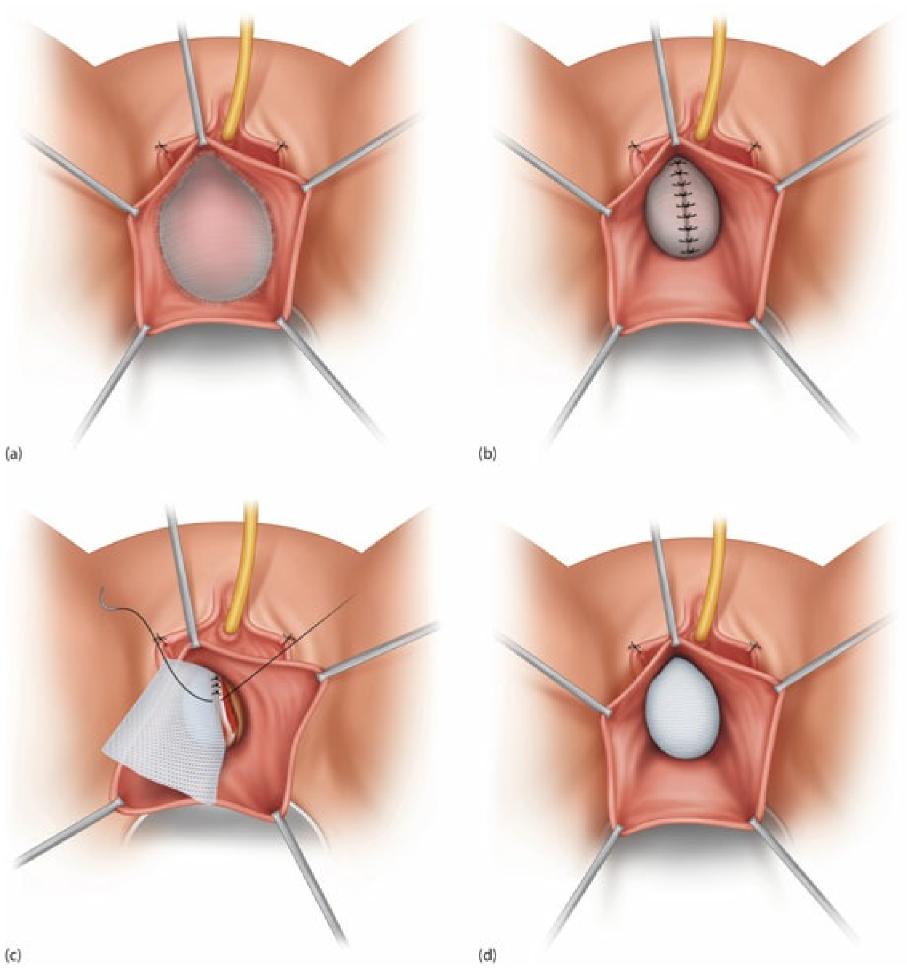

Figure 82.7 Cystocele repair with mesh: (a) the bladder is dissected bilaterally and off the vaginal apex; (b) midline plication is completed; (c) after entering the left paravaginal space and exposing the arcus tendineus fasciae pelvis (white line), the prosthetic mesh is sewn to it; and (d) the mesh is attached bilaterally and all sutures are tied, supporting the bladder.

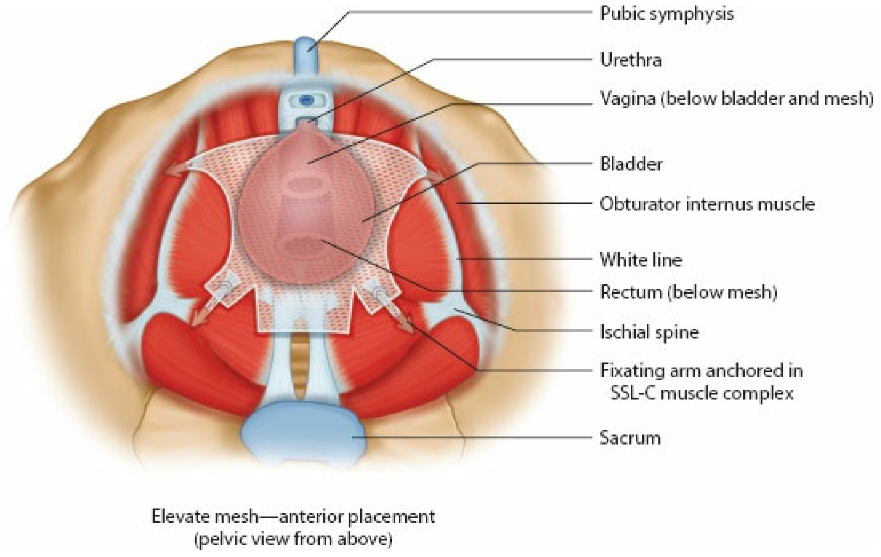
Pubic symphysis
Urethra
Vagina (below bladder and mesh)
Bladder
Obturator internus muscle
White line
Rectum (below mesh)
Ischial spine
Fixating arm anchored in SSL-C muscle complex
Sacrum
Elevate mesh—anterior placement
(pelvic view from above)

Figure 82.8 The Elevate incisionless mesh (American Medical Systems) is anchored bilaterally to the sacrospinous ligaments and obturator internus muscles near the distal end of the arcus tendineus fasciae pelvis. (Redrawn from Maher CF and Karram MM, Surgical management of anterior vaginal wall prolapse, in

Karram MM, ed., *Atlas of Surgical Management of Pelvic Organ Prolapse*, Saunders, Philadelphia, PA, 2013. With permission.)

Vaginal Paravaginal Repair

The aim of paravaginal defect repair for anterior vaginal prolapse is to reattach the detached lateral vagina to its normal place of attachment at the level of the ATFP. This can be accomplished using a vaginal or retropubic approach. Retropubic surgeries such as the Burch colposuspension are discussed in Chapter __.

The preparation for vaginal paravaginal repair begins as for an anterior colporrhaphy. Marking sutures are placed on the anterior vaginal wall on each side of the urethrovesical junction, identified by the location of the Foley balloon after gentle traction is placed on the catheter (Figure 82.9a). In patients who have had a hysterectomy, marking sutures are also placed at the vaginal apex. If a culdeplasty or apical suspension procedure is being performed, the stitches are placed but not tied until completion of the paravaginal repair and closure of the anterior vaginal wall. As for anterior colporrhaphy, vaginal flaps are developed by incising the vagina in the midline and dissecting the vaginal muscularis laterally. The dissection is performed bilaterally until a space is developed between the vaginal wall and retropubic space. Blunt dissection using the surgeon's index finger is used to extend the space anteriorly along the ischiopubic rami, medially to the pubic symphysis, and laterally toward the ischial spine. If the defect is present and dissection is occurring in the appropriate plane, one should easily enter the retropubic space, visualizing retropubic, and paravaginal adipose tissue. The ischial spine can then be palpated on each side. The ATFP coming off the spine can be followed to the back of the symphysis pubis. After dissection is complete, midline plication of the bladder adventitia can be performed, either at this point or after placement and tying of the paravaginal sutures (Figure 82.9b and c).

On the lateral pelvic sidewall, the obturator internus muscle and the ATFP are identified by palpation and then visualization. Retraction of the bladder and urethra medially is best accomplished with the Breisky–Navratil retractor, and posterior retraction could be provided with a lighted right-angle retractor. Using No. 0 nonabsorbable or delayed absorbable suture, the first stitch is placed around the tissue of the white line just anterior to the ischial spine. A Capio device (Boston Scientific, Natick, MA) works well to facilitate suture placement. If the white line is detached from the pelvic sidewall or clinically not felt to be durable, then the attachment should be to the fascia overlying the obturator internus muscle. The placement of subsequent sutures is aided by placing tension on the first suture. A series of three to six stitches are placed and held, working anteriorly along the white line from the ischial spine to the level of the urethrovesical junction (Figure 82.9d). Starting with the most anterior stitch, the surgeon picks up the edge of the periurethral tissue (vaginal muscularis or pubocervical fascia) at the level of the urethrovesical junction and then tissue from the undersurface of the vaginal flap at the previously marked sites. Subsequent stitches move posteriorly until the last stitch closest to the ischial spine is attached to the vagina nearest the apex, again using the previously placed marking sutures for guidance. Stitches in the vaginal wall must be placed carefully to allow adequate tissue for subsequent midline vaginal closure. After all the stitches are placed on one side, the same procedure is carried out on the other side. The stitches are then tied in order from the urethra to the apex, alternating from one side to the other. This repair is a three-point closure involving the vaginal epithelium, vaginal muscularis and endopelvic fascia (pubocervical fascia), and lateral pelvic sidewall at the level of the ATFP (Figure 82.9e and f). There must be tissue-to-tissue approximation between these structures. Suture bridges must be avoided by careful planning of suture placement. Vaginal tissue should not be trimmed until all the stitches are tied. The vaginal flaps are trimmed and closed with a running subcuticular or interlocking delayed absorbable suture.

Cystoscopy

Cystoscopy with visualization of ureteral flow is usually performed after cystocele repair, especially if slings or apical suspension procedures are also being performed. The purpose is to ensure that no sutures or mesh have been placed in the bladder and to verify patency of both ureters. The rate of ureteral obstruction after simple anterior colporrhaphy is only 0.4% [29], but the rate increases with the addition of some types of apical suspension. Intraoperative release of the offending sutures almost always releases the obstruction without further sequelae.

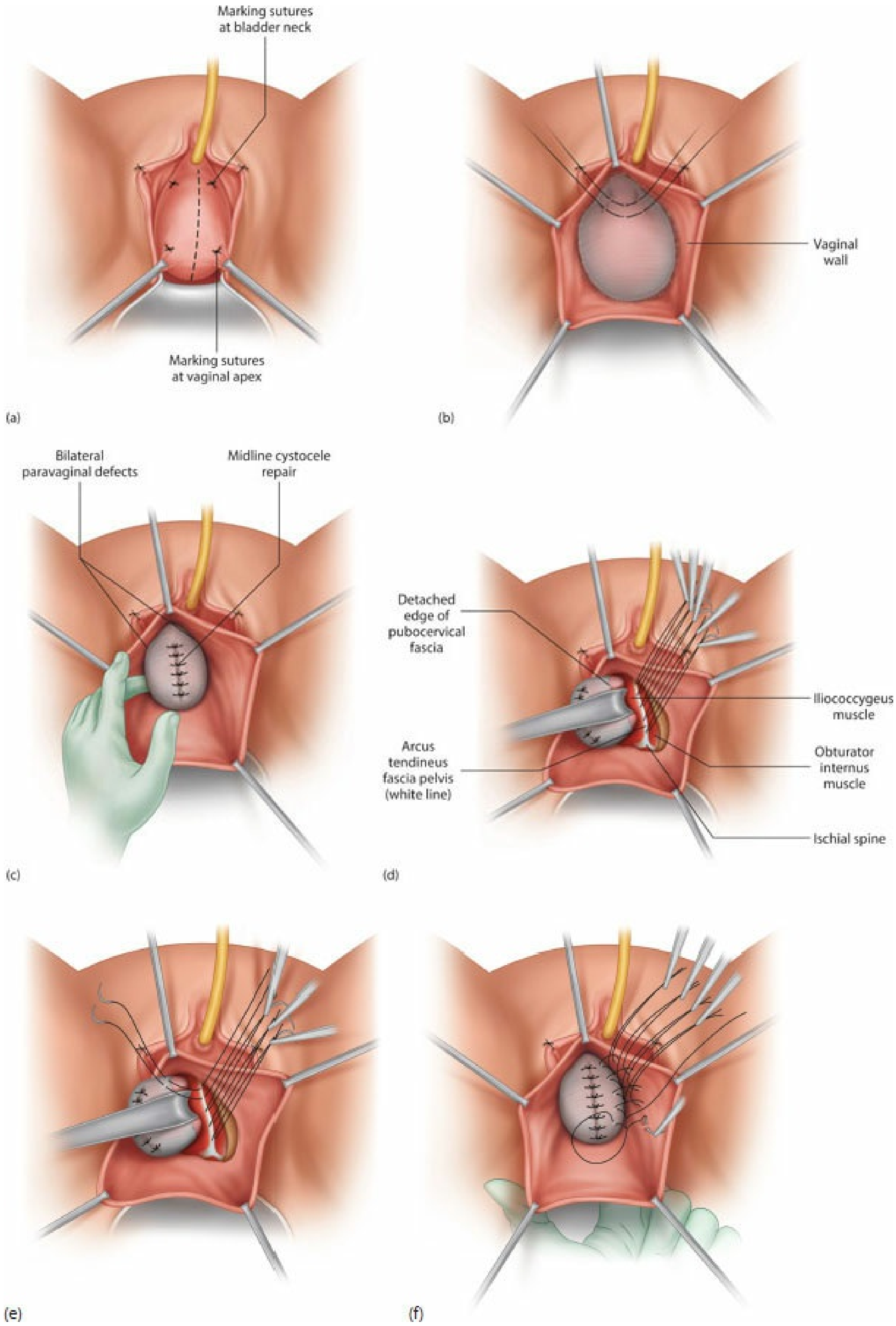
Marking sutures at bladder neck
Marking sutures at vaginal apex
(a)
Vaginal wall
(b)
Bilateral paravaginal defects
Midline cystocele repair
(c)
Detached edge of pubocervical fascia
Arcus tendineus fascia pelvis (white line)
Iliococcygeus muscle
Obturator internus muscle
Ischial spine
(d)
(e)
(f)

Figure 82.9 Technique of vaginal paravaginal repair. (a) Marking sutures are placed at the bladder neck and vaginal apex. A midline anterior vaginal wall incision is made. (b) The bladder is dissected bilaterally and off the vaginal apex. Midline plication is performed. (c) Midline plication is completed; obvious bilateral paravaginal defects are present. (d) The bladder is retracted medially and numerous sutures are passed through the arcus tendineus fasciae pelvis (white line). (e) Sutures are then passed through the detached pubocervical or endopelvic fascia. (f) Sutures are passed through the inside of the vaginal wall, thus completing the three-point closure. (Reproduced from Karram MM, Vaginal operations for prolapsed, in Baggish MS and Karram MM, eds., *Atlas of Pelvic Anatomy and Gynecologic Surgery*, 2nd edn., Saunders, Philadelphia, PA, 2001. With permission.)

Results

The main indication for surgical repair of anterior vaginal prolapse is to relieve symptoms when they exist or as part of a comprehensive reconstructive pelvic procedure for multiple sites of pelvic organ prolapse with or without stress urinary incontinence. Few studies have addressed the long-term success of surgical treatments for anterior vaginal prolapse. While the majority of studies evaluating anterior vaginal prolapse repairs are uncontrolled series, an increasing number of randomized surgical trials have been done in recent years. Success rates vary considerably depending upon the outcome measure used to define success. Historically, most studies evaluating the treatment of pelvic organ prolapse have focused exclusively on anatomic success without considering other important areas such as symptoms, vaginal compliance, quality of life, or socioeconomic outcomes. For an individual patient, the most important outcome of a surgical procedure is the relief of her symptoms and improvement in her quality of life, yet until recently these areas have largely been ignored. Reported success rates for native-tissue anterior colporrhaphy range from 37% to 100% with most cohorts reporting success rates greater than 80%.

In 2001, Weber et al. [30] studied three variations of anterior colporrhaphy using a prospective randomized study design and a strict definition of success (Aa and Ba points at –3 or –2 cm; stage 0 or I). Standard anterior colporrhaphy resulted in 30% of patients with an optimal or satisfactory anatomic result; anterior colporrhaphy with polyglactin 910 mesh overlay had 42% optimal or satisfactory result and ultralateral plication under tension a 46% optimal or satisfactory result. No difference was seen in anatomic or functional outcomes and most patients reported satisfaction with their symptom improvement. The low success rates found in the trial are used as evidence that anterior colporrhaphy should be augmented by either synthetic mesh or another approach used (e.g., sacrocolpopexy) for treatment of anterior vaginal prolapse. More recently, Chmielewski et al. [31] reanalyzed the data from this trial using more clinically relevant definitions of success and reported considerably better outcomes with only 10% of subjects developing anatomic recurrence beyond the hymen, 5% of subjects developing symptomatic recurrence, and less than 1% having another surgery for prolapse at 23 months follow-up. In general, it appears that native-tissue anterior colporrhaphy commonly results in asymptomatic anterior vaginal descent to within 1 cm of the hymen (POPQ stage 2); however, prolapse beyond the hymen, development of symptomatic prolapse (e.g., vaginal bulging symptoms), and reoperation for recurrent prolapse are uncommon events in the first 2–3 years after surgery. Long-term results of anterior colporrhaphy are largely unknown, although Gotthart et al. [32] reported only 13 reoperations for prolapse (2.9%) after 10 years in 456 patients who had vaginal hysterectomy and colporrhaphy. The median interval from the first surgery to the second was 5.5 years.

No randomized trials have been performed evaluating the efficacy of paravaginal defect repair for the treatment of anterior vaginal prolapse. Single-center uncontrolled case series suggest good anatomic results for both open retropubic (success rate 75%–97%) and vaginal (success rate 67%–100%) approaches [33,34]. However, the vaginal approach appears to be associated with high risk of hemorrhage, with one series reporting a 21% blood transfusion rate [33]. Few data are available on the efficacy or safety of the laparoscopic or robotic paravaginal defect repair.

Two studies evaluated the use of absorbable polyglactin 910 mesh to augment anterior colporrhaphy and reported mixed results. The Weber et al. trial [30] described earlier found no benefit, while a randomized trial by Sand et al. [35] found a 75% success rate 1 year after surgery in those receiving absorbable mesh compared with a 57% success in those receiving native-tissue anterior colporrhaphy. Based on the 2012 Cochrane meta-analysis of trials comparing biological graft overlay to anterior colporrhaphy and trials comparing biological graft to permanent synthetic graft, the review concluded that overall use of a biological graft overlay is associated with a lower risk of anatomic failure than anterior colporrhaphy alone (failure rate: anterior colporrhaphy 25% versus biological graft 14%; RR 1.44 [95% CI 1.20–2.63]) but with no difference in subjective cure or improvement in quality of life [36]. Not all trials included in the meta-analysis demonstrated anatomic benefit for biological grafts over native-tissue repair. Given the different characteristics of many of the biological grafts, it seems likely that the results will vary depending upon the specific biological graft used; however, no head-to-head comparisons have been performed.

At least six randomized trials have compared the efficacy of mesh augmentation with polypropylene to native-tissue anterior colporrhaphy for the treatment of anterior vaginal prolapse [27]. Altman et al. [37] published the largest of these studies in 2011. In this multicenter study, 389 women with stage II or greater anterior vaginal prolapse were randomized to Anterior Prolift (n = 186) or anterior colporrhaphy

($n = 182$). Of note, prolapse surgery was performed in the anterior compartment only; concomitant prolapse surgery for the other compartments or for incontinence was excluded. At 1 year, the success rate, defined as POPQ point Ba $< \mp 1$ and absence of vaginal bulge symptoms, was significantly greater after the mesh repair (61%) as compared to colporrhaphy group (35%). The subjective success rate was also significantly greater after the mesh repair (75% versus 62%, $p = 0.008$) as compared to the native-tissue repair, while no difference was detected on validated pelvic floor questionnaires (Urinary Distress Inventory) between the groups. The Prolift mesh procedure was associated with greater morbidity including longer operating time, greater blood loss, and higher rate of intraoperative cystotomy (3.5% versus 0.5%), greater rates of postoperative de novo stress urinary incontinence (12.3% versus 6.0%), and higher combined reoperation rates for stress incontinence, prolapse, and mesh exposure (6% versus 0.5%). De novo dyspareunia was seen in 7.3% after the mesh surgery as compared to 2% after anterior colporrhaphy ($p = 0.07$); however, no difference was detected in overall postoperative sexual function. Reoperation for mesh exposure occurred in 3.2% after the Anterior Prolift in this trial; the overall rate of mesh exposure was 11.5% [27,37].

A 2012 Cochrane review [36] concluded that the use of permanent synthetic mesh for anterior prolapse repair was associated with a decreased anatomic failure rate when compared to anterior colporrhaphy alone (14% versus 49%; RR 3.50, 95% CI 2.71–4.52), but no differences are found in the reoperation rate for prolapse or for improvement in quality of life measures. While the trial by Altman et al. [37] demonstrated improved subjective outcomes with the use of transvaginal mesh, this was not demonstrated in the other trials. However, because of the large size of the Altman study, the Cochrane meta-analysis concluded decreased subjective failure with transvaginal mesh in the anterior wall (17% versus 28%; RR 1.62, 95% CI 1.22–2.14) [36]. Of note, the use of mesh in the anterior vaginal wall appeared to predispose to prolapse in the apical and posterior segments in these trials compared to native-tissue repair. The Cochrane reviewers also found that anterior vaginal mesh placement was associated with greater operating time, greater blood loss, and a tendency for more cystotomies and de novo stress urinary incontinence. Also, the overall rate of reoperations including reoperation for recurrent prolapse, de novo stress incontinence, or mesh exposure was almost two times higher after anterior vaginal mesh than native-tissue repair (10.2% vs. 5.8%) [36].

Vaginal mesh erosions can be a particularly difficult problem and a small but significant number require reoperation for mesh removal due to chronic discharge, bleeding, pain, and other serious complications [38]. The average rate of mesh exposure reported in the literature in the first year after transvaginal mesh placement for pelvic organ prolapse is 10.9%. More than half of the women who experience erosion or exposure from nonabsorbable synthetic mesh after transvaginal placement require surgical excision in the operating room with some women requiring multiple operations. Creation of thicker vaginal flaps with an attached fibromuscularis, limiting vaginal trimming, and avoiding inverted "T" colpotomy incisions or concurrent vaginal hysterectomy probably decreases the mesh erosion rate.

It is worth emphasizing that the great majority of clinical trial evidence available for anterior transvaginal mesh placement involves using trocar-based mesh products that are no longer commercially available in the United States. In recent years, there has been a significant shift toward the nontrocar-based mesh kits for which there are currently few data. Moore et al. [39] performed a prospective multicenter cohort of 60 women receiving Anterior Elevate® (American Medical Systems, Minnetonka, MN) for anterior vaginal prolapse. They reported an anatomic success rate of 92% and a mesh exposure rate of 0%. Vu et al. [40] reported a retrospective analysis of the Uphold system for the treatment of anterior/apical prolapse that included 115 women including 53 who underwent a hysteropexy and reported an anatomic recurrence rate of 5% and a mesh exposure rate of 2.3%. Similarly, Rivaux et al. reported a case series of 59 patients who underwent Uphold hysteropexy and reported a 93% anatomic success rate and 3.5% mesh exposure rate at 12 months [41]. As of the writing of this chapter, no clinical trials comparing nontrocar-based mesh kits for anterior vaginal prolapse have been published.

Risk factors for failure of anterior vaginal prolapse repair have not been specifically studied separate from studies of total prolapse. Vaginal prolapse in general recurs with increasing age and length of follow-up, but the actual frequency is unknown and tends to vary with different definitions of prolapse. Recurrence of anterior prolapse is more likely to occur with more severe initial prolapse and probably with transvaginal, compared to abdominal, repairs [42]. Recurrence may represent a failure to identify and repair all support defects, or weakening, stretching, or breaking of patients' tissues, as it occurs with advancing age and after menopause. Sacrospinous ligament suspension of the vaginal apex, with exaggerated retrosuspension of the vagina, may predispose patients to recurrence of anterior vaginal prolapse; however, a recent clinical trial comparing sacrospinous ligament fixation to uterosacral ligament suspension did not demonstrate a difference in anterior recurrence between these two apical procedures [43]. Other characteristics that may increase chances of recurrence are genetic predisposition, subsequent pregnancy, heavy lifting, chronic pulmonary disease, chronic straining at stool, smoking, and obesity.

Complications

Intraoperative complications are uncommon with native-tissue anterior vaginal prolapse repair. Excessive blood loss may occur, requiring blood transfusion, or a hematoma may develop in the anterior vagina; this is probably more common after vaginal paravaginal repair than anterior colporrhaphy. The lumen of the bladder or urethra may be entered in the course of dissection. Accidental cystotomy should be repaired in layers at the time of the injury. After repair of cystotomy, the bladder is generally drained for 7–14 days to allow adequate healing. Ureteral damage or obstruction occurs rarely (0%–2%), usually with very large cystoceles or with apical prolapse [29,44]. Other rare complications include intravesical or urethral suture placement (and associated urologic problems) and fistulae, either urethrovaginal or vesicovaginal.

Complications unique to synthetic mesh use in the vagina include vaginal mesh exposure or extrusion; mesh erosion or perforation into an adjacent organ including the bladder, urethra, and rectum; and vaginal mesh contraction with associated pain and dyspareunia [45,46]. Complications that can occur with any pelvic reconstructive surgery but that can be made more severe or complicated by the presence of synthetic mesh include bleeding, infection, fistulas, pelvic pain, sexual dysfunction, and dysfunction of the lower urinary and lower gastrointestinal tract. While many of these complications can be managed nonsurgically, a significant proportion will require one or more surgical excision of some or all of the mesh [47]. The incidence of these complications varies from 3% to 39%. A systematic review of 110 studies by Abed et al. [45] found the average rate of graft erosion or exposure to be 10.3% with permanent synthetic grafts and 10.1% after biological grafts. Wound granulation was seen in 7.8%. Approximately, two-thirds of women with a mesh exposure after permanent synthetic mesh placement require some surgery to correct the exposure; in some cases, multiple procedures are required. For a more detailed discussion of incidence and management of mesh or graft complications see Chapter __.

De novo stress incontinence occurs in up to two-thirds of women after anterior vaginal prolapse repair. This risk is higher in women who demonstrate a positive cough stress test with prolapse reduction prior to surgery than those who do not. However, performance of an anti-incontinence procedure such as a midurethral sling or Burch colposuspension decreases this risk whether the preoperative stress test is positive or not [22].

Voiding difficulty can occur after anterior vaginal prolapse repair. This problem may occur more often in women with subclinical preoperative voiding dysfunction, especially if a suburethral plication is done [48]. Treatment is continuous bladder drainage or intermittent self-catheterization until spontaneous voiding resumes, usually within 2 weeks. Urinary tract infections are common (especially with concurrent catheter usage), but other infections such as pelvic or vaginal abscesses are uncommon.

Sexual function may be positively or negatively affected by vaginal operations for anterior vaginal prolapse [49]. Most prospective studies demonstrate that sexual function either does not change or improves in the majority of women after vaginal reconstructive surgery for pelvic organ prolapse; however, worsening sexual function can be seen in some patients. As many as 50% of patients with advanced prolapse report dyspareunia prior to surgery. In general, dyspareunia rates go down after prolapse surgery; however, de novo dyspareunia can be seen, especially if a posterior colporrhaphy is also performed. Vaginal topography, except for perhaps vaginal length, appears to have little relationship with postoperative sexual satisfaction [49]. In a comprehensive study by Kuhn et al. [50] of male and female sexual function after primary repair of vaginal prolapse without the use of mesh, female patients reported improvement in sexual desire, arousal, lubrication, pain, and overall satisfaction, but not orgasm. De novo dyspareunia only occurred in 2 of 70 women. Male partner function improved as well in domains of interest, sexual desire, and overall satisfaction [50]. One prospective comparison of patients undergoing vaginal versus nonvaginal (open or robotic) prolapse repair found that sexual function improved overall after surgery with no difference between groups [51]. Comparisons of sexual outcomes between native-tissue and mesh-augmented repairs have had mixed results with some showing worse sexual function after mesh repairs and others show no difference between the groups. The Cochrane reviewers found no difference in postoperative de novo dyspareunia between native-tissue prolapse repair and those augmented with synthetic or biological grafts [36,52].

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83 Enterocele

Kaven Baessler

DEFINITION AND SCOPE

The term “enterocele” is derived from the roots “enter,” meaning intestine, and “cele,” meaning hernia. It is a herniation of the bowel. In general, hernia occurs when a rupture in the smooth muscle or connective tissue allows a bodily structure to protrude. An enterocele is usually referred to as a herniation through or into the vagina typically as a posterior enterocele, which develops in the rectovaginal space (pouch of Douglas or cul-de-sac). The anterior enterocele in the vesicovaginal space is a rare entity [1], which might occur after cystectomy or after hysterectomy [2].

An enterocele is a form of pelvic organ prolapse with the bowel protruding into the vagina. Why and how are etiological and pathophysiological issues which are illustrated in this chapter. Surgical treatment of an enterocele is often concurrent or identical to operations for vaginal vault prolapse. Preventative and therapeutic procedures will be described.

ANATOMY, ETIOLOGY, DEFECTS, AND PATHOPHYSIOLOGY

Normal Anatomy

The important anatomical structures, with regard to enterocele formation, are consistent with normal pelvic organ support mechanisms. An enterocele develops in the pouch of Douglas. Therefore, the pouch of Douglas is an anatomical structure that plays an important and probably predisposing part. The pouch of Douglas is normally closed and does not contain intestine or omentum. In anatomy textbooks, the extent of the pouch of Douglas has traditionally been described as 2–3 cm below the uterosacral ligaments (e.g., Gray’s Anatomy). Histological studies by Uhlenhuth and colleagues have demonstrated that in the fetus the pouch of Douglas may extend to the perineal body [3]. The consecutive fusion of the anterior and posterior peritoneum forms the rectovaginal septum and determines the depth of the pouch of Douglas [3–5]. According to Uhlenhuth, the rectovaginal septum is distinguishable from the “fascial” capsule of the vagina and rectum. In contrast to anatomy textbooks, intra-abdominal measurements of the depth of the pouch of Douglas in young nulliparous women revealed great variations with 25%–75% of the posterior vaginal wall covered with peritoneum [6]. The mean depth of the pouch of Douglas was 49% of vaginal length in nulliparas, 46% in parous women, and was significantly deeper (72%) in patients with posterior vaginal wall prolapse. The mean vaginal length was 10 cm. Age and parity did not have an influence. It would appear that the deep pouch of Douglas is frequently present in young nulliparous women without pelvic organ prolapse, which implies a congenital variation and predisposition [6].

A sophisticated concept of normal pelvic organ support accentuates the imperative role of several factors including integrity of the anterior and posterior endopelvic fascia with intact attachments as well as normal tone, position, and functionality of the levator ani muscle. Normal pelvic floor muscle and fascial structures are required to hold the perineum in place and ensure normal bladder, bowel, and sexual function. It is apparent that fascial defects in the three levels of vaginal support and the posterior compartment may contribute to pelvic organ prolapse including enteroceles [7,8]: the normal pelvic floor tone is essential for the nearly horizontal axis of the vagina, which in turn is necessary to allow for a normal pelvic floor protecting intra-abdominal pressure distribution. These elements might be most important in keeping the pouch of Douglas closed.

Deep Pouch of Douglas as a Predisposing Factor (Figure 83.1)

Principally, a posterior enterocele develops in the pouch of Douglas, which is normally closed. Figure 83.1 illustrates the different characteristics in the development of enteroceles. Intra-abdominal measurements of the depth of the pouch of Douglas have shown that in women with posterior vaginal wall and anterior rectal wall prolapse the pouch of Douglas is significantly deeper and may reach the level of the perineal body [6]. In addition, the anatomy of the pouch of Douglas is considerably different, which is a recognized feature in some studies. In women with severe pelvic organ prolapse, a large or voluminous rectovaginal pouch was a consistent anatomic finding, requiring obliteration during pelvic reconstructive surgery [9–11]. Apart from a mobile vaginal axis and a dehiscence of the levator hiatus, French authors reported a “grande fosse pelvi-périnéale”—a large pelvic pouch—to be the principal lesion in women with enteroceles [12]. Other authors described this phenomenon as an abnormally deep and wide cul-de-sac with a 3D enlargement [13]. Their anatomical observations included a deep and wide rectovaginal pouch and a rectosigmoid colon, which closely follows the sacral curve (Figure 83.2). Although different positions and courses of the sigmoid colon and its mesentery are known [14], systematic descriptions in women with pelvic organ prolapse are scarce. Baessler and Schuessler found 64% of women with enteroceles and all women with anterior rectal wall procidentia to have these features, termed as “grande fosse pelvienne.” A grande fosse pelvienne was also present in 6 of 43 women (14%) in the control group who did not have pelvic organ prolapse. Three of them were nulliparous [15]. Given these findings, it seems reasonable to regard a deep pouch of Douglas as a risk factor for enterocele formation. However, a deep pouch of Douglas does not necessarily result in an enterocele. An enterocele can only develop when other factors open and expose the deep pouch of Douglas.

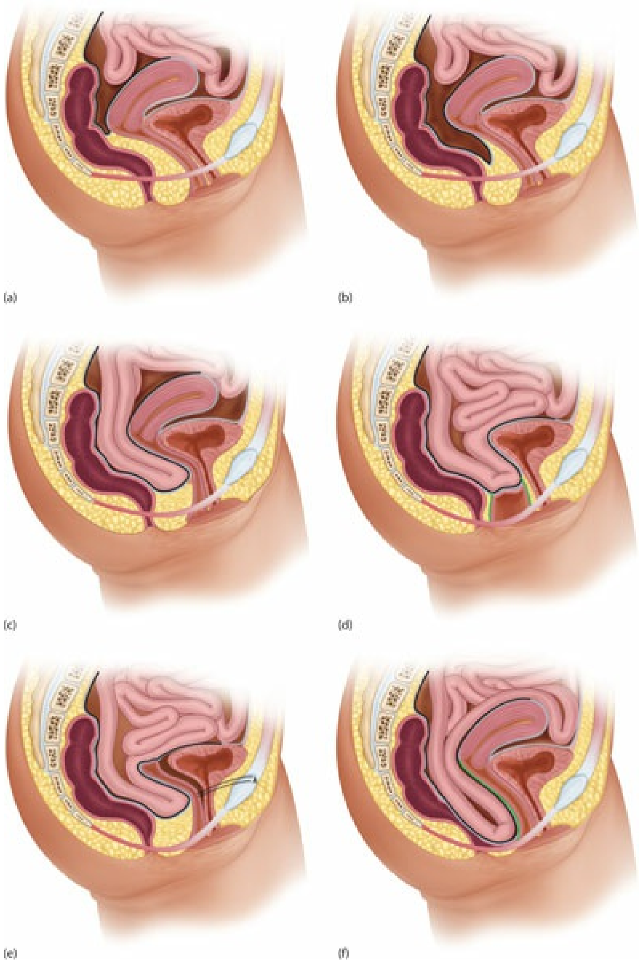

Figure 83.1 The pouch of Douglas—“normal” depth, deep, grande fosse pelvienne. (a) “Normal” pouch of Douglas: the pouch of Douglas covers approximately one-third of the posterior vaginal wall and is closed. (b) Deep pouch of Douglas: peritoneum covers the posterior vaginal wall down to the level of the levator ani. Normal pelvic floor support prevents opening and exposure of the pouch of Douglas. (c) An enterocele has developed in the rectovaginal space displacing the posterior vaginal wall: the vaginal and rectal course is more vertical and the pelvic floor position is lower leaving the pouch of Douglas unprotected. (d) Apical enterocele with separation of the anterior and posterior endopelvic fascia after hysterectomy. (e) Enterocele after Burch

colposuspension with ventral displacement of anterior compartment: the pouch of Douglas was not protected. (f) Enterocele bulging primarily into the rectum: anterior rectal wall procidentia. Intact posterior endopelvic fascia (green line).

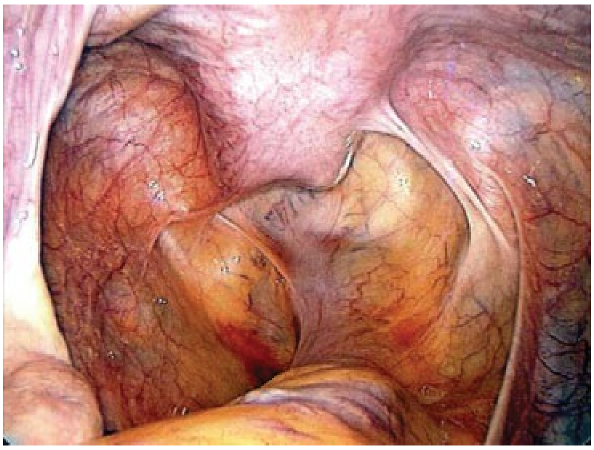

Figure 83.2 Laparoscopic view of a grande fosse pelvienne: note the deep and wide pouch of Douglas, the lack of prominent uterosacral ligaments, and the rectal course close to the sacrum with a short mesentery.

Vaginal Axis

In a woman with normal pelvic organ support, the pouch of Douglas is closed, irrespective of its depth, and lies nearly horizontally between the levator plate and the vagina [16–18]. A recent MRI study measured the mean levator–vaginal angle with a horizontal line at 35°–53° in different ethnic nulliparous populations [19]. It is known that operations that change the vaginal axis can lead to increased prolapse in the “unprotected” area. This is true for the higher incidence of cystoceles after sacrospinous fixations, where the position of the vagina is more posterior and also for the considerate rate of rectoceles and enteroceles after Burch colposuspensions or ventrofixations where the vagina is displaced anteriorly.

A further process that changes the vaginal axis is excessive perineal descent (or descending perineum syndrome), which is often seen clinically in women with significant posterior vaginal wall prolapse (Figure 83.3). A deep pouch of Douglas is likely to accentuate the process of enterocele development once the vaginal axis is changed.

Endopelvic “Fascia”

The integrity of the anterior and posterior endopelvic *fascia* or connective tissue and its attachments is essential for normal pelvic organ support [8]. A defect in the endopelvic *fascia* or insufficiency is necessary for an enterocele to protrude. However, an intact endopelvic connective tissue might only prevent the enterocele from bulging into the vagina but not into the rectum causing an anterior rectal wall procidentia (Figure 83.1f).

It is not entirely apparent whether the endopelvic *fascia* is identical to the rectovaginal septum as the latter can be rather short [20], depending on the depth of the pouch of Douglas. Whole-thickness biopsies of the leading edge of radiologically proven enteroceles showed that in none of the 13 women examined the vaginal epithelium was in direct contact with the perineum and all had a well-defined vaginal wall muscularis [21]. These findings add to the ongoing controversy on whether the *fascia* exists or not. It has been suggested that it is a structure that is artificially created during surgical dissection. This debate is complicated by inconsistent histological studies, some of which do not substantiate the concept of a fascia between the rectum and vagina. However, it might simply be a question of definition: the fascia is a connective tissue usually with smooth muscle cells and it might also contain fatty or areolar tissue [22] (Figure 83.4). Whether the fascia is part of the vagina or rectum or whether it is a separate structure is of scientific but not clinical value. *Fascia* in the clinical sense means connective tissue that has tensile strength and is strong enough to hold sutures and support the underlying organs.

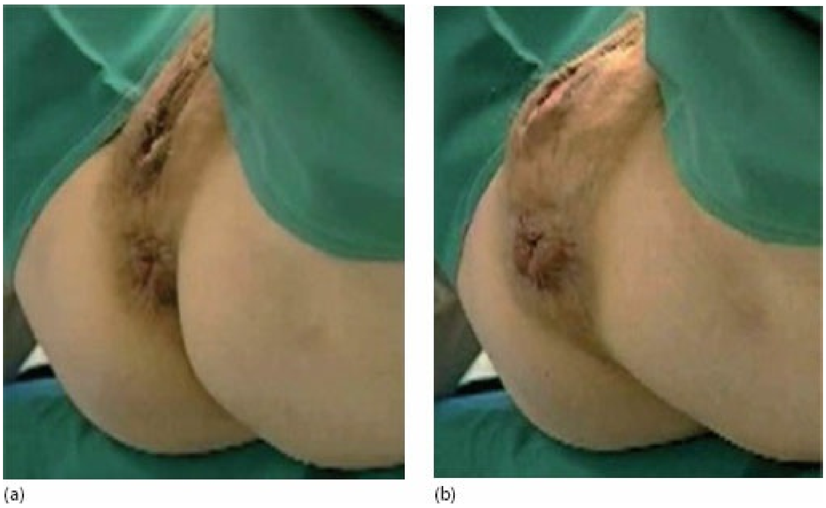

Figure 83.3 Excessive perineal descent. These photos demonstrate a nearly normal position of the perineum at rest (a) but a “ballooning” of the perineum on straining (b). This patient had a large rectoenterocele that did not protrude outside the introitus.

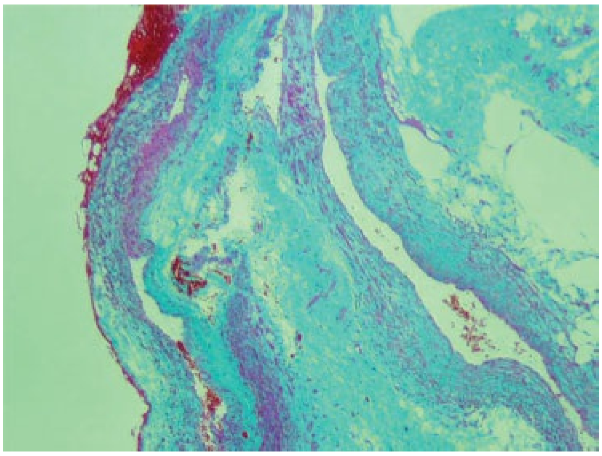

Figure 83.4 The Mallory trichrome stain of a biopsy taken from the tissue used in posterior vaginal wall repairs. The biopsy site was approximately 2 cm below the ischial spine. This stain is used to differentiate fibrous tissue (green) and smooth muscle (red). Note the amount of smooth muscle, organized connective tissue, and areolar tissue. (Courtesy of Dr. Christopher Maher.)

Descending Perineum Syndrome

This syndrome has been described by colorectal surgeons as a “ballooning” of the perineum during straining (Figure 83.3) [23]. Apart from bowel symptoms, which can be similar to complaints of patients with rectoceles or enteroceles, excessive perineal descent of more than 2 cm (measured in relation to the ischial tuberosities) is seen more frequently in women with posterior vaginal wall prolapse [24]. Solitary rectal ulcer, rectal prolapse, and intussusception are common concomitant findings [24,25]. The etiology is unclear, but reduced pelvic floor tone [26] with insufficient perineal and endopelvic *fascial* attachment and a deep pouch of Douglas and sigmoid colon elongation have been discussed. The term “ballooning” is also used to describe an enlargement of the genital hiatus during straining on perineal 3D ultrasound and is associated with pelvic organ prolapse [27].

Pulsion, Traction, Sliding, True, and Congenital: Concepts of Enterocele Development

There are different concepts, and each one of them might be true in an individual patient. The idea of finding a one-fits-all theory is probably in vain. Enteroceles may develop as a *true hernia* with a hernial sac and neck. A defect in the endopelvic connective tissue is then a prerequisite. It is argued that a *traction enterocele* is accompanied by the loss of pelvic organ support [17] and a greater vault descent with normal anatomical connections between the pouch of Douglas and vagina [28,29]. In contrast, according to Nichols and Genadry [17], a *pulsion enterocele* is secondary to increased abdominal pressure, whereas Zacharin states that a pulsion enterocele occurs as a late complication of pelvic surgery like hysterectomies and is associated with a large rectovaginal pouch [28]. However, Zacharin is convinced that the depth of the pouch of Douglas has no bearing on enterocele development. He considers levator incompetence and relaxation of the *fascial* support to be the primary defects. Nichols and Genadry describe *iatrogenic enteroceles* as a sequela to operations that alter the vaginal axis like Burch colposuspension and *congenital enteroceles*, which are associated with an "unusually" deep pouch of Douglas (Figure 83.1e).

In theory, an enterocele can only develop when important anatomical factors change: the vagina becomes more vertical and the (deep) pouch of Douglas opens or the pubocervical and rectovaginal *fascia* are separated. Whether a discrete defect in the endopelvic connective tissue is also required remains a topic for discussion. Therefore, Zacharin's observation of a common deep pouch of Douglas found only in Chinese females corroborates the ones mentioned earlier: their pelvic floor status including tone and support prevents an exposure of the rectovaginal pouch.

Rectal Prolapse

Colorectal surgeons view prolapse with a different attitude but have similar problems defining the pathophysiology of rectal prolapse, which might originate from the pouch of Douglas [30]. Altemeier described three types: type 1 is a false prolapse due to mucosal redundancy, type 2 is an intussusception without an association with the pouch of Douglas, and type 3 is a sliding hernia of the rectovaginal pouch [31]. Enteroptoses, or elongation of the rectosigmoid colon, are considered contributing factors [32]. Similar to vaginal enteroceles, type 3 rectal prolapse develops in the pouch of Douglas and basically is an enterocele bulging into the rectum, sometimes termed anterior rectal wall prolapse (Figures 83.1f and 83.6c).

Further Factors

Old textbooks often quote other factors that might contribute to enterocele formation. Apart from established confounders for pelvic organ prolapse like aging, obesity, and constipation with excessive defecatory straining, connective tissue diseases, parity, and malnutrition especially in war times are also mentioned [33].

Increased intra-abdominal pressure may also play a role as it is associated with increased BMI and leads to a larger genital hiatus [34]. Obesity and constipation have been established as risk factors for pelvic organ prolapse [35–37]. A chylous ascites has been described to accentuate pelvic floor defects and cause an enterocele [38].

EPIDEMIOLOGY

The prevalence of enteroceles is inseparable from other pelvic organ prolapse. Isolated enteroceles may occur after pelvic surgery. The classical example is the development of enteroceles after Burch colposuspension in up to 32% [39–41], which has not been described for suburethral tapes. It has also been recognized that enteroceles and rectal prolapse frequently coexist with other defects of pelvic floor support [42–44].

Specific data on enteroceles from women in the community are scarce. In a prevalence study of 639 women aged 45–85 years using the pelvic organ prolapse quantification of the International Continence Society, only 22% had no prolapse at all, 37% had stage 1, 29% had stage 2, 9% had stage 3, and 3% had complete eversion [45].

SYMPTOMS

As with any other kind of pelvic organ prolapse, an enterocele can cause prolapse symptoms including the feeling of a bulge and a dragging sensation, and it can also interfere with bladder, bowel, and sexual function. Unlike a cystocele or rectocele, an enterocele does not appear to cause any stereotypical and pathognomonic symptoms, and very often symptoms cannot be distinguished from those of any coexisting pelvic organ prolapse. Some women primarily complain of rectal symptoms like fullness and incomplete or difficult bowel emptying; however, in others, the prolapse symptoms are predominant [46]. There might be dyschezia and a frequent, unproductive urge to defecate. Anorectal symptoms and degree of posterior prolapse do not seem to correlate [47,48].

Partial or complete obstruction of the urethra might result in voiding difficulties or retention [49,50]. Dyspareunia, "slackness at intercourse," vaginal dryness, and coital incontinence are frequently reported by women with pelvic organ prolapse [51]. Mainly, a complication of previous pelvic floor surgery and hysterectomy, vaginal rupture, and evisceration has been reported in women with enteroceles [52].

CLINICAL ASSESSMENT AND INVESTIGATIONS

Vaginal and rectal examination with special attention to the endopelvic connective tissue is probably capable of identifying most enteroceles although some studies claim an inferiority of clinical examination to radiological studies [48]. Defects in the endopelvic connective tissue and their location with diminished vaginal rugae are a clue (Figure 83.5). Simultaneous bimanual examination of the tissues between the vagina and rectum under straining or in the standing position usually helps. An enterocele can be located in the anterior vaginal wall where it divides the pubocervical *fascia* in the posterior vaginal wall through the pouch of Douglas or it might separate the anterior and posterior endopelvic *fascia* at the vaginal vault (apical enterocele). Occasionally, peristalsis of the intestine bulging into the vagina establishes the diagnosis. If in doubt and a diagnosis is necessary, intraoperative evaluation during dissection will ascertain the presence or absence of an enterocele. However, perineal ultrasonography has gained popularity and has become the investigation of choice.

Perineal ultrasound may depict an enterocele [53], especially when performed in an upright position. This is its advantage over MRI; it can be performed standing, during straining or coughing, and even during simulated defecation using ultrasound where using gel in the rectum is possible. No opacification is required and the equipment is widely available. In Figure 83.6a, an enterocele descends between the rectum and vagina in a patient after hysterectomy. In a different patient, bulging into the rectum is also noted, explaining the patient's evacuation problems (Figure 83.6b and c). Three-dimensional ultrasound can also produce astounding images (Figure 83.7). Although limited in the evaluation of structures located more proximally, it may provide information on endopelvic connective tissue defects and pelvic floor dynamics (Figures 83.6 and 83.7) and may replace defecography [54,55]. But even with conventional 2D perineal ultrasound, an enterocele can be identified. Rectal ultrasound can also be helpful; sonographic diagnosis of an enterocele was confirmed intraoperatively in 27 of 29 cases in one study [56].

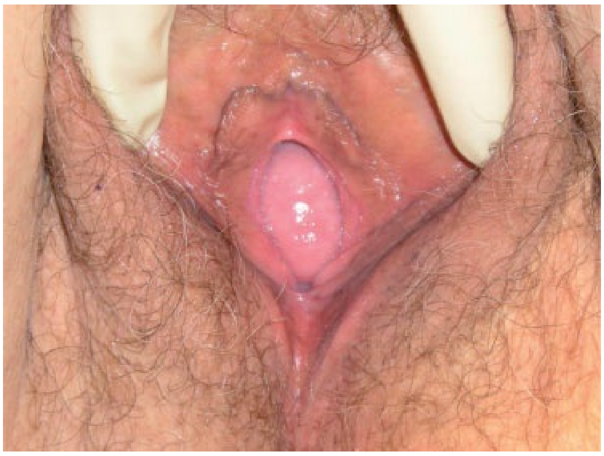

Figure 83.5 A rectoenterocele with diminished vaginal rugae.

Viscerography or fluoroscopic imaging includes the opacification of the bladder, rectum, and vagina with contrast medium. An additional barium meal will show the small bowel on x-ray. Ideally, the investigation is performed dynamically during straining or coughing and comprises defecography. The bowel evacuation gives room and is crucial for some enteroceles to descend. It will also provide further information on bowel emptying, rectal prolapse, or intussusception [47,57] although there are great variations of “normal” findings. Shorvon et al. could demonstrate that rectoceles and intussusception are frequently present in young and asymptomatic women [58]. It is therefore most valuable when the clinician performs the radiological investigations and interprets the findings in context with the symptoms.

Dynamic MRI including defecation MRI provides superb images but has major disadvantages: it is expensive, not widely available, and, at present, performed in the supine position only. Defecation in this situation might be impossible for some patients, and for the diagnoses of enteroceles, it may be inferior to defecating fluoroscopy studies [59]. However, the pictures obtained are remarkable and usually provide an accurate diagnosis (Figure 83.8) [60].

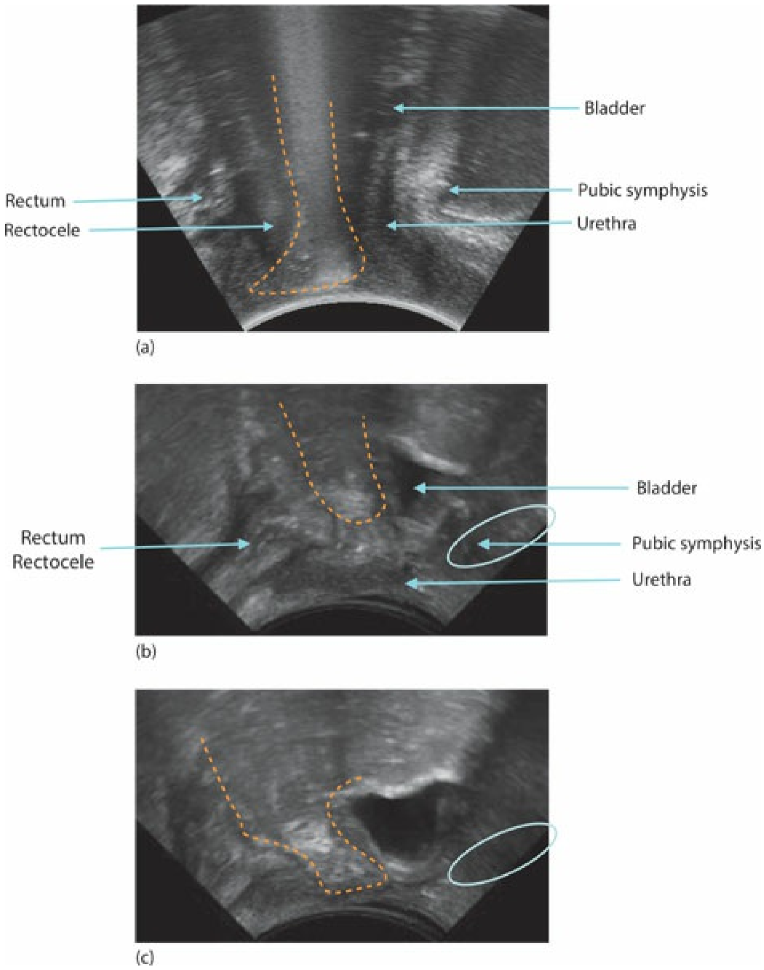

Figure 83.6 (a) Enterocele between the vagina and rectum (dotted line). Note the shadow caused by gas in the bowel. (b) Enterocele between the vagina and rectum at rest (dotted line). (c) On straining, the enterocele descends more not only into the vagina but also into the rectum, causing anterior rectal wall descent.

PREVENTION OF ENTEROCELE

Theoretically, obliteration of the pouch of Douglas and maintaining a normal vaginal axis should prevent enteroceles from developing. Controlled studies assessing prevention of enteroceles are scarce but support modified McCall sutures with reattachment of the uterosacral ligaments to the vaginal vault during hysterectomy [61]. This has long been advocated and several techniques are widely used. At the time of hysterectomy, Cruikshank and Kovac compared three available methods to prevent an enterocele in a randomized controlled trial [62]: obliteration of the pouch of Douglas by suturing the uterosacral ligaments in the midline, called the vaginal Moschcowitz-type operation; the McCall-type culdoplasty, where the uterosacral ligaments are plicated and attached to the vaginal vault and the sutures externalized; and the closing of the peritoneum with a purse-string suture. Up to 3 months postoperatively, all procedures were equally successful (100%). After 3 years, the McCall-type method was found to be superior for enterocele prevention with none of the 32 patients developing a symptomatic enterocele [62].

The prevention of an enterocele after a Burch colposuspension with or without additional pouch of Douglas obliteration by either approximation of the uterosacral ligaments or Moschcowitz-type horizontal purse-string sutures was reported recently [39]. Without Douglas obliteration, postoperative enterocele formation after 3–16 years (mean 9 years) occurred in 19%, whereas after the additional Moschcowitz procedure the incidence was 11% and after uterosacral ligament plication 2%. These differences were significant [39].

Whether extensive distal preparation of the bladder during abdominal hysterectomy with exposure of the pubocervical fascia might contribute to the development of anterior enteroceles is unclear. Also, the utilization of intrafascial hysterectomy might be of value but this has not been assessed systematically. During intrafascial hysterectomy, parts of the endopelvic fascia are maintained in their normal position and plicated over the vaginal vault to prevent separation and subsequent enterocele formation.

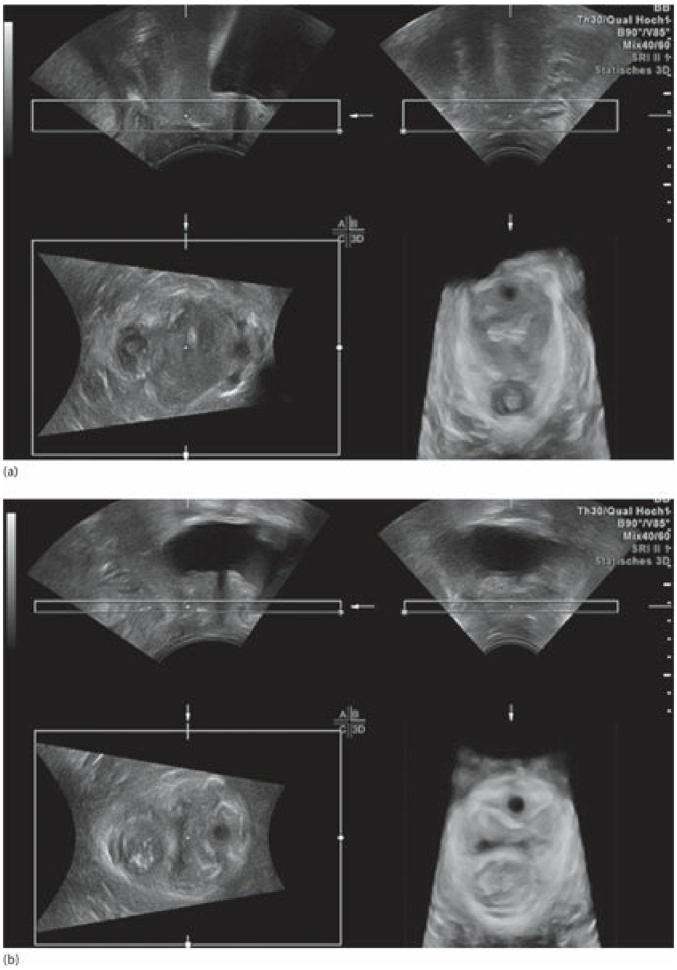

Figure 83.7 Three-dimensional ultrasound. (a) The enterocele between the vagina and rectum can be seen in all three dimensions; the levator is partly damaged but the 3D modulation shows it to be intact in some levels. (b) In comparison, the image shows a rectocele with an intact levator ani, and in the 3D image, the ventral displacement of the posterior vaginal wall is visible.

CONSERVATIVE TREATMENT

Treatment of pelvic organ prolapse depends on the patient's preferences for management, associated symptoms, extent of prolapse, and whether the patient has completed her family. As subjective and objective success and durability of our current surgical prolapse repairs remain limited and the women's longevity is increasing, more patients might ask for conservative options. Conservative treatment of pelvic organ prolapse in general includes the use of pessaries [63] and pelvic floor muscle training [64]. Vaginal pessaries might prevent deterioration of the prolapse and alleviate symptoms of prolapse and are especially useful if there is a long waiting list for surgery [63]. There is an extensive range of mechanical devices available to reduce the prolapse, but literature on success and complications is inadequate especially if isolated enteroceles are considered. Pessaries are an option, and a trial of pessary fitting can easily be performed in clinics and can be managed by educated nurses or continence advisers. In a comparative study, pessaries alleviated pelvic floor symptoms similarly to prolapse surgery [63]. Dissatisfaction with pessary treatment was associated with the development of occult stress urinary incontinence [65].

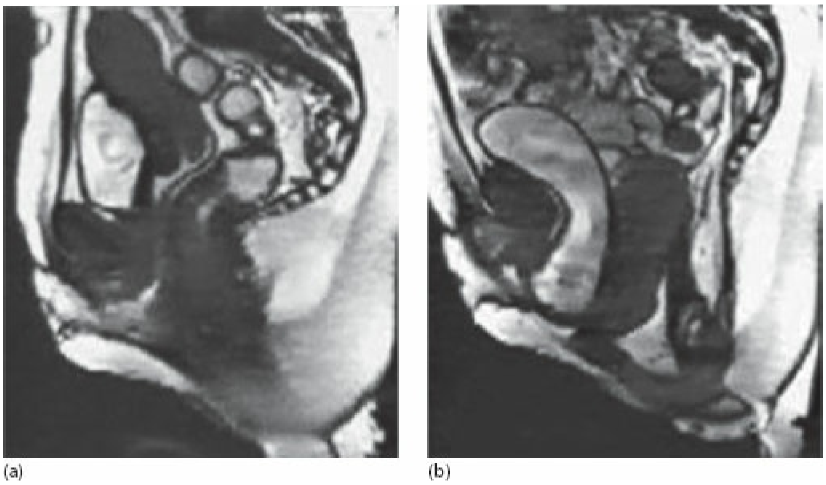

Figure 83.8 Enterocele, considerable pelvic floor and perineal descent, uterine, and bladder prolapse: MRI pictures (a) at rest and (b) during straining.

SURGICAL TREATMENT

There are procedures that only obliterate the pouch of Douglas by plicating the peritoneum like the Moschcowitz or Halban operations or the uterosacral ligaments like the McCall procedure (Figure 83.9). The failure rates are high if there is insufficient pelvic floor support present and an additional solid repair is omitted. Peritoneum alone is not a supportive structure. Therefore, best results might only be achieved when the pouch of Douglas obliteration is combined with surgery to support the vaginal vault or uterus. This can be achieved by native tissue repairs like sacrospinous or uterosacral ligament fixation by using mesh interposition between the vaginal vault and the sacrum (abdominal or laparoscopic sacrocolpopexy) or by vaginal mesh placement (transischiorectal mesh arm placement or direct mesh attachment to the sacrospinous ligament) [66]. An enterocele has been recognized as a risk factor for recurrence of prolapse and for persistence of obstructive symptoms [67,68].

Synthetic mesh is increasingly used in the treatment of posterior vaginal wall prolapse and is meant to reinforce the rectovaginal septum [69]. However, there are few studies that address enteroceles directly. To date, there is no evidence to encourage the use of mesh in the posterior compartment [70]. In the Cochrane review of surgical management of pelvic organ prolapse, the lack of randomized controlled trials for enterocele repair was apparent [70].

The stapled transanal rectal resection for obstructive defecation, rectocele, and/or intussusception has gained popularity although data are limited and ambiguous [71,72].

Operations to Obliterate the Pouch of Douglas

Several horizontal, circular, purse-string-type sutures beginning at the most distal part of the pouch of Douglas/enterocele form the so-called Moschcowitz procedure, which was described by him in 1912 after extensive anatomical studies of rectal prolapse [30]. Although he found it a successful operation in his patients, it has subsequently been associated with a high failure rate and complications like ureteral kinking and small bowel obstruction [73]—although there is a lack of controlled studies. Currently, it is usually used only as an adjunct to major pelvic floor surgery.

Occlusion of the pouch of Douglas as described by *Halban* in his textbook in 1912 includes several sagittal sutures positioned along the pouch in a vertical direction (Figure 83.10) [33]. Although there is less risk for ureteral damage, the ureters should be checked carefully. As with the Moschcowitz operation, this approach has not been studied systematically and is currently performed concomitantly with other pelvic floor surgeries.

Both the Moschcowitz and Halban obliteration were initially described as abdominal procedures but can also be achieved transvaginally or laparoscopically [74,75]. The McCall, Halban, and Moschcowitz procedures and their plentiful variations can be performed prophylactically to obliterate a deep pouch of Douglas or therapeutically to correct an enterocele.

As described earlier in the prevention of enterocele, there are several methods available to close the rectovaginal pouch vaginally but also abdominally. A popular approach is the simple *plication of the uterosacral ligaments* in the midline and the *McCall culdoplasty* with its numerous modifications (Figures 83.9 and 83.10). The principal structure employed is the uterosacral ligament, which is sutured together in the midline with several interrupted stitches or one continuous stitch. Modifications include the incorporation of the vaginal vault or cervix into the sutures. After the suture is passed through the uterosacral ligaments on either side with or without inclusion of the rectosigmoid serosa, it is tied, and the ends are passed through the medial aspect of the upper vaginal wall. Permanent or delayed absorbable sutures should be used although there are no controlled studies to corroborate this. Nonabsorbable sutures should not be passed through the vagina to avoid any sinus formation or abscess. Long-term success rates at 5 and 7 years are very good after the McCall culdoplasty and Douglas obliteration [66,76,77].

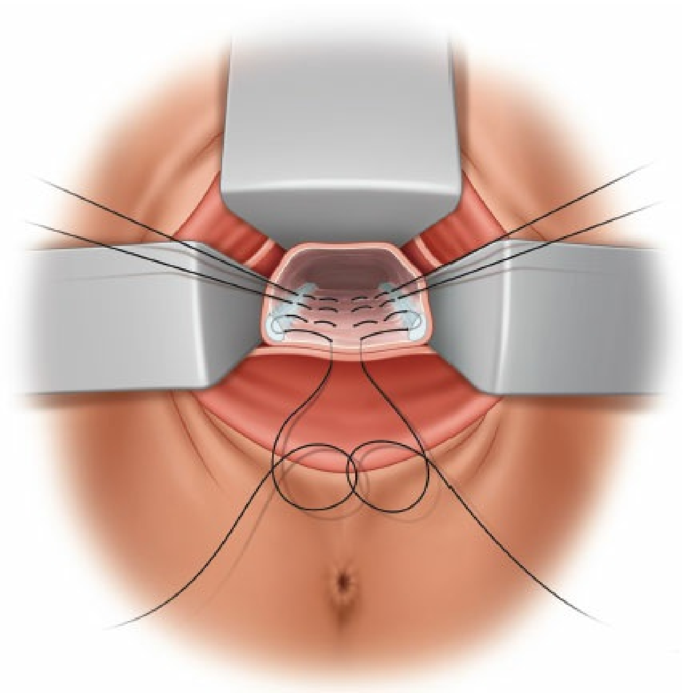

Figure 83.9 McCall procedure: this is one of several different methods of suture placement.

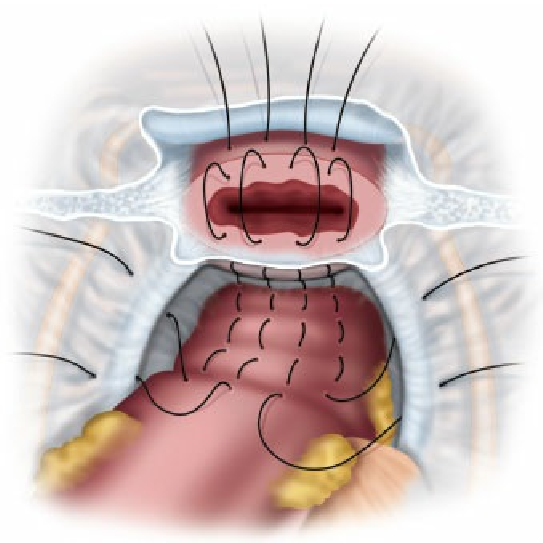

Figure 83.10 **A** combination of a Halban-type pouch of Douglas obliteration with sagittal sutures and a McCall-part with incorporation of the uterosacral ligaments after concomitant abdominal hysterectomy. Note that the anterior and posterior endopelvic fascia are joined over the vaginal vault and incorporated in the pouch of Douglas obliteration.

Vaginal enterocele repair comprises identification, preparation, and opening of the enterocele sac, high closure of the peritoneum with a purse-string suture, and excision of the sac if preferred. The failure rate with this repair was reported at 33% in one study although 72% of women also received a posterior repair and 22% had a Burch colposuspension [78]. A site-specific fascial defect repair with reattachment of the disruption might complete the vaginal repair. Although there are many studies employing grafts and mesh in the posterior vaginal compartment, only few analyze enteroceles separately. Graft reinforcement may reduce enterocele recurrence [79] but controlled studies are lacking.

Effect of Pelvic Organ Prolapse Operations on Enterocele Formation

A surgical technique to suspend the vaginal vault and reattach the endopelvic fascia to the uterosacral ligaments has been studied by Shull et al. [80]. During repair, the concept of prolapse as a hernia is meticulously followed. Using one suture, the anterior and posterior endopelvic connective tissue is connected to the uterosacral ligaments thereby completely covering the vault with this endopelvic connective tissue. Two or three permanent stitches along the ligament might be passed; the more proximal sutures correspond with, the more lateral placements in the anterior and posterior endopelvic connective tissue. The success rate for vault prolapse and enteroceles was reported to be 99% [80]. This method was originally described as a vaginal procedure but using these principal steps and some modification allows it to be performed (at least partly) laparoscopically as illustrated by Miklos et al. [81] and Paraiso et al. [75]. Laparoscopically, the sutures are placed through the uterosacral ligaments, which are later, during the vaginal part of the operation, passed through the anterior and posterior endopelvic connective tissue. Early success rates were 100%, with no recurrent enteroceles [81]. Similar vaginal procedures that include some form of uterosacral ligament plication and address an enterocele have been described by Karram et al. with a 7% enterocele recurrence rate [82].

There are two randomized controlled trials comparing the transvaginal and transanal rectocele repair [83,84]. The authors reported a higher incidence of enteroceles and rectoenteroceles in the transanal repair group. It was suggested that the transvaginal posterior repair with continuous plication of the endopelvic connective tissue from the perineal body to the vaginal apex offers protection against enterocele formation [85]. A posterior colporrhaphy augmented with Vicryl mesh is not superior to a simple posterior repair in terms of recurrent enterocele, according to one randomized controlled trial [86].

Combined Operations for Pelvic Organ Prolapse and Concomitant Enterocele

There are several vaginal, abdominal, and laparoscopic operations that address vaginal vault or uterine prolapse and concomitant enteroceles, but there is a paucity of studies that assess long-term objective and subjective outcomes. Open abdominal [87–89] and laparoscopic sacrocolpopexy [66,75,90,91] may include pouch of Douglas obliteration. Obliteration of the pouch of Douglas with Moschcowitz or Halban sutures or rectovaginal mesh interposition as advocated by Villet et al. [92] has been emphasized by several authors because posterior enteroceles behind the mesh have been observed [88,93]. However, on reviewing the available literature, there seems to be no higher incidence of enteroceles in women who did not undergo any form of pouch of Douglas obliteration [88]. There were 12 cases (2.2%) of recurrent vault prolapse or enterocele described out of 549 patients in whom the pouch of Douglas was obliterated. In 548 patients with no obliteration of the pouch of Douglas, the failure rate of vault prolapse was 4.0% (22 of 548 cases) [94].

In a meta-analysis of two randomized controlled trials, the abdominal sacrocolpopexy with mesh and vaginal sacrospinous colpopexy were equally effective with regard to occurrence of postoperative enterocele (OR 0.77; 95% CI 0.28–2.06) [95,96]. Nonrandomized comparisons of sacrospinous and iliococcygeus colpopexy did not reveal any difference with respect to postoperative enteroceles [97]. The same applies to fixation of the cervix/uterus or vaginal vault to the sacrospinous ligament [98]. Sacrospinous ligament fixation, sacrocolpopexy, and rectopexy appear to be effective in controlling enteroceles [66,87,95,99–101].

SYNOPSIS

An isolated enterocele is rare and usually occurs after pelvic surgery that displaces the vaginal axis, leads to disruption of the anterior and posterior endopelvic connective tissue, or exposes the pouch of Douglas. A deep pouch of Douglas might predispose to enterocele formation. Enteroceles are frequently associated with pelvic organ prolapse in other compartments. Symptoms vary widely and include prolapse sensation, disturbance of defecation and micturition, and dyspareunia. During careful clinical vaginal and rectal examination, enteroceles can usually be identified, but imaging techniques such as ultrasound, viscerography and MRI are helpful.

There are two procedures that close the peritoneum of the pouch of Douglas only: the Moschcowitz operation with horizontal sutures and the Halban method with vertical suture placement. Several other procedures and modifications utilize the uterosacral ligaments. These repairs can be performed vaginally, abdominally, or laparoscopically and are usually combined with other pelvic floor reconstructive surgeries. Operations that address vaginal vault prolapse might be necessary to accomplish a good anatomic and symptomatic result. To date, there are no data available to recommend one particular procedure.

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84 Rectocele: Anatomic and Functional Repair

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INTRODUCTION

Disorders of the posterior pelvic floor are associated with disturbances in the integrity of the pelvic floor musculature and disordered defecation. Since the early nineteenth century, surgeons have performed posterior colporrhaphy to manage tears of the perineum. The supports of the genital organs were largely a mystery, and there was little distinction between prolapse of the rectum, bladder, and uterus. As anatomic concepts developed, surgeons ascertained that the main support of the uterus was the vagina, which in turn is supported by the insertion of the levator ani muscles into the perineum. This concept was the basis for the incorporation of plication of the levator ani muscles into posterior colpoperineorrhaphy, with the surgical goals of restoring the anatomic support of the vagina and rectum without compromising functionality. Until recently, very little attention has been given to the functional derangements that are commonly associated with rectoceles.

In 2010, an estimated 166,000 women underwent surgery for pelvic organ prolapse with a rectocele procedure occurring in approximately half of the cases [1]. The prevalence of rectoceles ranges from 12.9% to 18.6% with an average annual incidence estimated to be 5.7 cases per 100 women years [2,3]. A rectocele is an outpocketing of the anterior rectal and the posterior vaginal wall into the lumen of the vagina and is fundamentally a defect of the rectovaginal septum, not of the rectum. Some rectoceles may be asymptomatic, whereas others may cause such symptoms as incomplete bowel emptying, sensation of a vaginal mass, pain, and pressure. The size of the defect does not necessarily correlate with the amount of functional derangement or severity of bowel symptomatology [4,5]. This chapter reviews the anatomy, pathophysiology, diagnosis, and management of rectoceles.

ANATOMY

In 1839, Denonvilliers first described a layer of fascia found in males, which he named the “rectovesical septum.” Nichols and Milley later recorded the existence of this septum in surgical dissections and autopsies of fresh female cadavers [6]. This layer of connective tissue is fused to the undersurface of the posterior vaginal wall. The rectovaginal “fascia” extends downward from the posterior aspect of the cervix and the cardinal–uterosacral ligaments to its attachment on the upper margin of the perineal body (PB) and laterally to the fascia over the levator ani muscle. Richardson [6] states that the rectovaginal septum and uterosacral ligaments provide suspensory support of the PB from the sacrum. Histologically, the rectovaginal septum shows that the distal portion contains dense connective tissue; the midportion contains fibrous tissue, fat, and neurovascular tissue; and the proximal portion is mostly fat cells [7]. Hence, it is recognized that this is not a true fascial layer. Posterior to the rectovaginal septum lies the rectovaginal space, which provides a plane for dissection. In between the rectovaginal septum and the rectum is the pararectal “fascia”; inside this fibromuscular layer lies blood vessels, nerves, and lymph nodes, which supply the rectum. The pararectal fascia, originating from the pelvic sidewalls, divides into fibrous anterior and posterior sheaths, which encompass the rectum. These layers provide additional support to the anterior rectal wall [7]. Histological study of the smooth muscle content of the posterior vaginal wall of women with prolapse revealed significantly reduced smooth muscle content compared to women without prolapse [8].

Further support is provided by the levator ani, which are composed of paired iliococcygeus, puborectalis, and pubococcygeus muscles. These muscles function to maintain a constant level of baseline tone and a closed urogenital hiatus. This constant basal tone prevents descent of the pelvic viscera on a daily basis. The puborectalis muscle act as a sling that angles the posterior wall about 45° from the vertical and closes the potential space of the vagina. These levator ani muscles also provide a contraction reflex to increased intra-abdominal pressures, preventing incontinence and prolapse. The PB fuses anteriorly in the distal posterior vaginal wall. The anterior portion of the external anal sphincter and its attachment to the internal anal sphincter makes up the posterior portion of the PB. The anterior sacral nerve roots S2–S4, which innervate these muscles, cross the pelvic floor, and are stretched and compressed during labor, increasing the risk of injury [7,9].

ETIOLOGY

Rectoceles were once thought to be a condition affecting only multiparous females and resulting from obstetric damage or increased tissue laxity with aging and menopausal atrophy. However, rectoceles and enteroceles have been noted to occur in approximately 40% of asymptomatic parous women [10]. Shorvon et al. performed defecography on healthy, young, nulliparous, asymptomatic volunteers, noting that 17/21 women had small or moderate-sized rectoceles. Rectoceles may be more prevalent than previously thought and may not be a result of parity [11].

The most common causes of rectoceles are obstetric events. Traumatic obstetric events, which usually occur when the presenting fetal part descends quickly in the second stage of labor, can predispose to rectocele formation. The forces of labor may separate, tear, or distend the pelvic floor, altering the functional and anatomic position of the muscles, nerves, and connective tissues. The rectal “fascia” may separate from the PB, causing a transverse defect and low rectocele. Low rectoceles are isolated defects in the suprasphincteric portion of the rectovaginal “fascia.” They are usually caused by obstetric trauma that disrupts the attachments of the levator ani fascia and bulbocavernosus muscles. A palpable defect at the level of the introitus will be noted on the physical examination.

If middle or high rectoceles form, they may alter the vaginal axis. Laxity of the levator ani secondary to the levator detaching from the PB along the vaginal axis allows the pelvic organs to slide downward, following the newly altered axis. High rectoceles often occur from pathological overstretching of the posterior vaginal wall as the rectovaginal “fascia” does not exist at this level. They may also coexist with congenital deepness of the pouch of Douglas [12].

Rectoceles may occur as a result of pathologic stretching of the pudendal nerves during descent of the fetal head, causing atrophy, and denervation of the pelvic floor muscles. Sultan reported that most damage to the pelvic support occurs in the first vaginal delivery [13,14]. Denervation will probably recover after the postpartum period; however, it has been demonstrated that injury may be cumulative with increasing parity [9]. Increased labor duration and weight of the baby directly influence the perineal damage and denervation of the pelvic floor. This neuropathy can lead to the weakening of pelvic floor muscles and development of a rectocele.

Defecation disorders may account for a subgroup of rectoceles. They may lead to the weakening of the rectovaginal septum by continuous straining against an obstruction. Some patients may suffer from paradoxical sphincter reaction (anismus), which is the unconscious contraction of the voluntary striated muscles when attempting to defecate. This constant straining with bowel movements has been shown to cause or worsen a preexisting rectocele and to increasingly weaken the rectovaginal septum by denervation injury [15]. Anismus eventually leads to the accumulation of stool in the rectum, which may complicate pelvic outlet obstruction and cause a progressive cycle, worsening the rectocele.

Congenital absence of the perineum may mimic a rectocele. This pseudorectocele has its posterior vaginal wall exposed because of the lack of inferior support; this may be corrected by surgical reconstruction of the perineum. Congenital absence allows for deepening of the cul-de-sac and weakening of the rectovaginal septum, leading to the development of a high rectocele and enterocele [10,12].

Clinical Presentation

The symptoms associated with a rectocele are summarized in Table 84.1. Clinical symptoms vary from being nonexistent to severe defecatory dysfunction. A common complaint is constipation, which can occur in 20%–58% of patients with rectoceles [16]. Patients may also complain of incomplete rectal emptying, a sense of rectal pressure, or a vaginal bulge. Patients may describe stool becoming trapped in the rectocele pocket itself. Vaginal digitation/splinting or perineal support is sometimes necessary to facilitate defecation [5,17–19]. It is also important to note that many women with rectoceles do not have to splint with defecation, and women without rectoceles may require splinting [4]. Constipation and straining may worsen the symptoms and lead to left lower quadrant abdominal pain if impaction occurs.

Many nonspecific symptoms, such as rectal pain, bleeding, fecal or gas incontinence, low back pain worsening throughout the day but relieved by lying down, and dyspareunia may occur, as well as many other defecatory disorders.

Table 84.1 Symptoms Associated with a Rectocele

Pelvic pressure
Lower abdominal and/or back pain
Sensation of a vaginal bulge
Dyspareunia
Constipation
Stool trapping in the rectum
Incomplete stool evacuation
Fecal incontinence
Asymptomatic

Physical Examination

A rectocele is detected by observing the bulge in the posterior vaginal wall during maximum Valsalva or cough. The patient may be in the dorsal lithotomy position (for the gynecologist) or in the left lateral decubitus position (for the colorectal surgeon). The use of the split blade of a Sims or Graves speculum will support the apex and the anterior compartment and can aid in visualization. A rectocele can be confirmed with a rectal examination during which anterior displacement of the vaginal wall adjacent to the rectum and the PB is noted. An exam should also be performed with the patient standing, as a vaginal exam in this position may identify a more prominent rectocele and rectovaginal examination will reveal small bowel herniating into this space when an enterocele is present. Of women with rectoceles, up to 80% are asymptomatic and can only be diagnosed on physical examination [9,20]. A rectal examination should be performed to evaluate anal sphincter tone and symmetry along with the integrity of the PB. Finally, it is important to evaluate for rectal prolapse or intussusception.

The current standardized system used for prolapse assessment is termed the pelvic organ prolapse quantification (POPQ) system and was described by Bump et al. [21]. The POPQ is a descriptive system that contains a series of site-specific measurements of a patient’s anterior, apical, and posterior pelvic organ support. This nomenclature has replaced the respective terms cystocele, enterocele, and rectocele as it is often uncertain which specific structures are contributing to prolapse at each segment. Prolapse is measured in centimeters relative to the hymenal ring in relation to the six defined points. Points proximal to the hymen are denoted as negative and points distal as positive. The other landmarks that complete the examination are the genital hiatus, PB, and total vaginal length.

In the POPQ system, the posterior segment includes analogous points ascribed to the anterior segment. Point Ba corresponds to a point 3 cm proximal to the hymen in the midline of the posterior segment. Possible values range from –3 to +3 cm from the hymenal ring. Point Bp represents the most distal portion of the posterior vaginal wall. The minimum value is –3 in the absence of any posterior wall prolapse. In the presence of complete vaginal eversion, the maximum value equals the value of C. The PB is measured from the posterior margin of the genital hiatus to the midanal opening. It is very important to note if the PB is truly a firm palpable muscular structure or just an exaggerated skin flap from previous surgical repair.

Richardson described site-specific defects in the rectovaginal septum that occur in various locations including the superior, inferior, right, left, and midline areas [6]. These defects are often noted at the time of surgical intervention [22]. One study has suggested that locating defects during clinical evaluation of the posterior vaginal wall is often inaccurate when compared to surgical assessment at the time of defect-specific repair [18].

DIAGNOSTIC STUDIES

Imaging Studies

Clinical examination has excellent sensitivity for the indication of a rectocele, making the routine use of imaging studies not indicated for the patient with an isolated rectocele. However, the use of imaging studies does become useful when combined with other ancillary data, especially history and symptomatology for the following patients: (1) symptomatology and physical findings do not correlate, (2) the pelvic anatomy is unusual or altered due to previous pelvic surgery or a congenital defect, and (3) the patient is unable to exert maximal straining during pelvic examination. Imaging results should not be used alone to make treatment decisions as studies have noted that radiographic findings of posterior compartment defects do not necessarily correlate with patient symptomatology [23,24].

Currently, universally accepted radiologic criteria for defining pelvic organ prolapse are lacking [25]. In order to identify a rectocele on imaging, a measurement is made from a reference line to a predefined point. Multiple reference lines have been described in the literature, i.e., midpelvic line, pubococcygeal line, or midperineal line [26,27], leading to the difficulty with interpreting and comparing radiographic results.

Dynamic Proctography or Defecography

The use of contrast media in pelvic fluoroscopy allows the various prolapsed organs to be opacified and seen in real time providing a two-dimensional view of rectal emptying. Traditionally, it has mainly been used in the study of anorectal dysfunction as evacuation proctography, which is also known as defecography. The addition of a cystogram (dynamic cystoproctography) to this modality allows further information to be gained during the assessment especially when the possibility of an enterocele or sigmoidocele exists [28].

The equipment required includes a thick barium paste, a radiolucent toilet, and video equipment. Images are taken at rest, during straining effort, and during and after evacuation.

A rectocele is seen radiographically as an anterior rectal bulge that is usually measured as the distance from the anterior border of the anal canal to the maximal point of the bulge of the anterior rectum into the posterior vagina wall. The cutoff value has not been universally agreed, but some authors consider a depth of >3 cm to be abnormal (many asymptomatic women will be found to have a small rectocele 2 cm or less in depth) [11,29]. Identification of posterior anatomic defects on defecography does not always indicate the need for evaluation. In a study of 52 symptomatic women over the age of 75, posterior compartment defects that were found on imaging did not correlate with reported bowel symptoms [23].

Proctography will also note the finding of postevacuation barium trapping, which may help to explain any evacuation dysfunction [30]. During testing, patients can be taught how to apply manual pressure in the vagina to obtain relief from the symptoms associated with incomplete emptying. Defecography may suggest the diagnosis of anismus, which may be the main contributor to a patient’s bowel dysfunction rather than a rectocele [31]. This has important implications because anismus is treated with biofeedback therapy rather than with surgery.

An enterocele is noted as a herniation of the small bowel into the vagina, rectovaginal space, or both. The vagina and small bowel in the pelvis need to be opacified to obtain this diagnosis. They are most evident after evacuation as a full rectum may obscure its visualization. Sigmoidoceles are noted in approximately 5% of proctograms [25]. However, there still may be false negatives with proctography due to insufficient filling of contrast media into the sigmoid. Identification of a sigmoidocele is important in that a patient may require a sigmoid resection or sigmoidopexy as treatment. Vaginal vault prolapse can also be assessed on postevacuation studies. Proctography will detect many enteroceles and sigmoidoceles not seen on pelvic examination [32]. Studies have shown that enteroceles are only identified approximately 50% of the time on physical examination, which is less than the rates of identifying rectoceles and cystoceles [20,33]. This has been attributed to the failure of the patient to strain maximally during pelvic examination, an impediment that is removed during the evacuation phase of cystoproctography. One study by Altringer et al. found that patient diagnosis was changed in 75% of cases after dynamic cystoproctography [33]. Another benefit is that fluoroscopy will identify the specific organs involved in the prolapse.

Magnetic Resonance Imaging

MRI was first introduced as a diagnostic modality for pelvic organ prolapse by Yang et al. [34]. It has many advantages over dynamic proctography:

- It is able to contrast soft tissue structures well.
- It provides images in numerous different planes; it can examine subtle pelvic floor changes such as superior rectovaginal, paravaginal, and uterine defects.
- It can assess pelvic floor musculature.
- Bony landmarks are easier to identify.
- No catheterization is necessary.
- The patient is not exposed to ionizing radiation.

The main limitation is the supine position usually employed by this modality.

It also shares some of the same advantages, including identifying prolapse not noted on physical examination. In addition, MRI defecography facilitates the diagnosis of anismus and intussusception. Another advantage is that the cervix and vaginal vault are often easier to see on MRI imaging than on fluoroscopy due to leakage of vaginal contrast during fluoroscopy. Fluoroscopy may not detect enteroceles in 20% of cases in which small portions of peritoneal fat enter the rectovaginal space [35]. However, due to greater soft tissue contrast with MRI, the various tissue components can be seen with relative clarity. A systematic review of the use of dynamic MRI in imaging of pelvic organ prolapse revealed that there is lack of any standardization of prolapse assessment and the posterior segment is the most promising segment where imaging can better aid in diagnosis [26].

Disadvantages of MRI include

- Limited access to a vertical configuration magnet
- Increased relative cost to fluoroscopy
- Less physiologic modality than fluoroscopy if performed supine and without evacuation studies
- Most importantly, lack of correlation with clinical staging [36,37]

Ultrasonography

Transperineal ultrasound has been described in the assessment of dynamic function of the pelvic floor [38]. Dynamic anorectal endosonography has also been described and may detect the presence of enteroceles [39]. Dietz and Lekskulchai performed translabial ultrasound to define cutoff points for prolapse on the basis of patient’s symptoms. They concluded that descent of the rectum >15 mm below the symphysis pubis was associated with symptoms [40]. Another study has compared the clinical evaluation using the POPQ system and compared it with the ultrasound assessment to discriminate between women with or without symptoms and found that the ultrasound assessment was not any better [41]. The use of endoanal ultrasound may be indicated on patients with decreased anal sphincter tone to evaluate the integrity of anal sphincter complex, which, if damaged, may lead to consideration of a sphincteroplasty. The role of these alternate modalities in regard to posterior compartment defects has not been fully elucidated and needs further study.

Anal Manometry

Anal manometry measures rectal pressures by a transducer or balloon. Its measurement of rectal sensation evaluates the first feeling, urge, and discomfort; this information is used to distinguish causes of constipation. When an individual is able to tolerate increased volumes without signs of increased discomfort or the urge to defecate, overflow incontinence may occur. Careful consideration must be given to this evaluation process because individuals able to tolerate only small volumes in the rectum may have an irritable rectum, causing incontinence or urgency. Overflow incontinence and irritable bowel syndrome may mimic rectocele symptoms such as incontinence or incomplete emptying. If misdiagnosis of a rectocele is made, rectocele repair may exacerbate these disorders by causing a worsening of symptoms [15,42].

Electromyography and Nerve Conduction Studies

EMG and nerve conduction studies also have been used to evaluate defecation disorders. Obstetrical trauma denervates and causes atrophy of the pelvic floor muscles and tissue, which may lead to subsequent pelvic floor weakness. This denervation may be detected by EMG studies, and pudendal nerve terminal motor latency can be used as a method to detect the causes of pelvic floor weakness.

However, the clinical utility of these evaluations is limited.

Colonic Transit Studies

In colonic transit studies, the patient ingests radiopaque markers, which are measured, and the patient undergoes serial abdominal imaging, typically over a period of 5 days, to follow the markers through the right colon, left colon, sigmoid colon, and rectum. A normal transit time is defined as 80% of the ingested markers being expelled by day 5 [43]. Clinically slow transit time is defined as less than two bowel movements per week over several years. The utility of this test in individuals with rectoceles is controversial; some have normal transit times whereas others have prolonged times [44]. Patients whose symptoms did not improve after repair were found to have longer transit times preoperatively [17].

Management

Treatment should only be undertaken if the patient is symptomatic. Once the clinical diagnosis has been made and (if necessary) confirmed by ancillary studies, the decision to operate or to treat conservatively must be made. Most nonsurgical treatments consist of proper bowel training, following an active lifestyle, and eating an appropriate amount of dietary fiber. These steps are the most important when the main complaint is constipation.

Nonsurgical therapies available for posterior prolapse symptoms include expectant management and/or the use of a vaginal pessary. In a study of 100 patients with symptomatic pelvic organ prolapse, patients successfully fitted with a pessary noted significant decreases in vaginal bulge, pelvic pressure, and the need to splint with defecation (14% down to 0%) [45]. For patients diagnosed with anismus, the use of pelvic physical therapy and/or biofeedback is the mainstay therapy [46,47].

Symptoms that respond well to surgery include pelvic pressure, vaginal bulge, vaginal digitation or splinting (which occurs in 20%–75% of symptomatic patients) and outlet obstruction constipation. Gustilo-Ashby et al. analyzed bowel function at 1 year after vaginal reconstruction in a randomized trial of three techniques of rectocele repair. They concluded that posterior vaginal wall repair was specifically associated with a reduction in symptoms of incomplete emptying and straining [48]. Janssen and van Dijke noted that repair increased rectal sensitivity, causing the urge to defecate earlier as a positive predictor of a good outcome [42]. In the colorectal literature, it has been noted that defecography showing a rectocele >2 cm with symptoms is also a good indicator for surgery; however, this finding has not been conclusive in all studies [16]. All patients who undergo a surgical repair should be appropriately counseled that some bowel dysfunction may persist following surgical repair, especially if a motility disorder is present.

Signs and symptoms that are predictive of a poor surgical outcome include a history of the use of potent laxatives, incidence of preoperative pain, and (possibly) large rectoceles in women who had previously undergone hysterectomy [17,42,49]. A few studies in the colorectal literature have noted that hysterectomy disrupts parasympathetic nerves, causing decreased rectal sensation as well as increased rectal compliance, which may not be improved after anatomic correction [42,49]. The persistence or development of dyspareunia after rectocele repair has been variable and is dependent on the surgical technique. Levator plication and overnarrowing of the introitus may lead to increased dyspareunia, whereas site-specific repair has been suggested to improve dyspareunia [22].

SURGICAL REPAIR

Traditionally, the vaginal and transrectal approaches have been used by gynecologists and colorectal surgeons, respectively, as a result of training and familiarity with each technique.

The transrectal approach is often used if perianal/rectal pathology such as hemorrhoids, anterior rectal wall prolapse, or rectal mucosal redundancy is surgically treated concurrently with the rectocele. A vaginal approach is advocated when

- Other genital prolapse (i.e., enterocele, perineocele, apical, or anterior vaginal wall prolapse) is to be repaired, thus avoiding a second incision
- Compromised anal function exists (a transanal retractor may further compromise function) [57,58]
- An anal sphincteroplasty is also performed

- A high rectocele exists (as the posterior fornix or vaginal apex is not reached through the transanal approach) [50]

When performing transvaginal repair of the posterior compartment, two main methods exist: site-specific repair and traditional posterior colporrhaphy.

Site-Specific Rectocele Repair

According to Richardson, rectoceles are caused by a variety of breaks in the rectovaginal fascia [6]. He described the most common break as being a transverse separation above the attachment to the PB, resulting in a low rectocele. Another common fascial break was considered to result from an obstetrical tear or episiotomy that was incorrectly repaired. This midline vertical defect may involve the lower vagina and extend to the vaginal apex. Less common separations involving a lateral separation down one side of the "fascia" were also found to exist. Richardson also stated that a U- or L-shaped tear in the "fascia" might occur. Since Richardson's observation, there has been an increased movement among gynecologists toward site-specific rectocele repair. Richardson recommended performing the repair with a finger in the rectum, so that defects can be easily identified and "fascia" can be appropriately approximated with interrupted sutures.

Before starting any rectocele repair, the surgeon should approximate the introitus by using Allis clamps bilaterally to help determine the amount of, if any, perineal and vaginal tissue that should be excised to correct a gaping introitus. The repaired opening should accommodate three fingerbreadths, taking into account that the levator ani and perineal muscles are relaxed from general anesthesia and may further constrict postoperatively and with postmenopausal atrophy. This is of great importance in a sexually active patient as overcorrection of the gaping introitus can cause narrowing of the vagina and dyspareunia. Initially, an injection of lidocaine with dilute epinephrine or vasopressin below the vaginal epithelium aids with hydrodissection and hemostasis. Next, Allis clamps are placed on the posterior perineum and a diamond-shaped perineal incision is made with the overlying skin excised. However, if the introitus is already narrow, a vertical perineal incision is performed to maintain adequate vaginal caliber. The length and width of the perineal incision are dependent on the epithelium needed for restoration of the PB. Sharp dissection is usually required over the PB because of previous scarring, and caution should be taken during the dissection of the PB, as entry into the rectum usually occurs within 3 cm of the PB (see Figure 84.1). Mayo scissors are used to dissect a plane in the rectovaginal space bilaterally. The posterior vaginal epithelium is dissected away from the underlying fibromuscularis (see Figure 84.2). This is continued laterally to the tendinous arch of the levator ani and extends inferiorly to the PB as seen in Figure 84.3. The surgeon performs blunt and sharp dissection to a level proximal to the bulge, which may correspond with the vaginal apex as seen in Figure 84.4.

Hemostasis is ensured and irrigation may be used to attain a clean operative field to allow inspection for defects. The rectovaginal "fascia" is inspected by the surgeon inserting a finger of the nondominant hand into the rectum. The rectal wall is brought forward, distinguishing the uncovered muscularis (fascial defect) from the muscularis covered by the smooth semitransparent rectovaginal septum. According to the plane of dissection and the location of the defect, frequently the rectovaginal "fascia" must be mobilized off the lateral vaginal epithelium. Defects are individually isolated and repaired with an absorbable No. 0 or No. 2-0 suture. Figure 84.5 is highlighting a transverse defect followed by Figure 84.6 with surgical reapproximation. The surgeon must continuously examine the vaginal caliber to ensure a smooth contour and a diameter of three fingerbreadths. A perineorrhaphy is performed, if indicated, followed by closure of the vaginal epithelium with a running No. 2-0 absorbable suture.

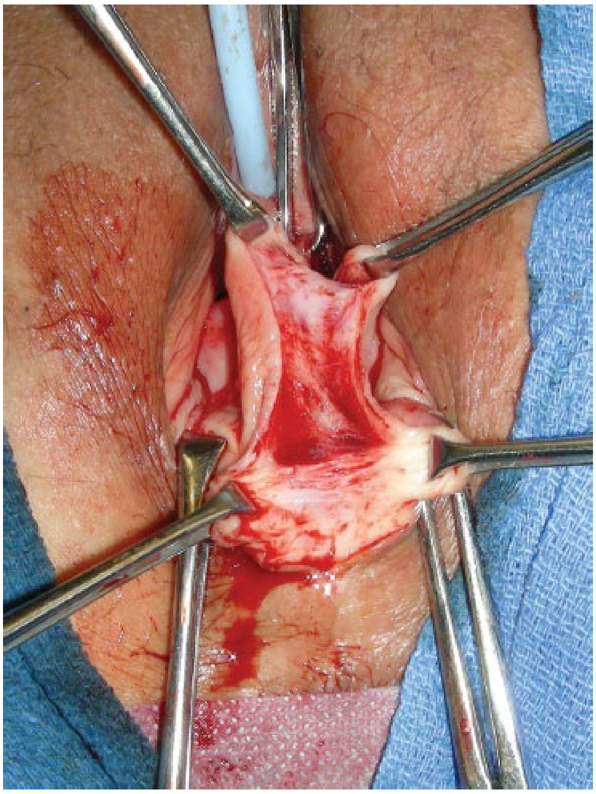

Figure 84.1 Initial view following incision of posterior vaginal epithelium.

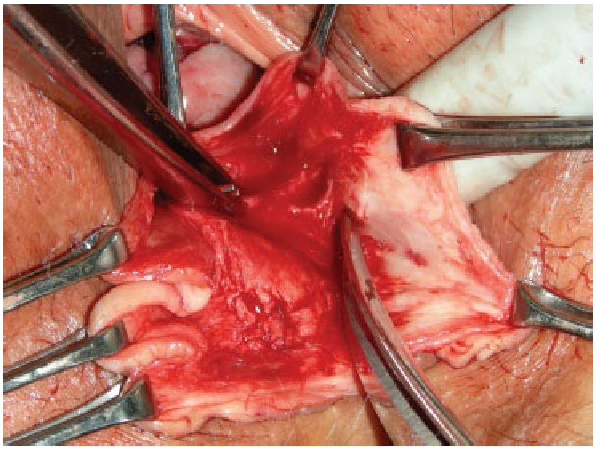

Figure 84.2 Dissection of the fibromuscularis from the lateral posterior vaginal epithelium.

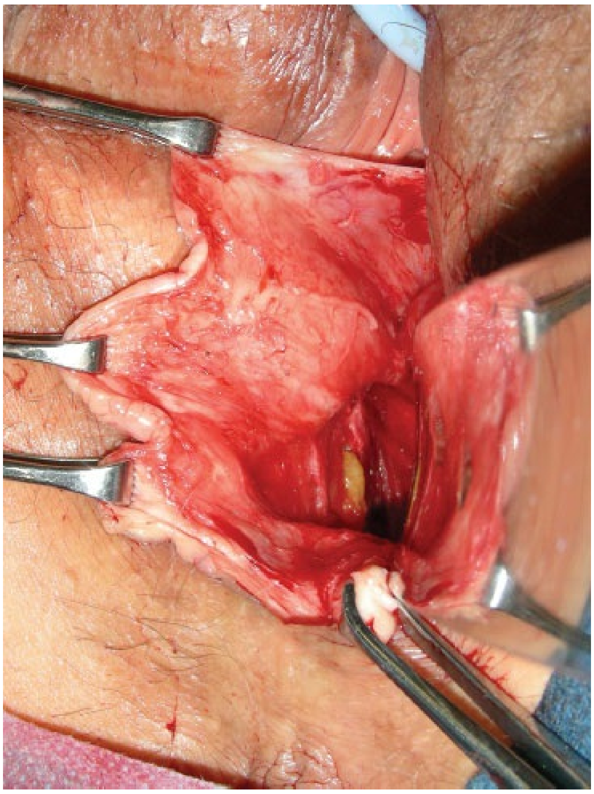

Figure 84.3 Lateral dissection to the level of the levator ani tendon.

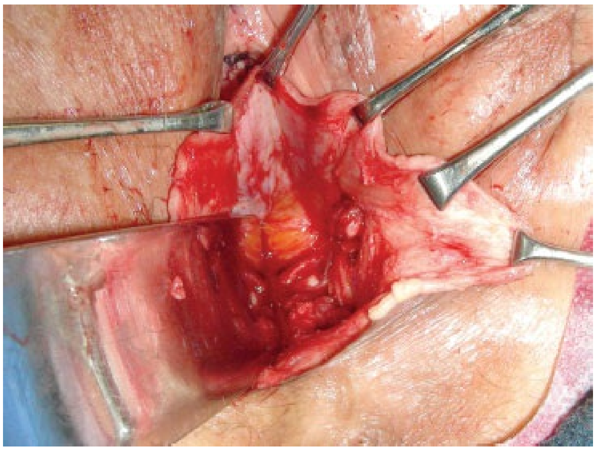

Figure 84.4 Apical dissection to a level beyond the identified defect.

Perineorrhaphy is routinely performed along with a rectocele repair. The goal of a perineorrhaphy is to reconstruct the PB and restore anatomic support. The PB consists of the anal sphincter, the superficial and deep transverse perineal muscles, the bulbocavernosus muscles, and the junction of the rectovaginal fascia with the anal sphincter. A triangular incision is made at the level of the posterior hymen extending to the midline of the perineal skin, and the vaginal epithelium is dissected off the underlying musculofascial complex. The bulbocavernosus muscles are then plicated in the midline using No. 0 absorbable suture in an interrupted fashion followed by the plication of the transverse perinei muscles. Care should be taken to prevent ridging and narrowing of the introitus in a sexually active woman. If dyspareunia is a concern, a triangular incision at the perineum and/or plication of the bulbocavernosus muscles should be avoided.

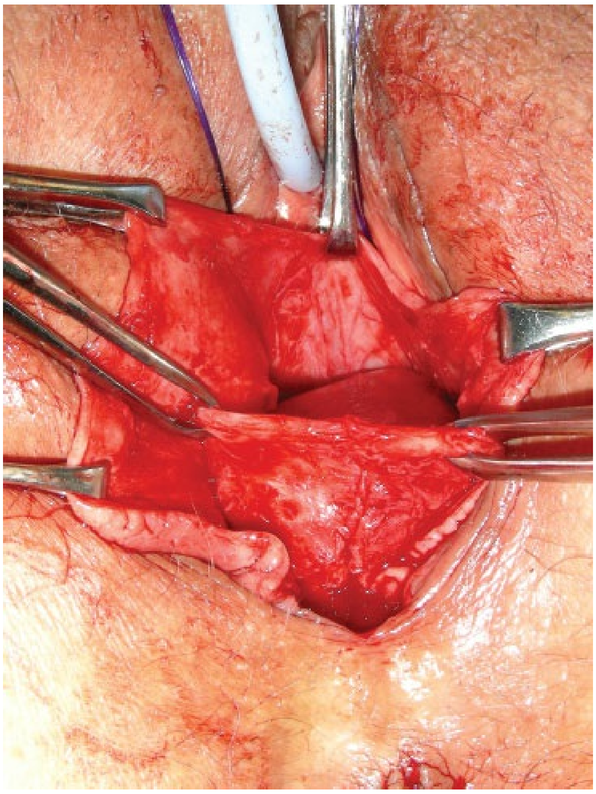

Figure 84.5 Transverse rectocele defect grasped between the Allis clamps.

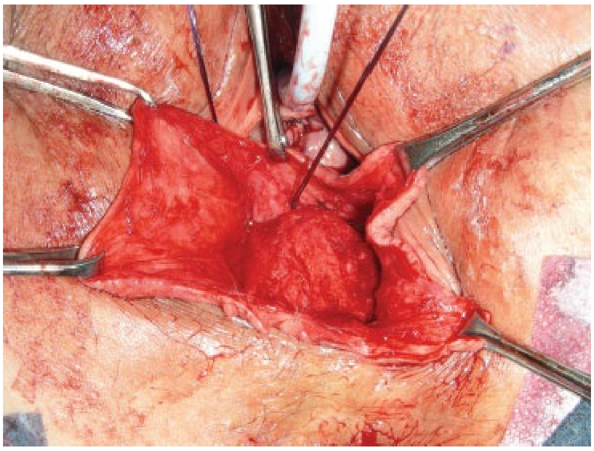

Figure 84.6 Site-specific surgical correction of defect.

Whereas rectocele repair is accomplished for identification of the fascial defect and reapproximation of the connective tissue, evaluation of the levator hiatus is an entirely different issue. In women who have an enlarged levator hiatus, it may be appropriate to place another set of interrupted sutures horizontally to provide a muscular posterior shelf and narrowing of the levator hiatus. This may be a source of postoperative pain and/or dyspareunia. This portion of the operation is not necessary in all patients and is independent of rectocele repair.

Traditional Posterior Colporrhaphy

The traditional rectocele approach has been described and illustrated by Nichols, Wheeless, and others. The opening of the vagina is previously described, via a midline incision or by removal of a triangular wedge of vaginal wall. Some surgeons will place an initial row of No. 2-0 interrupted sutures reapproximating the rectovaginal fascia. The rectocele is then depressed in the midline with the surgeon's finger to reveal the margin of the puborectalis portion of the levator ani muscle. With the rectocele still depressed, a No. 2-0 absorbable suture is used to plicate the fibromuscularis in an interrupted fashion as seen in Figure 84.7. These sutures should be placed in close proximity to each other to repair any noticeable defects. The surgeon should intermittently evaluate the repair both vaginally and rectally to ensure minimal ridging or narrowing of the vagina. The posterior vaginal wall epithelium is trimmed if necessary and closed with continuous 2-0 absorbable suture. The PB is repaired as previously described.

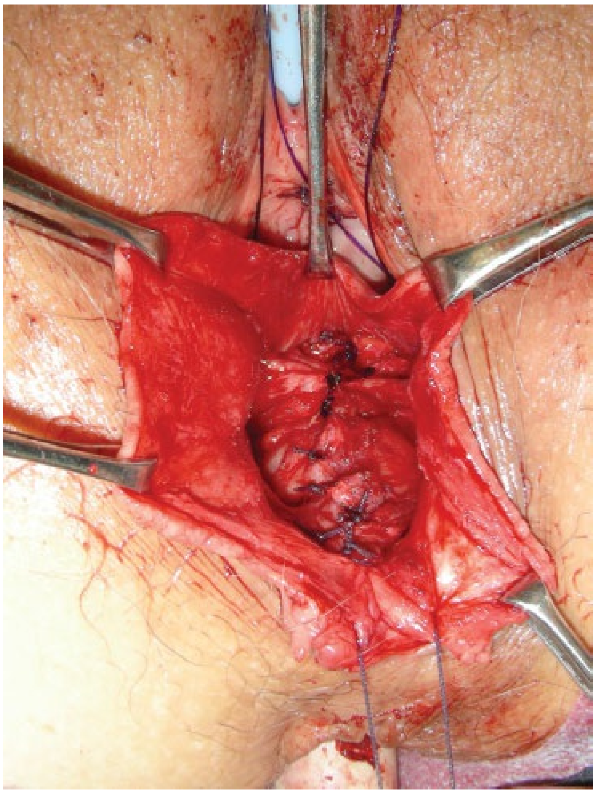

Figure 84.7 Traditional colporrhaphy with tissue plication in the midline.

Transrectal Approach

The transrectal approach was described by Sarles et al. [51] and is routinely utilized by colorectal surgeons in repairing distal rectoceles. Patients are placed in a prone or jackknife position. An anal retractor is used expose the anterior rectal surface. An incision of the anterior rectal mucosa is made 1 cm above the dentate line. The submucosal plane is sharply dissected 8–10 cm from the anal verge. Bleeding is controlled by electrosurgical coagulation. Dissection is performed anteriorly and laterally; the resulting bare areas are plicated using interrupted absorbable suture; the suture includes the rectal muscle and the rectovaginal septum. If the vaginal mucosa is perforated, the stitch is removed. The rectal mucosal flap is excised and a second layer of 3-0 absorbable sutures closes the mucosal defect. The advantage of this approach is that it allows for correction of rectal prolapse and hemorrhoids simultaneously. The disadvantage is that a perineorrhaphy or sphincteroplasty cannot be performed simultaneously. Also, a high rectocele repair is difficult to perform with the same incision.

The stapled transanal rectal resection procedure is another form of endorectal repair that is utilized for the treatment of outlet dysfunction constipation associated with rectocele. A circular stapler and a purse-string suture anoscope are introduced. A portion of the rectocele and the internal rectal prolapse, including the mucosa and muscularis, are resected and stapled off. Varying success rates have been reported following the procedure; however, complications such as fecal urgency, fistula formation, or postsurgical stenosis may occur [52,53].

Graft Augmentation

Graft materials have been employed in both the traditional posterior colporrhaphy and the site-specific technique in an attempt to strengthen the repair and prevent recurrences. Graft materials that have been used are xenografts, allografts, and permanent synthetic material. Some authors advocate the use of mesh or graft in recurrent rectoceles in patients with deficient rectovaginal fascia and weak tissue, in the presence of advanced prolapse, or with the coexistence of risk factors such as obesity and/or chronic constipation [54]. Following repair of the rectocele, either via a traditional colporrhaphy or via a site-specific repair, the graft is then attached to the rectovaginal and pubocervical fascia proximally, levator ani muscles laterally, and PB distally with a series of interrupted sutures [54]. The repair of a high rectocele can be challenging as there is commonly a deficiency of rectovaginal and pubocervical fascia proximally. However, this repair can be facilitated by entry into an associated enterocele with attachment of the graft to the distal uterosacral ligaments.

Abdominal Sacral Colpopexy (Colpoperineopexy)

An abdominal approach may be utilized for the correction of a rectocele when accompanied by apical prolapse. This may be performed through an open incision or laparoscopically with or without robotic assistance. Identification of the right ureter is confirmed prior to opening the pelvic peritoneum. The peritoneum is opened in a vertical fashion from the sacral promontory to the pelvic cul-de-sac along the lateral border of the right colon and medial to the right ureter. Next, sharp and blunt dissection is used to expose the anterior longitudinal ligament of the sacrum over S1–S2 being mindful of the surrounding vasculature. With the aid of an end-to-end anastomosis sizer placed in the vagina and the rectum, the rectovaginal space is identified and entered sharply. This is an avascular space and if one is in the correct plane, limited bleeding should occur. This plane is then dissected down to the level of the PB and bilateral pubococcygeus muscles for correction of a distal rectocele and perineal descent (colpoperineopexy) if indicated. Following this, dissection of the bladder off the anterior vaginal wall is performed to the level of the bladder neck. The mesh is then attached to the PB and levator musculature (if indicated) and posterior and anterior vaginal wall with a series of interrupted No. 2-0 absorbable sutures. Finally, the mesh is affixed to the anterior longitudinal ligament with two separate sutures of No. 0 permanent suture taking care not to place the mesh on excess tension and avoiding the middle sacral vessels. The mesh is then trimmed and the peritoneum is closed over the mesh using a No. 2-0 absorbable suture. Of note, this procedure may also be combined with a vaginal approach to further correct a distal rectocele.

RESULTS AND COMPLICATIONS

Posterior Colporrhaphy without or with Levatorplasty

Anatomic cure rates after posterior colporrhaphy with or without levator plication range from 76% to 96% after a mean follow-up period of 12–42 months [44,55–59]. Results are shown in Table 84.2. One study revealed an improvement from 100% to 88% cure rate for constipation in 24 patients that were prospectively followed and evaluated pre- and postoperatively with standardized questionnaires, defecography, colon transit studies, anorectal manometry, and electrophysiology. This study also showed improvement in symptoms of vaginal bulge from 21% preoperatively to 4% postoperatively. The rate of de novo dyspareunia was 8% [55].

In comparison, two studies showed a modest improvement (<50%) [56] or an increase [60] in the constipation rate (from 22% to 33% after a mean follow-up of 52 months). Reasons suggested for these observations include (1) unselective approach used in offering surgical treatment for persistent constipation [69], (2) retrospective analysis of the data [1], and (3) the possibility that patients with a pathologic transit study might have a less favorable outcome with respect to constipation [55,59]. In addition, the study by Kahn and Stanton showed an increase in rates of incomplete bowel emptying and fecal incontinence (4% preoperatively vs. 11% postoperatively) after posterior colpoperineorrhaphy [60]. In contrast, Maher et al. reported an anatomic cure rate of 87% and 79% at 12 and 24 months, respectively. All bowel function parameters showed improvement with overall patient satisfaction of 97% [61]. Additionally, a prospective study of 60 women who underwent posterior colporrhaphy with or without perineorrhaphy reported significant improvement of subjective bowel symptoms within 3–6 months postoperatively. Bowel evacuation scores improved by 42% and continence by 37% based on a validated questionnaire given pre- and postoperatively [62]. Both subjective and objective outcomes following repair of the posterior compartment vary due to the various surgical procedures that routinely accompany rectocele repair, making the ability to compare and contrast the current studies difficult.

Table 84.2 Posterior Colporrhaphy

Study	*n*	Mean follow-up (months)	Levator plication	Anatomic cure (%)	Defecatory dysfunction (%)	Vaginal bulge (%)	Vaginal digitation (%)	Fecal incontinence (%)	Dyspareunia (%)	De novo dyspareunia in sexually active patients, *n* (%)
Mellgren										
Preoperative	25	12	Yes	96	100	21	50	8		2 (8)
Postoperative	25				88	4	0	8		
Kahn[a]										
Preoperative	231	42	Yes	76	22	64	33	4		27 (16)
Postoperative	171				33	31		11		
Weber										
Preoperative	53	12	No[b]							14 (26)
Postoperative	53									
Sand										
Preoperative	70	12	No	90						
Postoperative	70									
Maher										
Preoperative	38	12.5	No	89	100	100	100	3	37	1 (4)
Postoperative	38				13	5	16	0	5	
Abramov[a]										
Preoperative	183	12	No	82				17	8	18 (11)
Postoperative	183							18	17	
Paraiso										
Preoperative	37	12	No	86	80		43		56	
Postoperative	33				32		19		45	

[a] Prospective, all other studies retrospective.

[b] One of the patients had a levator plication.

Dyspareunia appears to be associated with posterior colporrhaphy. Komesu et al. compared women who underwent posterior repair to those who did not in a cohort study. Preoperatively, there was no difference in dyspareunia in both groups, but postoperatively, the prevalence of dyspareunia was significantly lower in the group without posterior repair [63]. De novo dyspareunia rates after levatorplasty have been reported to range from 12.5% to 16%. An additional study showed an increased rate of sexual dysfunction (18%–27%) after levatorplasty [60]. A study by Weber et al. reported an even higher dyspareunia rate of 26% after posterior repair only (except for one patient who had a levator plication) and 38% after a posterior repair with Burch colposuspension [57]. The postoperative introital calibers in patients with or without dyspareunia were not different. The reasons for the unexpectedly high rate of dyspareunia in that study are unclear.

Site-Specific Rectocele Repair

The surgical outcomes after a defect-specific rectocele repair are summarized in Table 84.3 [22,63–67]. Anatomic cure rates range from 56% to 100% after a mean follow-up period of 3–18 months. Improvements in constipation were seen in 43%–84% of patients [22,64,67] with de novo constipation rate of 3%–4%; however, Kenton et al. found that the rate of constipation was not statistically significantly different after 1 year of follow-up and attributed this to the predominantly medical etiology for the disorder. In addition, the lack of a standardized definition of constipation contributes to the difference in constipation rates seen in the literature after rectocele repair. Improvements in the symptoms of manual evacuation was noted in 36%–63% [22,64,67] with a de novo rate of 7% in one study [22].

Most studies report some improvement in dyspareunia after site-specific repair (35%–92%) [22,64–67] (Table 84.3). The only study where site-specific rectocele repair was not combined with other prolapse or incontinence surgery followed 42 women for a period of 18 months. Improvement in sexual function was reported in 35% and there were no patients who developed de novo dyspareunia [66]. Other studies report a de novo dyspareunia rate of 0%–8% [22,64–67]. Abramov et al. compared outcomes of site-specific repair to posterior colporrhaphy. This study showed higher anatomic recurrence rate in the site-specific repair group with similar rates of dyspareunia and bowel symptoms [68].

One prospective randomized trial by Paraiso et al. compared three surgical techniques of rectocele repair: traditional colporrhaphy, site-specific repair, and site-specific rectocele repair augmented with a porcine-derived graft on 106 patients. The results included both anatomic results and subjective condition-specific validated quality of life questionnaires. Anatomic cure of prolapse ≤ Stage II at 1 year was comparable between the traditional colporrhaphy and the site-specific groups (86% vs. 78%). When compared to the site-specific graft-augmented group, both the traditional colporrhaphy and site-specific rectocele repair were improved (54%) and statistically significant. Also, recurrence of the prolapse to or beyond the level of the hymen developed in 20% of those who underwent a graft-augmented approach, compared to 7.1% in the traditional colporrhaphy group and 7.4% in the site-specific repair group. There was no significant difference between the groups in regard to preoperative or postoperative dyspareunia, but improvement in sexual function was noted after rectocele repair, regardless of the technique used [69].

Graft-Augmented Approach

The ideal mesh or graft material used to augment repairs of pelvic fascial defects remains elusive. It should be inexpensive and improve recurrence rates, should not be rejected, and should cause no detriment to sexual and bowel function. The results of graft augmentation are summarized in Table 84.4 [54,59,61,70–73]. Anatomic cure rates range from 92% to 100% (12–30-month follow-up) with the transvaginal approach and 89% to 95% (12–29-month follow-up) with the transperineal approach. De novo dyspareunia rates range from 3% to 20%.

In a prospective, controlled trial, Sand et al. randomly assigned 160 patients to undergo anterior and posterior colporrhaphy with (80 patients) or without (80 patients) polyglactin 910 mesh reinforcement.

Preoperatively, 91 women had a rectocele to the midvaginal plane, 31 to the hymenal ring, and 22 beyond the introitus. In the treatment group, a strip of mesh was incorporated into the imbricating endopelvic “fascia” during the midline plication. Thirteen recurrent rectoceles were noted at 1 year follow-up, with no differences observed between the two groups (10% vs. 8%) [59].

Another randomized trial by Sung et al. evaluated the use of porcine subintestinal submucosal graft as an augmentation for rectocele repair compared to native tissue repair alone. A total of 80 patients were allocated to each group with results reported at 12 months. In the nongraft group, 8.6% (6/70) compared to the graft group 12% (8/67) experienced anatomic failure that was defined as points Ap or Bp −1 or greater with a p value of 0.5. Subjectively, there were no statistically significant differences between the groups for vaginal bulge symptoms or defecatory dysfunction. The authors concluded that augmentation with porcine submucosal graft was not superior to native tissue repair at 12 months [74].

Table 84.3 Site-Specific Repair

Study	*n*	Mean follow-up (months)	Anatomic cure (%)	Defecatory dysfunction (%)	Vaginal bulge (%)	Vaginal digitation (%)	Fecal incontinence (%)	Dyspareunia (%)	De novo dyspareunia in sexually active patients, *n* (%)
Cundiff									
Preoperative	69	12	82	71	100	39	13	29	1 (2)
Postoperative	61			39	28	25	8	19	
Kenton									
Preoperative	66	12	90	41	86	30	30	28	3 (7)
Postoperative	46			57	9	15		8	
Porter									
Preoperative	125	6	82	60	38	24	24	67	3 (4)
Postoperative	72			50	14	21	21	46	
Abramov									
Preoperative	124	12	56	33	11		15	8	12 (11)
Postoperative	124			37			19	16	
Singh[a]									
Preoperative	42	18	92	57	78		9	31	
Postoperative	33			27	7		5	38	
Glavind[a]									
Preoperative	67	3	100	40				12	2 (3)
Postoperative	67			4				6	
Sardelli[a]									
Preoperative	51	27	59	59			14	3	1 (2)
Postoperative	51			45			8	4	
Paraiso[a]									
Preoperative	37	12	78	85		58		48	
Postoperative	29			35		21		28	

[a] Prospective, all other studies retrospective.

Table 84.4 Graft-Augmented Rectocele Repair

Study	*n*	Mean follow-up (months)	Anatomic cure (%)	Graft type	Defecatory dysfunction (%)	Vaginal bulge (%)	Vaginal digitation (%)	De novo dyspareunia in sexually active patients, *n* (%)	complications
Oster									
Preoperative	15	30	100	Autologous dermis		80	100		1 infection
Postoperative	15				33	0	12	3 (20)	
Watson									
Preoperative	9	29	89	Polypropylene	100	100	100		
Postoperative	9				12	0	12	1 (14)	
Mercer-Jones									
Preoperative	22	12	95	14 polypropylene	95	86	64	1 (5)	2 superficial and 1 deep infections
Postoperative	22			8 Vipro II (polypropylene/ polyglactin)	32	23	23		
de Tayrac									
Preoperative	26	13	92	Cadaveric dermis	19				1 de novo fecal incontinence
Postoperative	25				16			1 (7)	3 mesh erosions 2 de novo defecation disorders
Lim									
Preoperative	90	3	84	Polypropylene/polyglactin					2 hematomas
Postoperative	90							2 (3)	9 mesh erosions
Milani[a]									
Preoperative	63		94	Prolene	45				13% mesh erosion rate
Postoperative					30			4 (6)	
Altman[a]									
Preoperative	32	38	62	Acellular porcine dermis (Pelvicol)	100				
Postoperative	23				<50				
Sand[a]									
Preoperative	73	12	92	Polyglactin					
Postoperative	65								
Paraiso[a]									
Preoperative	31	12	54	Acellular porcine dermis (Fortagen)	97		51	50	
Postoperative	29				21		7	28	
Sung[a]									
Preoperative	79	12	88	Porcine subintestinal submucosal graft					
Postoperative	67					11.9		7 (12.5)	

[a] Prospective, all other studies retrospective.

The use of nonsynthetic grafts may have a lower erosion rate, although this has yet to be confirmed in randomized controlled trials. In a retrospective review by Dwyer and O'Reilly, polypropylene mesh was used as an overlay for repair of large or recurrent anterior and posterior compartment prolapse. Forty-seven women had mesh placed in the anterior compartment, 33 in the posterior compartment, and 17 had mesh placed in the both compartments. Of the erosions that occurred in nine women (9%), six lesions were in the posterior segment. One woman required surgical repair of a rectovaginal fistula [75]. Milani et al., in a series of 31 women, undergoing posterior colporrhaphy with polypropylene mesh, showed anatomic cure rate of 100%. The rate of dyspareunia increased from 6% preoperatively to 69% postoperatively. The rate of mesh erosion was 6.5% [73]. In contrast, at 12 months of follow-up, Kohli and Miklos reported no complications (including erosion or fistula) in 43 women after placement of a cadaveric dermal graft [54]. At 1-year follow-up of 35 women, Dell and O'Kelley noted no erosions after the use of a porcine collagen mesh that contained fenestrations in the graft material. They also described 6/41 patients that experienced wound separation and delayed vaginal healing when they previously employed the nonfenestrated form of the same material. The authors suggested that the fenestrations allowed immediate contact between the vaginal mucosa and underlying host tissues, thus facilitating appropriate tissue ingrowth [72].

The use of synthetic mesh for vaginal reconstruction has become a highly discussed topic in the past few years. In 2008, the Food and Drug Administration (FDA) released a public health notification that was followed by an update in 2011 regarding the use of transvaginal mesh. The results of a systematic review from 1996 to 2011 stated the routine use of vaginal mesh compared to native tissue repairs, particularly in the posterior compartment, was shown to be of no additional benefit [76]. Previously, the majority of studies comparing vaginal mesh kits to native tissue repair were retrospective in nature [73,77,78]. Since the FDA announcement, the prospective research for vaginal mesh kits has drastically increased. Many randomized controlled trials have been performed comparing native tissue repair to vaginal mesh kits in multiple compartments, with a few reporting results specifically for the posterior compartment [79–81]. In 2010, Iglesia et al. conducted a randomized controlled trial of 65 women comparing transvaginal mesh to native tissue repair that was halted due to a mesh extrusion rate of 15.7% at a median follow-up of 9.8 months [82]. Results after 1 year reported a rectocele recurrence rate of 21.9% in patients with mesh compared to 18.2% recurrence without mesh in the posterior compartment; however, the findings were not statistically significant. There were no significant differences identified with new onset dyspareunia between the two groups (9.1% [mesh] versus 21.4% [no mesh]) [79]. At 3 years, both subjective and objective data were evaluated between the two groups showing no statistically significant differences in cure rates. No differences were observed at 3 years in regard to prolapse stage or individual POPQ points in patients with or without vaginal mesh [83]. It is important to note that the subjects in this study underwent a wide range of vaginal reconstructive procedures and the results may not be generalizable to patients with rectoceles alone. Currently, there is insufficient evidence for the use of mesh or graft material in the repair of the posterior compartment [84,85], and based on the current data, native tissue repair appears to have similar objective and subjective cure rates without the risk of mesh extrusion.

Transanal Approach

The majority of studies are based on the experience of colorectal surgeons whose primary focus is defecatory dysfunction and anal incontinence. Anatomic cure rates range from 70% to 98% after a 12–74-month follow-up [17,42,86–92]. Reported rates of symptomatic improvement are 58%–100% after the transrectal approach. De novo anal incontinence may be a concern, especially in those with occult sphincter lacerations, as a transanal retractor may further compromise function. One study reported a 38% rate of new-onset fecal incontinence after this approach [56].

In a combined transvaginal/transanal approach, van Dam et al. found an anatomic cure rate of 72% in 89 women after a mean follow-up period of 52 months. Rates of constipation were 63% preoperatively and 33% postoperatively, while difficulty in evacuation decreased from 92% to 27%. However, rates of dyspareunia were found to be 28% preoperatively and 44% postoperatively, in which the authors attributed to the transvaginal portion of the operation [93].

Studies comparing the transvaginal and transanal approaches have been mainly retrospective [56,94] or prospective and nonrandomized [93]. Previously, retrospective reviews suggested equivalence between transanal and transvaginal rectocele repairs [56,94]; however, current evidence appears to suggest transvaginal repair is superior to the transanal approach. A retrospective study in 2005 by Roman et al. identified 71 females who underwent transanal rectocele repair from 1992 to 2000. All procedures were performed by a single surgeon. In a survival analysis, a 50% rectocele recurrence rate was noted over a mean 6-year time frame [92].

Also, in 2004, in a randomized controlled trial of 30 patients by Nieminen et al. [95], 15 patients underwent transanal rectocele repair, while the other 15 underwent vaginal posterior colporrhaphy. They excluded patients with other symptomatic prolapse or compromised anal sphincter function as evidenced by colon transit study. At 12 months follow-up, 14 (93%) patients in the vaginal group and 11 (73%) in the transanal group reported improvement in symptoms ($p = 0.08$). The need to digitally assist rectal emptying decreased significantly in both groups, from 11 to 1 (73%–7%) for the vaginal group and from 10 to 4 (66%–27%) for the transanal group ($p = 0.17$ between groups). Rectocele recurrence rates were 7% and 40%, respectively ($p = 0.04$), and enterocele rates were 0% and 27%, respectively ($p = 0.05$). A 27% improvement rate in dyspareunia was noted; none of the patients developed de novo dyspareunia.

The Cochrane review on surgery for pelvic organ prolapse identified three studies comparing transvaginal and transanal rectocele repairs. After review, patients who underwent transvaginal repair were found to have fewer subjective and objective findings of recurrent prolapse. Therefore, with the current evidence available, transvaginal correction of the posterior compartment appears to be superior over a transanal approach in the prevention of recurrent rectocele [58].

CONCLUSIONS

Posterior compartment defects are often identified on physical exam and may or may not be symptomatic. Rectocele repair is a common surgical procedure and occurs in approximately half of the patients undergoing prolapse repair. A thorough history and physical examination is paramount before considering surgical or nonsurgical interventions. The use of pelvic floor imaging may complement the clinical assessment of the pelvic floor, but its use needs to be further studied and defined prior to advocating its routine use. Numerous surgical techniques and materials exist for repairing the posterior compartment. These surgical decisions should be made based on the current evidence and the surgeon's experience.

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85 Vaginal Approach to Fixation of Vaginal Apex

May Alarab, Salomon Zebede, and Harold P. Drutz

INTRODUCTION

Caring for women with pelvic floor disorders has become an increasingly important component of women's health care. Pelvic organ prolapse (POP) is a major health issue for women; it affects almost half of all women over 50 years of age, with a lifetime prevalence of 30%–50% [1]. It is estimated that the lifetime risk of surgery for either stress urinary incontinence (SUI) or POP is 20.0% by the age of 80 years [2]. With the current generation of women maintaining a more active lifestyle into an older age, it is likely that an increasing number of women will seek treatment for prolapse, conditions requiring increasing expertise on the part of the urogynecologist and pelvic reconstructive surgeons in the management of these conditions. It has been projected that the demand for care for pelvic floor disorders will increase by 35% between 2010 and 2030 [3].

Conservative management of POP using vaginal pessaries is a known and effective method in treating this problem; however, patients are more inclined toward more permanent solutions to correct their symptoms, while maintaining body image and coital function. Numerous surgical operations have been described for the support of the vaginal apex at the time of hysterectomy or for the posthysterectomy vault prolapse and are performed either abdominally or vaginally. In this chapter, we will describe the different vaginal approaches for fixation of the vaginal apex.

HISTORY

Genital prolapse in antiquity finds its roots in the Ebers Papyrus (1500 BC) [4].

Soranus of Ephesus (AD 98–138) is commonly considered the foremost gynecologic authority of antiquity. He proposed vaginal hysterectomy for uterine prolapse in AD 120 [5]. The vaginal reconstructive approach was first described by Zweifel in 1892 [6] and involved suspension of the prolapsed vagina to the sacrotuberous ligament. In 1909, White suspended vaginal vault to the tendinous arch of the obturator fascia via a transvaginal approach [7]. A transvaginal technique suspending the vaginal vault to the sacrouterine ligaments just below the sacral promontory was reported by Miller in 1927 and then popularized by Shull in the late 1990s [8,9]. In 1951, Amreich described a transgluteal and later a transvaginal approach to attach an everted vagina to the sacrotuberous ligament [10]. Sederl first tried the use of sacrospinous ligament for this purpose in 1958 [11]. Richter, in 1967, introduced the sacrotuberous fixation in Europe [12] and 1 year later described the use of the sacrospinous ligament as an improvement technique for the suspension of the vaginal vault; the procedure that was made popular in the United States by Randall and Nichols in 1971 [13]. Since then, it has been increasingly popular. Cruikshank and Cox have described the use of sacrospinous ligament fixation as an adjuvant to vaginal hysterectomy and colporrhaphy for marked uterovaginal prolapse in the presence of poor integrity of the endopelvic fascia [14]. In 2001, the FDA approved the first "mesh kit" for the correction of POP in the United States (Posterior IVS Tunneller, Tyco Healthcare LP, Norwalk, CT). While initial publications regarding this device looked promising, the IVS Tunneller is now rarely used, presumably due to reports of high failure and complication rates [15–17]. However, the IVS Tunneller remains important in the history of transvaginal "mesh kits" because it served as the "predicate" device for subsequent kits. In the year 2004, the first transvaginal mesh trocar-based kits that use a transobturator or transgluteal approach to suspend the vagina were introduced. In 2006–2007, the nontrocar or single-incision kits were introduced to the market.

ANATOMICAL CONSIDERATION

The normal support of the pelvic floor is based on three mechanical principles: (1) the uterus and vagina are attached to the walls of the pelvis by the endopelvic *fascia* that suspends the organs from the pelvic side walls, (2) the levator ani muscles constrict the lumens of these organs until they are closed forming an occlusive layer on which the pelvic organs may rest [18], and (3) the flap valve, where the vagina suspended in such a way that it rests against the supporting wall adjacent to it, increases in pressure forces the vagina against the wall pinning it in place [19]. The part of the pelvic *fascia* that attaches the uterus to the pelvic walls (i.e., the broad, cardinal, and uterosacral ligaments) is called the parametrium; a similar tissue that attaches the vagina to the pelvic walls is called the paracolpium. Unlike other ligaments in the body that are made of dense connective tissue, these ligaments contain blood vessels, nerves, and fibrous connective tissue (smooth muscle, collagen, and elastin), a composition that reflects their function as neurovascular and supportive structures. The paracolpium is attached to the upper two-thirds of the vagina and consists of two portions: apical supporting tissues consist of a relatively long sheet of tissue that converges from their broad origin on the lateral pelvic walls and sacrum to their attachment to the lateral walls of the vagina. Defective suspension at this level presents clinically as uterine or vaginal vault prolapse. The midportion of the vagina is attached laterally and more directly to the pelvic sidewalls. This connective tissue stretches across the vagina transversely between the bladder and the rectum and includes the pubocervical anteriorly and the rectovaginal *fascia* posteriorly. At this level, the vagina becomes closer to the pelvic sidewall, and failure of midvaginal support presents as a cystocele, rectocele, or both. In the distal vagina, the vaginal wall fuses from 2 to 3 cm above the hymenal ring laterally to the levator ani muscle, posteriorly to the perineal body, and anteriorly it blends with the urethra and is embedded in the connective tissue of the perineal membrane, with no intervening paracolpium. The attachment at this level is so dense that it leaves the vagina with no mobility, and displacement of the levator muscle, the perineal body, or the urethra will carry the vagina along with it [20].

SURGICAL ANATOMY

Pelvic endopelvic connective tissue (often called *fascia*) and the pelvic ligaments have been used to suspend the prolapsed vagina. The nerves and vessels surrounding these anchoring structures may be susceptible to injury during surgical repair. In order to reduce the hemorrhage and postoperative pain secondary to colpopexy operations, it is essential to understand the anatomical relationships of the pelvic organs and their adjacent neurovascular structures. The pararectal space is filled with fat and loose areolar tissue through which the middle rectal artery and the nerve of the levator ani muscle course [21]. The sacrospinous ligament, located within the substance of the coccygeal muscle [22], extends from the lateral sacrum to the ischial spine (Figure 85.1a). The average length of the sacrospinous ligament was measured to be 43.04 ± 6.58 mm [23], and it divides the sciatic notch into the greater and lesser sciatic foramina. The inferior gluteal artery, after originating from the internal iliac artery, descends inferolaterally passing through the greater sciatic foramen leaving the pelvis and crossing the upper border of the sacrospinous ligament 8.54 mm from the ischial spine, accompanied by the inferior gluteal vein. After emerging from the sacral plexus, the inferior gluteal nerve passes close to the vessels and leaves the infrapiriform foramen crossing the upper border of the sacrospinous ligament 13.82 mm from the ischial spine. Leaving the pelvis, the inferior gluteal complex crosses the sciatic nerve posteriorly and branches inside the gluteus maximus muscle. The internal pudendal artery, after originating from the anterior branch of the internal iliac artery and accompanied by the internal pudendal vein, reaches the upper border of the ligament and leaves the infrapiriform foramen accompanied by the pudendal nerve. The pudendal complex lies a maximum of 5.5 mm medial to the ischial spine. The sciatic nerve is situated the most laterally among the structures emerging from the infrapiriform foramen; on average, it is measured to be 25.14 ± 3.94 mm lateral to the ischial spine [23] (Figure 85.1b). The coccygeal branch of the inferior gluteal artery passes immediately behind the midportion of the sacrospinous ligament and pierces the sacrotuberous ligament in multiple sites. During the procedure of sacrospinous vault suspension, placing the sutures immediately medial and inferior to the ischial spine may have a potential of injury to the pudendal vessels. However, placing the sutures superior to the midportion of the ligament may cause injury to the inferior gluteal artery. The coccygeal branches of the inferior gluteal artery might be injured by any deep suture that traverses the full thickness of the ligament. Thompson has shown, by dissecting 23 female cadavers, that placing the sutures through the sacrospinous ligament 2.5 cm or more medial to the ischial spine along the superior border of the ligament and not through the full thickness reduces the risk of complications [24].

ETIOLOGY AND PATHOPHYSIOLOGY

The opening in the levator ani muscle, through which the vagina and urethra pass, is called the urogenital hiatus of the levator ani (through which prolapse occurs); the rectum, although passes through the opening, is not included in the hiatus because the levator ani muscle attaches directly to the anus and the external anal sphincter. The hiatus is surrounded by the pubic bones anteriorly, the levator ani muscle laterally, and the perineal body and the external anal sphincter posteriorly. The levator ani muscle is always tonically contracting, keeping the urogenital hiatus closed. It closes the vagina, urethra, and rectum by compressing them against the pubic bone. The continuous contraction of the levator ani muscle keeps the hiatus closed and prevents any opening in the pelvic floor through which prolapse may occur. As long as the levator ani muscle functions normally, the pelvic floor is closed; the ligaments and fascia are under no tension. When the muscles relax or are damaged, the pelvic floor opens and the pelvic organs lie between the high abdominal pressure and the low atmospheric pressure of the introitus. Then, the organs must be held in place by the ligaments, which can sustain the load for short periods of time but eventually become damaged and fail to hold the vagina in place. This failure is due not only to acute damage of the ligaments and connective tissue but also from inability of these structures to repair themselves. The injury to the connective tissue in the pelvis is due to rupture rather than stretching [25]. Neuromuscular injuries to the pelvic floor are associated with the development of POP [26]. The health and function of the pelvic floor muscles provide significant protection to the ligaments to avoid POP. The neuromuscular damage of the pelvic floor that occurs during parturition plays a major role in the etiology of prolapse; however, the repetitive loads on the pelvic floor resulting from increases in abdominal pressure also play a significant role in the development of this disorder. This results from continuous heavy lifting, chronic obstructive pulmonary disease, obesity, chronic constipation, and large fibroids or tumors; direct damage to the muscle that may result from previous pelvic surgery, spinal cord conditions and injury, and thinning of the muscle and fascia that happens with postmenopausal atrophy and attenuation; and finally the collagen status of these patients. It has been shown that women with Marfan or Ehlers–Danlos syndrome have high rates of urinary incontinence and POP. This finding supports the hypothesized etiologic role of connective tissue disorders as a factor in the pathogenesis of these conditions [27]. These facts have been confirmed by recent studies showing decreased collagen and smooth muscle content in women with POP with or without SUI regardless of age, parity, BMI, or smoking [28] and increased collagen breakdown in SUI and POP groups compared to controls [29].

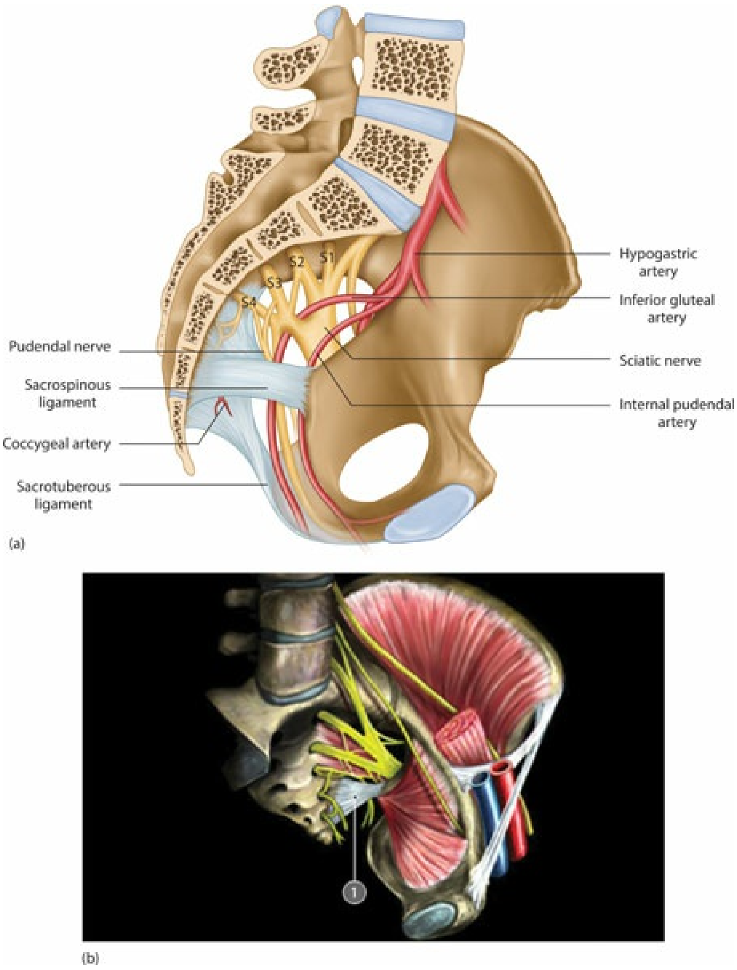

Figure 85.1 (a) Left hemipelvis. The sacrospinous ligament covered by the coccygeus muscle extends from the ischial spine to the sacrum. The pudendal neurovascular structures pass beneath the sacrospinous ligament at the ischial spine. The inferior gluteal artery passes between the sciatic nerve and the sacrospinous ligament. (b) The roots of the sciatic plexus converge obliquely toward the subpyramidal canal that is limited superiorly by the pyramidal muscle and inferiorly by the sacrospinous ligament itself (1 = sacrospinous ligament). (a: From Thompson J et al., *Obstet Gynecol*, 94, 973, 1999. With permission; b: Redrawn from www.websurg.com with courtesy of M. Cosson and IUGA.)

SYMPTOMS, PRESENTATION, AND EVALUATION

Patients' symptoms of vaginal apical prolapse can vary from being asymptomatic to various complaints of vaginal pressure, feeling a bulge or something coming down, coital difficulties, and urinary symptoms (urgency, frequency, incontinence, or voiding dysfunction) or bowel emptying difficulties due to concomitant anterior and posterior vaginal wall defect. Burrows et al. looked at the correlation of symptoms with the severity of POP and concluded that the more advanced the pelvic prolapse, the less likely the women will have SUI and the more likely to manually reduce prolapse to void; however, prolapse severity was not associated with sexual or bowel symptoms [30]. A study correlating symptoms in women with or without enterocele showed that women with enterocele were likely to be older and postmenopausal, have had hysterectomy or vaginal prolapse surgery, had more advanced apical and posterior vaginal prolapse, but showed no significant difference in bowel function symptoms [31].

Patients may present to a gynecologist, urologist, or colorectal surgeon depending on their major complaint. A detailed history is undertaken, including the chief complaint, urinary and bowl symptoms, obstetrical history, medical history, and current medication. A traditional clinical history taken in women presenting with prolapse should ideally be supplemented by a tool to assess the symptoms and impact of the POP on the patient's life. This lends some degree of objectivity to the preliminary assessment and can be compared with a postintervention questionnaire to evaluate the efficacy of the intervention. The Pelvic Floor Distress Inventory (PFDI) and the Pelvic Floor Impact Questionnaire (PFIQ) and their shortened versions PFDI-20 and PFIQ-7, are popular, reliable, and validated quality of life questionnaires for women with pelvic floor disorders [32].

A careful speculum and digital examination at rest and with straining is performed to quantify POP. By placing the Sims speculum along the posterior vaginal wall and asking the patient to bear down, we look for anterior compartment prolapse, and the opposite is done to examine the posterior vaginal wall. A digital rectal–vaginal examination while the patient is straining is performed to differentiate between a high rectocele and an enterocele. There are numerous grading systems for prolapse [29–31,33–36], the Pelvic Organ Prolapse Quantification (POPQ) system [36] produced by the International Continence Society has gained popularity among urogynecologists to describe, measure, and stage prolapse. The careful vaginal examination is vital to clearly identify the site specific vaginal wall prolapse. Other variables should be taken into consideration at the time of assessment of the prolapse. The time of the day the examination is done should be recorded. Prolapse can change throughout the day, with it being more pronounced at the end of the day, especially after prolonged standing. Position of the patient during examination, straining, and traction on the prolapse and fullness of the bladder are other variables that can influence the assessment [37].

SUI has been strongly associated with POP [38,39], and it has been shown that mild to moderate POP is often associated with SUI; however, women with severe POP rarely complain of urine leakage because of urethral kinking and increased urethral resistance with the urogenital prolapse in an unreduced state [40–42]. After correction of the prolapse, the leakage problem will be manifested in what is called occult or latent SUI—which is one of the common problems seen with complex vault prolapse [43]. The incidence of occult SUI can vary from 22% to 80% and can be quite distressing [44,45]. As a result, it is recommended to perform a prolapse reduction stress test to identify patients at risk of developing SUI after their reconstructive surgery. Although a negative preoperative prolapse reduction stress test alone may reduce the risk of de novo SUI, some recent studies suggest that this test alone may not be sufficient to determine the need for anti-incontinence surgery at the time of reconstructive pelvic surgery [46,47]. A recent study has demonstrated that prophylactic incontinence surgery using a midurethral sling during vaginal prolapse surgery will result in a lower rate of urinary incontinence at 12 months; however, this benefit should be weighed against higher rates of adverse events [47]. In order to balance the risks and benefits and to help us better counsel patients, a model for predicting the risk of de novo SUI in women undergoing POP surgery has been developed and published by the Pelvic Floor Disorders Network [48]. This model has shown that it outperforms preoperative stress testing, prediction by experts, and preoperative reduction cough stress testing [48].

The investigations, which may be required prior to any prolapse repair, are accurate preoperative urodynamic studies, with prolapse reduced to examine the expected outcome after repair, cystourethroscopy, and abdominal–pelvic ultrasound. In addition, transanal studies may be required if there is a history of fecal incontinence. Other tests include defecography, anorectal motility studies, pudendal motor nerve latency studies, and magnetic resonance imaging of the pelvic floor.

VAGINAL SURGICAL TECHNIQUES IN SUPPORTING THE VAGINAL APEX

The vaginal approach to prolapse surgery carries significant low postoperative morbidity. It does not require additional skill or the cost of laparoscopy; however, it requires a well-trained pelvic surgeon, who is well versed in different techniques and has the ability to repair other pelvic defects simultaneously. In addition, it provides the option to perform the operation under regional or general anesthesia. Various techniques have been described for the treatment of vault prolapse, these include sacrospinous vault suspension, iliococcygeus muscle fixation, uterosacral ligament fixation, McCall culdoplasty, posterior intravaginal slingplasty (IVS), and more recently total vaginal mesh (TVM) kits. We will outline the different techniques of restoration of the vaginal apical defect.

Sacrospinous Vault Suspension

Indications

The main indication for sacrospinous ligament suspension is to correct total procidentia, posthysterectomy vaginal vault prolapse with an associated weak cardinal uterosacral ligament complex, and posthysterectomy enterocele [49,50]. This procedure suspends the vaginal apex to the sacrospinous ligament, either unilaterally or bilaterally, typically using an extraperitoneal approach [51]. Bilateral sacrospinous ligament fixation has been described and recommended in patients with recurrent vault prolapse [52,53] or a desire to maintain a wide vaginal vault [54]. The procedure has also been described as a prophylactic step at the time of vaginal hysterectomy against subsequent vaginal vault prolapse [13,55], as well as in young and elderly patients with marked prolapse, who wish to retain their uterus [56–60].

Contraindications

A short vagina, usually attributed to prior repairs is considered to be a contraindication to performing sacrospinous colpopexy; the surgeon needs to ensure that there is an adequate vaginal depth to allow the attachment of the vault to the ligament without any tension. Surgical inexperience is another contraindication, and the procedure should only be performed by experienced reconstructive pelvic surgeons.

Surgical Techniques

Postmenopausal patients with vaginal atrophy usually benefit from preoperative local hormone treatment to improve the quality of the tissues and help to improve the vascularity of the operative site. Rahn et al. have shown that using vaginal estrogen application for 6 weeks preoperatively increased the synthesis of mature collagen, decreased the degradative enzyme activity, and increased the thickness of the vaginal wall, suggesting that this intervention improves both the substrate for suture placement at the time of surgical repair and the maintenance of the connective tissue integrity of the pelvic floor [61]. Preoperative intravenous prophylactic antibiotics and prophylaxis against venous thromboembolism (with intermittent pneumatic compression devices and/or pharmacological thromboprophylaxis with unfractionated heparin or low-molecular-weight heparin depending on the surgical risk following the guidelines set forth by the American College of Chest Physicians and supported by the American College of Obstetrics and Gynecology) [62,63]. After the patient receives the appropriate anesthesia, having in mind the feasibility of regional anesthesia with the vaginal approach, the surgery is performed with the patient in dorsolithotomy position. An intraoperative assessment allows the surgeon to identify the extent of the prolapse and to confirm that the vault can reach the ligament without tension. In a marked uterovaginal prolapse, a vaginal hysterectomy is performed first in the usual fashion, if a cystocele is present; it will be dealt with next. Some authors have suggested that the addition of polyglactin mesh may provide extra support to the anterior vaginal wall; however, a randomized trial by Weber et al. used the absorbable mesh as an overlay, which did not improve the cure rate compared to the standard anterior colporrhaphy [64]. Sand et al., in a larger prospective randomized controlled trial, found the addition of mesh of polyglactin 910 mesh placed in the plication to be useful in the prevention of recurrent cystocele at 1-year follow-up [65]. Altman et al., in a randomized controlled trial, compared the use of a trocar-guided, transvaginal polypropylene mesh repair kit with traditional colporrhaphy in women with anterior vaginal wall prolapse and found that the trocar-guided mesh kit for cystocele repair resulted in higher short-term rates of successful treatment at a price of higher rates of surgical complications and postoperative adverse events including mesh extrusion, de novo SUI, and surgical reintervention to correct mesh exposure [66]. When an enterocele is identified, usually noted as a distinct loss of the rectovaginal fascia with a sudden protrusion of the enterocele sac, it’s demarcated by the pubocervical *fascia* anteriorly and the rectovaginal septum posteriorly. The sac is dissected free, opened, and a high ligation is performed with a 2-0 delayed absorbable purse-string suture [67]. The sacrospinous ligament suspension is usually performed via the posterior approach and is started with a longitudinal incision in the posterior vaginal wall, after infiltration with a dilute solution of epinephrine (1:200,000). The incision extends from the introitus to the vaginal apex. The epithelium is dissected laterally on both sides, penetrating the right rectal pillar into the pararectal space near the ischial spine (Figure 85.2a). The right ischial spine is palpated and using a combination of sharp and blunt dissection, a window is created between the ligament and the rectovaginal space (Figure 85.2b). It is important to split the *fascia* in front of the ligament that is palpated as a cord-like structure or visualized, to ensure that the suture placement will involve the body of the ligament (Figure 85.2c). The rectum is mobilized medially with the fingers and with a Heaney or Breisky vaginal retractor protecting the rectum medially. Two delayed absorbable sutures (PDS I, Ethicon, San Angelo, TX) are placed into the ligament at two fingerbreadths medial to the spine and just inferior to the superior border of the ligament, hence avoiding injury to the pudendal complex (Figure 85.2d). Care must be taken not to penetrate the full thickness of the ligament to avoid injury to the inferior gluteal vessels and nerve. The two sutures are paired, loaded separately onto a Mayo needle, and passed through the angles of the vaginal epithelium at the level of the vault, 1–2 cm apart, and held for later tying [68]. If bilateral suspension to be performed, one suture will be placed per site [69].

The anterior rectocele and the rectovaginal septum are repaired by interrupted absorbable sutures (Vicryl 2-0), the levator muscles are approximated separately with (Vicryl No. I) suture, but left untied at this stage, and the ends are held. The bulbocavernosus muscle is approximated and held, and the vaginal skin is closed with continuous locking suture until the level of the introitus. The sacrospinous sutures are tied, pulling the vault onto the ligament. It is important to ensure a close approximation, avoiding a suture bridge between the vault and the ligament. Finally, the levator and bulbocavernosus muscle sutures are tied, and the vaginal skin is closed. A slight deviation of the vaginal apex to the right would be noted at the end of the procedure, this may be of benefit as the vault will be no longer subject to the intra-abdominal pressure after the operation [50]. At the end of the surgery, the bladder is drained transurethrally; a vaginal pack is inserted in the reconstructed vagina, all to be removed after 24 hours.

The earlier description of the procedure involves exposure of the ligament and placement of the sutures under direct vision [50,70], the ligament is grasped with an Allis forceps, and Deschamps ligature carrier is used to place the suture onto the ligament. This technique requires more dissection in the pararectal space [70]. Another option is to use the Miya hook ligature carrier (Figure 85.3a). Also, the Sharp technique has been described using the Shutt suture punch system [71]; with its automatic suture retrieval, this method proved to be a quick and easy way especially in obese patients. The downside is that the sutures have to be of rigid material such as nylon or polypropylene. Watson has described using the Endo Stitch (a laparoscopic suturing instrument) to pass the suture through the sacrospinous ligament. With this tool, the depth of the penetration is predictable, without the need for a retrieval hook [72]. The same advantages have been described with the Raz Anchoring System [73]. More recently, some authors have described using the Capio suture-capturing device demonstrating a low risk of complications and a reduction in operative time and blood loss when compared to the traditional technique [74–76] (Figure 85.3b). On the other hand, Morley and DeLancey [50] found that with the help of traditional retractors, a straight or curved needle holder could position the suture without much difficulty. Their other modifications include creating a neovaginal apex via a circumscribing incision at the apex [50]. They have recently published on the long-term patient satisfaction using this technique and a supplemental video in the article that better describe their technique [77,78].

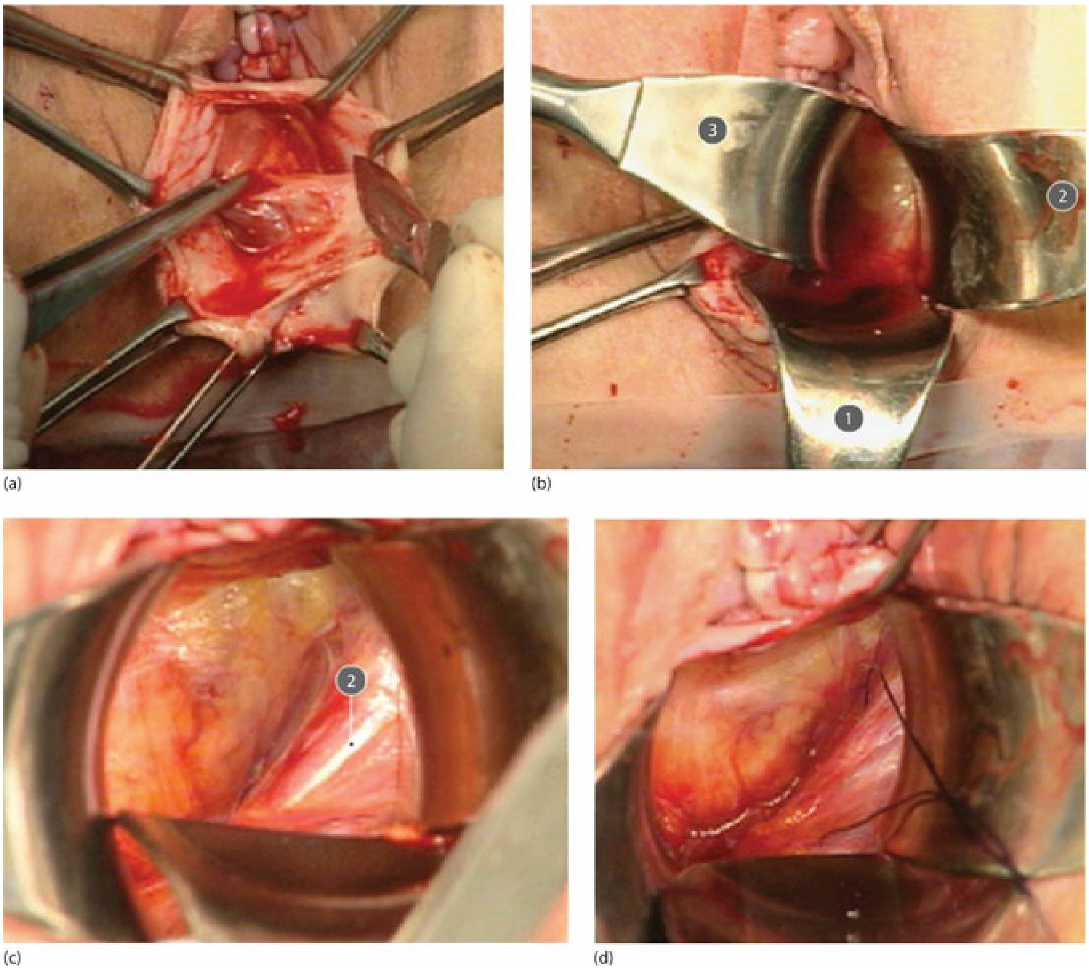

Figure 85.2 (a) Rectovaginal dissection. (b) Opening the fossa (1–3 = proper positioning of the Briesky retractors). (c) Ligament location and visualization (2 = left sacrospinous ligament). (d) Suture placement. (Redrawn from www.websurg.com with courtesy of M. Cosson and IUGA.)

The anterior sacrospinous vault suspension has been described, where the ligament is approached through an anterior vaginal incision; Goldberg et al. had shown that with this technique, there was a slight increase of the vaginal length, with a decrease in the recurrence of the anterior vaginal wall prolapse [79].

The choice of the suture used remains controversial; some advocate the use of absorbable sutures [11,12,21,50,80], and others use delayed absorbable or permanent sutures [13,49,50,52,68,81,82] to allow adequate time for fibrosis and scarring between the sacrospinous ligament and the vaginal apex. When absorbable sutures are used, they are passed through the full thickness of the vagina and tied over the vaginal epithelium. This is unlike permanent sutures where they should be passed submucosally in a double helix and tied beneath the vaginal epithelium [68,69].

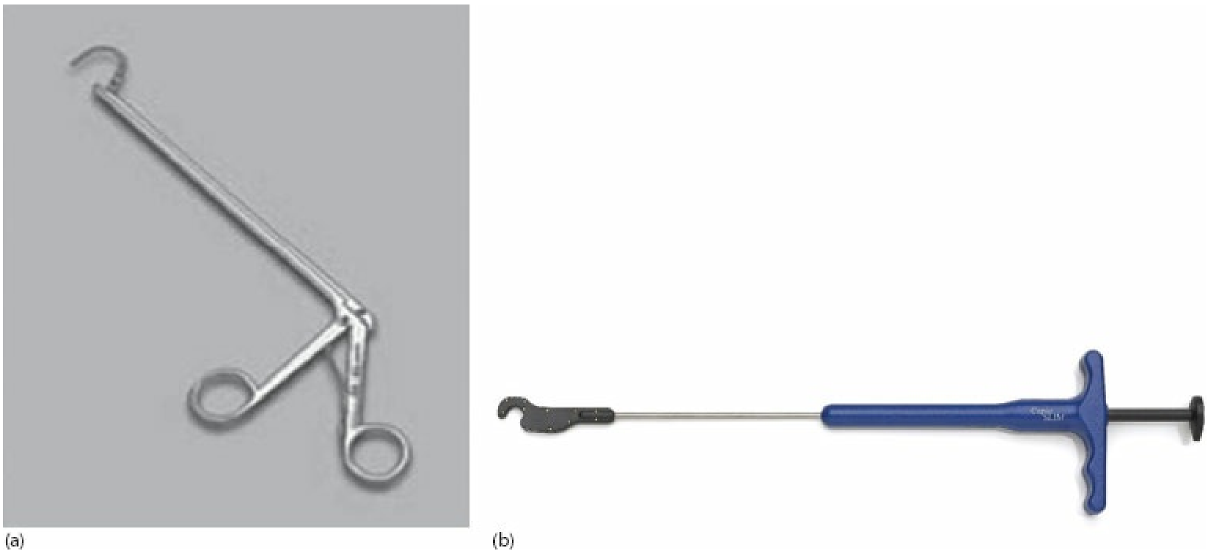

Figure 85.3 (a) Miya hook. (b) Capio suture-capturing device.

Results

Numerous studies on sacrospinous colpopexy have been published, including multiple retrospective studies, three prospective studies, three randomized controlled trials including sacrospinous vault suspension compared with abdominal sacrocolpopexy, and one randomized control trial comparing it to uterosacral vault suspension [50,52,69,77,78,82–97]. Most of these data were recently summarized by Barber and Maher in a review article [51]. The lack of objective outcome measures and the variety of definitions of success made the data difficult to collate.

Morgan et al. had published a systematic review on anatomical outcomes of sacrospinous ligament fixation for prolapse [98]. In this review, they included 17 studies. They reported an overall failure rate at any site of 28.8% (95% CI 18.4%–36.3%), with failure of the anterior segment seen in 21.3% (17.3%–25.3%), the apical segment in 7.2% (95% CI 4.0%–10.4%), and the posterior segment in 6.3% (95% CI 4.2%–8.4%) with follow-up varying widely from 12 to 83 months [98]. When subjective outcomes were assessed using the definition of failure to provide relief of prolapse symptoms, an analysis of the pooled data showed a 10.3% subjective failure rate (95% CI 4.4%–16.2%) [98].

Goldberg et al. have shown, in a retrospective analysis, that anterior sacrospinous vault suspension showed a subtle but statistically significant decrease in the anterior wall relaxation compared to the traditional posterior approach [79]. Lovatsis and Drutz [69], in a 5-year case series, with a total of 293 cases, had a cure rate of 97% for those with at least 1 year of follow-up. The incidence of de novo SUI was 3.1% and anal incontinence was 6%. However, 38 out of 43 patients, who had preoperative anal incontinence, denied any symptoms after surgery, giving a cure rate of 88.4%. The incidence of postoperative cystocele was 8.5%, and rectocele was 3.5%. Nieminen and Heinonen looked at sacrospinous ligament fixation in women over 80 years old with massive genital prolapse [92]. They showed comparable results with younger women and concluded that in the absence of major vascular diseases, this operation is as safe as the obliterative procedures, and in high-risk patients, intraoperative bleeding control is important.

Complications

- *Hemorrhage*: This is the most commonly reported complication with an average blood loss ranging from 75 to 839 mL [94]; Sze and Karram reviewed 1229 cases of sacrospinous ligament suspension and found that only 27 (2%) cases required transfusion [89]. Barksdale et al. dissected 10 female cadaveric pelvises and concluded that the inferior gluteal artery is the vessel most likely to be injured. This is because of its perpendicular course relative to the sacrospinous ligament, approximately midway between the ischial spine and the sacrum, lying in a position immediately posterior to the most common location of suture placement. Injury of the pudendal vessels is uncommon because the pudendal neurovascular bundle was found to be relatively protected by the ischial spine and would respond to ligation of the internal iliac artery. Massive intraoperative bleeding should be dealt with by packing and vascular clips or packing and arterial embolization [105]. Other causes of bleeding are injury to the perirectal veins [13], sacral veins [49], and severe adhesions [83] from previous surgery.

- *Nerve injury*: Neural tissue was found in all parts of the sacrospinous ligament with the highest concentration at the center of the ligament [106]. Postoperative sciatic neuralgia, induced by traction of the suture in the ligament, may cause tension transmitted to the sciatic nerve. Usually, the pain resolves in 2–3 weeks but may be helped by transvaginal infiltration of xylocaine [106]. Gluteal pain has been reported after sacrospinous fixation with an incidence of 3% [89] to 6.1% [69] and usually resolves spontaneously within 6 months. Immediate postoperative gluteal pain radiating to the posterior surface of the leg, accompanied by paresthesia, usually indicates posterior cutaneous, pudendal, or sciatic nerve injury [70]. The recommended treatment is immediate reoperation to remove the offending suture and to reposition the new suture in a more medial position on the same or the opposite sacrospinous ligament [70].
- *Injury to pelvic organs*: such as the bladder and the rectum has been reported [21,50,70,100,107] because of their close proximity to the sacrospinous ligament. These injuries should be immediately repaired using conventional techniques. The surgeon must be vigilant about these complications and intraoperative cystoscopy and careful rectal examination after insertion of the suture to the ligament is mandatory.
- *Dyspareunia*: Sexual function following sacrospinous ligament suspension has been evaluated in numerous studies [21,99–103]. The vaginal length is maintained after sacrospinous suspension procedure. Richter and Albright [21] reported that eight of their patients were afraid to attempt coitus because of narrowed vagina, while Given et al. [104] found that the procedure did not interfere with coital function. Holley et al. [101] compared preoperative and postoperative sexual activity of 35 patients and found a higher frequency of sexual intercourse postoperatively, with no association with dyspareunia.
- *Postoperative* SUI: This complication may result from vesicourethral junction straightening that results from restoration of vaginal length and depth and/or a significant reduction of urethral closure pressure when the vaginal vault is replaced intra-abdominally [70,108]. It is recommended that all patients with large prolapse be evaluated preoperatively to rule out the presence of occult urinary stress incontinence.
- *Voiding dysfunction*: Temporary voiding dysfunction has been described especially when the sacrospinous ligament fixation has been performed in conjunction with an anti-incontinence procedure. This can be attributed to the dislocation of the vesicourethral region to the right and ventral fixation when done in combination with the colposuspension [106].
- Other reported rare complications are death from postoperative coronary thrombosis (two patients) [70,109], and one patient died of pulmonary embolism [92]. Evisceration through the vaginal incision has also been reported [110].

Failures

Failure to maintain the support of the vault after sacrospinous suspension procedure may be attributed to a variety of reasons. Poor approximation of the vault to ligament may play a major role; the presence of a suture bridge will prevent fibrosis between the ligament and the vault, leaving the support mainly dependent on the suture material. This is the main reason why this procedure is contraindicated in patients with short vaginas. There is no supportive evidence in the literature that permanent sutures reduce the incidence of recurrence. Although bilateral attachment offers excellent anatomical results with more surface area of attachment, it does not seem to reduce the failure rate of the procedure [53].

Nieminen et al. have shown that postoperative infection is an independent and important individual risk factor for recurrence of prolapsed. The lack of intravenous antibiotic prophylaxis, preoperative vaginal ulcerations, and low age at operation were significantly associated with infectious complications [92], and for that reason, prophylactic antibiotics are highly recommended and should be a routine. Vaginal ulcerations should be treated preoperatively.

When the sacrospinous procedure fails, it can be repeated on the opposite side or bilateral sacrospinous fixation can also be done. Fibrosis and scarring may make repeating the procedure on the same side extremely difficult.

Vault Prolapse Repair: Vaginal or Abdominal Repair, Which Route to Choose and Why?

Both sacrospinous ligament vault suspension and abdominal sacrocolpopexy (laparoscopy, robotics, or laparotomy) have their own indications with their pros and cons. Reconstructive pelvic surgeons need to have the surgical expertise to do both and choose for the individual patient taking into consideration the patient's age, weight, medical condition, coital activity, multiple previous laparotomies, and history of previous failed surgery.

The sacrospinous ligament vault suspension has the following advantages: (1) It significantly reduces postoperative morbidity and does not require the additional skills or cost of laparoscopy or robotics. (2) It offers the option to perform the procedure under local or regional anesthesia. (3) It allows the repair of other pelvic defects simultaneously. (4) It has shorter operating time. However, orthopedic deformities, coexisting intra-abdominal pathology, and compromised vaginal length may favor the abdominal route. Furthermore, the abdominal route whether open or laparoscopic has its own complications of lumbosacral osteomyelitis [111] and mesh erosion into the vagina [112], the bladder [113], and the rectum or colon [114].

Hardiman and Drutz, in a retrospective review comparing the vaginal sacrospinous colpopexy and the abdominal sacral colpopexy, found each of the two procedures to be equally effective [68]. Benson et al., in a prospective randomized study, found abdominal sacral colpopexy to be superior to bilateral sacrospinous suspension in the treatment of POP [82]. However, in both studies, 50% of women had uterovaginal prolapsed and the results may be not be generalized to women with posthysterectomy vault prolapse.

A prospective randomized study by Maher et al. found that both the abdominal and the vaginal procedures were highly effective in the treatment of vaginal vault prolapse. However, the abdominal route was associated with a longer operating time, slower return to activities, and more cost. Both procedures significantly improved patients' quality of life [93].

Maher et al., in a systematic review, found three trials that were considered to be similar enough to address the comparison of abdominal sacral colpopexy and vaginal sacrospinous colpopexy [115].

There were no statistically significant differences between the abdominal and vaginal approach in the number of women reporting prolapse symptoms. They found that abdominal sacral colpopexy had a lower rate of recurrent vault prolapsed, dyspareunia, and de novo SUI; however, abdominal sacrocolpopexy had a longer operating time, longer time to return to activities of daily living, and increased cost [115].

There aren't any randomized trials comparing laparoscopic or robotic sacral colpopexy to sacrospinous ligament suspension.

Different Vaginal Approaches for Fixation of the Vaginal Apex

Iliococcygeal Fixation

The suspension of the vaginal cuff to the iliococcygeal fascia was described by Inmon in 1963 [116] and was popularized by Shull et al. [117], with the proposed advantages of decreasing the risk of neurovascular injury or recurrent cystocele [117,118]. During this procedure, the vaginal vault is fixed to the iliococcygeus fascia on both sides just anterior to the ischial spine. The muscle can be approached by either an anterior or posterior vaginal incision. Usually, no vaginal epithelium needs to excised, as the upper vagina is attached bilaterally resulting in good vaginal length and circumference. Meeks et al., in a case series of 110 patients undergoing iliococcygeal vault suspension, reported a 96% objective cure rate following patients for up to 13 years [118]. Maher et al., in a case-controlled study, compared sacrospinous vault suspension to iliococcygeal fixation of the vaginal vault and found the two procedures to be equally effective in treating vaginal vault prolapse, with similar rates of postoperative cystocele, buttock pain, and hemorrhage requiring transfusion [119]. It was believed that fixation of the vault to this more distal location could potentially foreshorten the vagina; however, Medina et al., in a retrospective cohort study of vaginal length after iliococcygeus fixation and sacrospinous ligament fixation, found that iliococcygeus fixation did not significantly shorten the vaginal length whereas the sacrospinous ligament fixation procedure shortened the vaginal length [120].

Milani et al. retrospectively compared iliococcygeus fixation to abdominal sacral colpopexy and found that both procedures were effective in restoring normal anatomy in patients with vaginal vault prolapse and in relieving associated symptoms. They did not find any difference in subjective or objective outcomes [121].

Uterosacral Ligament Suspension

This procedure restores the vagina to its normal axis, avoiding the retroflexion that may be associated with sacrospinous vault suspension [51]. This apical suspension is ideal at the time of a vaginal hysterectomy and may also be used in patients with posthysterectomy vault prolapse.

Surgical Technique

The technique described later is the original technique described by Shull et al. [122].

The procedure starts by identifying the uterosacral ligaments. In cases where the suspension has been done at the time of a vaginal hysterectomy, the uterosacral ligaments are identified by marking the pedicles and using this to facilitate the location during the suspension. For patients that present with a posthysterectomy vault prolapse, the operation is performed through a vertical midline incision in the vaginal epithelium. The incision should be extended from the base of the urethra to the perineal body. After completion of the epithelial dissection, the enterocele sac is located and the hernia sac is opened and the bowel packed out of the operative field.

The uterosacral ligaments are identified posterior and medial to the ischial spines at the 4 o'clock and 8 o'clock positions. An Allis clamp is used to apply traction to the tissue, and the contralateral index finger is used to trace the strong suspensory tissue of the uterosacral ligament toward the sacrum. A retractor is used to retract the rectum medially, and a retractor is used to hold the bowel and surgical pack cephalad. With a long needle driver, the suture is placed through the ligament on the sacral side of the ischial spine. In an effort to minimize the risk of injury to the ureter, each needle is passed lateral to medial because the surgeon has better control over the entry point of the needle than over its exit point. In addition, the points of needle entry should be medial and posterior to the ischial spines. Two additional sutures are placed distal (on the sacral side) to the initial suture. The same procedure is carried out on the opposite side, with the goal of placing three suspensory sutures on each side (Figure 85.4a). Once all the suspensory sutures are placed, any midline (central) defects in the pubocervical and rectovaginal fascia are repaired by side-to-side plication. The suspensory sutures closest to the surgeon are placed most laterally in the *fascia* (Figure 85.4b). The more proximal sutures are placed more medially in the *fascia*. Before the suspensory sutures are tied, the patient is given 5 mL of indigo carmine dye intravenously and cystoscopy is performed to rule out ureteric injury. The sutures are tied in the sequence in which they are placed, bringing the transverse portions of pubocervical and rectovaginal *fascia* together at the apex (Figure 85.4c).

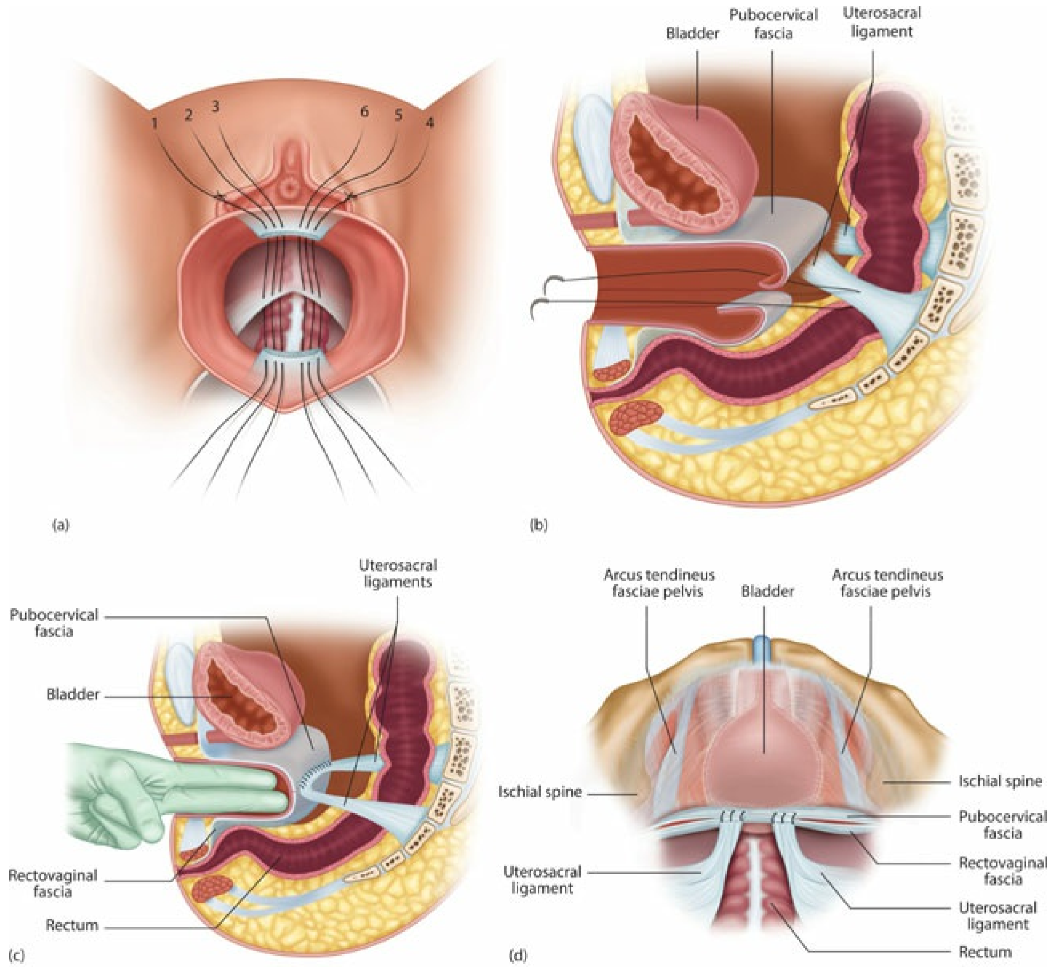

Figure 85.4 (a) Three sutures are placed in uterosacral ligament pedicles on each side. One arm of each suture is placed in transverse portion of pubocervical and rectovaginal fascia. (b) Sagittal view of suspensory suture in left uterosacral ligament (USL) with one arm through pubocervical fascia (PCF) and one arm through rectovaginal fascia (RVF). PS, pubic symphysis; B, bladder. (c) Sagittal view of PCF and RVF suspended to USLs. PS, pubic symphysis; B, bladder; R, rectum. (d) Abdominal view of completed repair. ATFP, arcus tendineus fasciae pelvis; B, bladder; IS, ischial spine; PCF, pubocervical fascia; RVF, rectovaginal fascia; USL, uterosacral ligament; R, rectum. (a–c: Courtesy of B. Shull.)

Dwyer and Fatton have described a different approach where the ischial spines are palpated extraperitoneally, and a delayed absorbable suture is placed through the ligaments bilaterally and suspended to the full thickness of the vaginal apex [123].

Results

A meta-analysis performed by Margulies et al. found pooled rates of anatomical success (POPQ stage 0–1) of 81.2% (95% CI 67.5%–94.5%) for the anterior segment, 98.3% (95% CI 95.7%–100%) for the apical segment, and 87.4% (95% CI 67.5%–94.5%) for the posterior segment. Subjective outcomes were reassuring; however, it was not possible to pool data because of methodological differences between studies [124].

There is only one randomized controlled trial comparing sacrospinous vault suspension with uterosacral ligament suspension (ULS), the OPTIMAL trial [125]. In this trial, they followed patients for 2 years, and they did not find any statistically significant difference in surgical success with the ULS 59.2% (93/154) vs. sacrospinous vaginal vault suspension 60.5% (92/152), OR 0.9 (95% CI 0.6%, 1.5%), or serious adverse event rates (ULS 16.5% [31/188] vs. SSLF 16.7% [31/186], OR 0.9 [95% CI 0.5%, 1.6%]). Prolapse symptoms were resolved in both groups [125].

Complications

The main concern with this procedure is the risk of ureteral kinking/injury. The rates have been reported to vary widely between 1% and 11% [124]. Gustilo-Ashby et al. reported a ureteral injury rate of 5.9% directly attributable to ULS [126]. They found that 87% were identified at cystoscopy. Only 3 of the 355 ULS (0.9%) performed in this series required additional procedures to relieve or correct ureteral obstruction or injury [126]. Other complications reported with this procedure are blood transfusions in 1.3%, bowel injury in 0.2%, and cystotomy in 0.1% [124].

McCall Culdoplasty

In 1957, McCall described suspension of the vaginal vault from the origins of the uterosacral ligament along with obliteration of the pouch of Douglas [127]. The difference between the uterosacral vault suspension and the McCall culdoplasty rests on the obliteration of the cul-de-sac. Elkins et al. described a high McCall culdoplasty technique to repair the prolapsed vault at hysterectomy, where the uterosacral ligaments (ULS) are plicated close to the pelvic sidewall [103]. Cruikshank and Kovac, in a randomized comparison of the three surgical methods used at the time of vaginal hysterectomy, concluded that McCall culdoplasty was superior to a vaginal Moschcowitz-type procedure and to simple peritoneal closure in preventing recurrence of enterocele [128]. Colombo and Milani, in a retrospective case-controlled study comparing the functional and anatomic outcomes of sacrospinous vault suspension and McCall culdoplasty, found no statistical difference in the recurrence of vault prolapse between the two procedures [87]. Webb et al. followed patients up to 8.8 years and reported 71% did not require any further prolapse operation. They also found that 82% were very satisfied [129].

Posterior Intravaginal Slingplasty

Papa Petros (2001) had first described the IVS in 75 patients aged 40–70 years with vault prolapse [130]. There were 71 patients who were followed up between 1 and 4.5 years. Vault prolapse recurred in 6%, and the main complication was tape erosion (5.3%). However, due to a high reported rate of adverse effects, the posterior intravaginal sling kit has now been withdrawn from the market and recruitment in this clinical trial stopped prematurely. Complications reported in other studies included tape erosion into the vagina, rectal perforation, pararectal hematoma, abscess, and rectovaginal fistula [17,131]. Gluteovaginal fistula and a rate up to 18% of mesh erosions have also been reported [132].

Total Vaginal Mesh

Placing graft material in the vagina, as an alternative to traditional surgical repairs, has been widely used by gynecologists over the last decade. This can be attributed to the proposition that the use of mesh will improve the outcome of the repair and reduce the recurrence risk. Based on the principles of synthetic mesh in abdominal surgery and after the successful introduction of synthetic vaginal tapes for SUI, in 2002 a group of French urogynecologists started a prospective multicenter study on transvaginal POP repair using a tension-free polypropylene mesh in patients with ≥stage III vaginal prolapse (Prolift^{TM}). The preliminary published reports were encouraging, and within a relatively short period of time, many gynecologists decided to introduce this technique or modifications of this technique into their practice [133].

Although these techniques were meant to replace or reinforce damaged pelvic tissue, a growing concern regarding the lack of long-term results and safety issues have been surfacing in relation to these kits.

On October 20, 2008, the FDA issued a Public Health Notification and Additional Patient Information on serious complications associated with surgical mesh placed through the vagina (transvaginal placement) to treat POP. Based on an updated analysis of adverse events reported to the FDA and complications described in the scientific literature, the FDA identified surgical mesh for transvaginal repair of POP as an area of continuing serious concern. They issued an update on July 13, 2011, to inform that serious complications associated with surgical mesh for transvaginal repair of POP are not rare. They state that it is not clear that transvaginal POP repairs with mesh is more effective than traditional nonmesh repairs in all patients with POP, and it may expose patients to greater risk [134].

Many of these products have been withdrawn from the market. Currently, American Congress of Obstetricians and Gynecologists (ACOG) and The American Urogynecologic Society (AUGS) recommend the use of vaginal mesh repair only in high-risk women for whom the benefit may justify the risk [135].

Results

There is only one prospective randomized trial comparing native-tissue repair (ULS or sacrospinous fixation) to a vaginal mesh kit (Prolift) for patients with vault prolapse [136]. At 12 months, both groups had improvement of POPQ test points with similar recurrence rates. The quality of life improved and did not differ between groups: 96.2% mesh vs. 90.9% nonmesh subjects reported a cure of bulge symptoms, 15.6% had mesh exposures, and reoperation rates were higher with mesh. Unfortunately, owing to the ethics committee imposing a stopping criterion of a 15.6% mesh exposure rate, the study was terminated and did not recruit the appropriate sample size and is underpowered to detect a significant difference between the groups—if it exists [136]. The 3-year follow-up from the same study was published, and there were no differences in cure rates between both groups [137].

There was one study comparing a vaginal mesh kit to laparoscopic sacrocolpopexy [138]. Maher et al. found that laparoscopic sacral colpopexy group had a longer operating time, reduced inpatient days, and quicker return to activities of daily living as compared with the TVM group. At the 2-year review, the total objective success rate at all vaginal sites was (77%) for laparoscopic sacral colpopexy as compared with (43%) in TVM group ($p < 0.001$). The reoperation rate was significantly higher after vaginal mesh surgery (22%) as compared with laparoscopic sacral colpopexy (5%) ($p = 0.006$). This study concluded that at 2 years, the laparoscopic sacral colpopexy group had a higher satisfaction rate and objective success rate than the TVM group with lower perioperative morbidity and reoperation rate [138].

A systematic review [139] on trocar-guided vaginal mesh kits for apical suspension reviewed the Posterior Prolift, Apogee, intravaginal slingplasty, and infracoccygeal sacropexy. They examined the success rate and complications of these minimally invasive “mesh kits” placed through small perianal skin incisions posteriorly through the ischioanal fossa designed to repair the vaginal apex.

Outcomes included both objective and subjective outcomes relating to prolapse; urinary, bowel, and sexual function; pain; mesh erosion/extrusion; and perioperative surgical complications.

Totaling in 2653 participants, 30 studies were reviewed for the analysis. For apical and posterior vaginal prolapse, eight studies on Apogee had a mesh extrusion rate of 11% and dyspareunia rate of 3%. Perineal, pelvic, or buttock pain was reported in 1%. The only severe intraoperative complication was proctotomy, documented in two women (0.4%).

Eight studies used the Prolift system with a varying proportion of women undergoing anterior, posterior, or total Prolift procedures. Only data relating to posterior and total Prolift were quoted with no randomized controlled trials available. Overall, posterior or total Prolift procedures were performed in 1295 women with mean follow-up time of 30 weeks (range 12–52 weeks). The mean objective success rate was 87% (range 75–94) and the mean complication rate was 16% (range 2–61). Some inconsistency in measuring success and failure following prolapse surgery among authors was noted partly due to the use of nonstandardized grading systems for prolapse quantification.

The most common complications using Prolift were mesh extrusion (7%) and dyspareunia (2%). Vaginal or buttock pain was reported in 2% and mesh contraction in 1.5%. While there was only a single woman with rectal injury, cystotomy occurred in 1% with 3 women developing fistula and 10 participants who received blood transfusions. There was a single woman with necrotizing fasciitis, which was treated by complete removal of the mesh, extensive perineal debridement, laparotomy, and colostomy followed by prolonged stay in the intensive care unit.

This review suggests that there is an overall high, short-term objective success rate (ranging from 87% to 95%) of the commonly used mesh kits in the treatment of apical vaginal prolapse. A significant limitation included management of mesh erosions. Management ranged from local estrogen, through operative excision and oversewing of the eroded mesh, to complete excision of the mesh. Additionally, repeated excisions may have occurred in the same subject and in different settings. Dyspareunia was reported between 1.5% and 3%. It is possible that the lower prevalence of dyspareunia following mesh kit procedures is attributed to the fact that fascial or levator placation is not performed with the mesh kits.

Complications associated with these trocar kits include cystotomies, proctotomies, and vascular injuries. Unlike mesh-related complications that can evolve at any stage during the postoperative course, trocar-related complications occur intraoperatively and can lead to extremely unfavorable consequences if not identified and treated meticulously at the time of occurrence.

Complication rates reported in more recent systematic reviews found rates of organ perforation (2.6%), bleeding (hematoma) (3.8%), and mesh exposure (5%–19%) (mean 10.3%) with 56% of the mesh exposure requiring surgical reintervention, vaginal scarring (8%–11%), dyspareunia (4.4%–7.7%), infection (1.6%–7.3%), pain (1.0%–9.8%), reoperation (5.5%–8.5%), and urinary problems (4.7%–10.2%) [133].

Few prospective cohort trials assessing the new single-incision transvaginal kits had been published with initial results showing promising efficacy and fewer complications when compared to trocar kits [140–142]. With these new kits, complications related to trocar passage are virtually eliminated, and initial reports show lower rates of mesh extrusion; however, these are still seen in 4.5%–6.5% of the cases [141–143]. Only short-term follow-up data are available. It is important to recognize that this rate may increase with time. Also with these kits, there is an evidence of an increased rate of de novo SUI after surgery [142]. Further research comparing single-incision kits with native-tissue repair are needed examining both objective and subjective outcomes.

In conclusion, based on limited peer-reviewed data, transvaginal mesh kits appear to be effective in restoring apical vaginal support, but data on functional outcomes and long-term follow-up are unclear. In the current literature, there is no level 1 evidence that vaginal mesh should be used in primary cases to correct vault prolapse. Surgeons should counsel women that device-related complications with these procedures are not rare; most are related to the use of mesh and their management might necessitate surgical intervention under an anesthetic. Future research should be directed toward well-conducted and adequately powered randomized controlled trials with longer follow-up, comparing vaginal mesh procedures with traditional native-tissue surgeries for apical prolapse and on how surgeons should manage device- and mesh-related complications. Functional outcomes following these procedures and their impact on prolapse symptoms and quality of life should also be thoroughly studied.

CONCLUSION

Optimal management of vault prolapse remains an enigma, and with an increasing aging and active population, there will be an increased need to manage women with complex vaginal prolapse utilizing procedures that restore anatomy and maintain bladder, bowel, and sexual function.

With the availability of different routes and procedures, it is important to individualize caretaking into consideration the patient’s age, medical status, sexual activity, reproductive history, previous surgery, and bowel and bladder function. Well-designed prospective randomized trials need to be done to determine whether or not any of these procedures can truly be considered the “gold standard.”

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86 Open Abdominal Approach to Supporting the Vaginal Apex

Kristina Cvach and Peter Dwyer

INTRODUCTION

Prolapse of the vaginal apex may occur with the uterus in situ or following a previous hysterectomy. The vaginal apex is normally supported by the uterosacral–cardinal ligament complex and the levator ani musculature, nominated by DeLancey [1] as Level 1 support. This defect in most cases occurs secondary to weakness in the muscular levator ani complex, which can occur as a result of obstetric injury with muscular tearing or denervation, aging, or even congenital defects such as spina bifida or bladder extrophy. Apical loss of support secondary to muscular injury may be unilateral or bilateral resulting in apical prolapse. This often occurs in the presence of anterior and/or posterior compartment prolapse. Identifying the extent of apical prolapse during the clinical examination and then addressing the apex during prolapse surgery is crucial to providing a durable repair.

The route by which prolapse surgery takes place is a decision based on patient characteristics as well as surgeon preference and experience. Both abdominal (open, laparoscopic, and robotic) and vaginal routes are utilized with varying surgical techniques performed in order to recreate Level 1 support. This chapter will focus on the open abdominal techniques used to repair apical prolapse, both in the posthysterectomy patient and in the patient with uterine descent wishing to preserve her uterus.

SACROCOLPOPEXY

Technique

Abdominal sacrocolpopexy (ASC) was first described by Frederick Lane in 1962 [2]. It is performed in the posthysterectomy patient and involves resupporting the vaginal apex to the sacrum with the use of an intervening graft, most commonly made of synthetic polypropylene mesh. In brief, the patient is placed in low lithotomy, and once the abdomen has been opened and with a probe in the vagina to aide dissection, the peritoneum, bladder, and rectum are dissected off the vagina. The graft material (either self-made strips, self-made “Y,” or precut “Y”) is then attached to the vagina using either delayed-absorbable or permanent sutures. The anterior longitudinal ligament overlying the sacral promontory is exposed by incising the overlying peritoneum. Care must be taken to identify the right ureter and right and left iliac vessels as these structures are all within 3 cm of the promontory [3]. The dissection is then continued caudally down the right paracolic gutter to the posterior vagina.

The tail of the graft is attached to the anterior longitudinal ligament just below the most prominent point of the sacral promontory (Figure 86.1). In an MRI study, Abernethy showed that the L5–S1 disc was situated at the prominence in 73% of cases [4]. Therefore, attaching the graft with permanent suture or surgical tacks just below the prominence may avoid the complication of discitis. Care must be taken not to over suspend the vagina—the graft material needs to be an adequate length (15–20 cm) in order to achieve tension-free attachment to the sacrum. Oversuspension in our opinion can lead to an increased incidence of de novo stress urinary incontinence and anterior compartment prolapse. The peritoneum is closed over the graft in order to avoid entrapment of the sigmoid colon and development of bowel adhesions to the graft. Vaginal assessment is performed to ascertain if any concomitant anterior or posterior compartment repairs are required. Anti-incontinence procedures may be performed concurrently, if indicated. Cystoscopy is performed to ensure bladder integrity and ureteric patency.

Patients with uterine prolapse may undergo a concomitant total hysterectomy at the time of sacrocolpopexy. However, any opening of the vagina, intentional or not, will increase the risk of subsequent vault mesh exposure (ME), with one study reporting an odds ratio of 4.9 when a concomitant total hysterectomy was performed [5]. In an effort to mitigate this risk, a number of authors advocate that supracervical hysterectomy be performed.

Efficacy

ASC has been shown to be an effective procedure for apical prolapse [6]. Nygaard published a comprehensive review of all studies reporting outcomes on ASC [7]. Efficacy was reported on 64 studies; with mean follow-up between 6 months and 3 years, the success rate for apical prolapse was reported as 78%–100%, and that for all compartment cure was 58%–100%. The median reoperation rate for prolapse was 4.4%. Many of these studies were retrospective case series or cohort studies with relatively short follow-up.

The Colpopexy and Urinary Reduction Efforts (CARE) trial assessing the utility of retropubic urethropexy performed at the time of ASC in stress-continent women recently reported outcomes at 7 years [8]. This is a very valuable study as it provides longer-term data on efficacy of ASC in the framework of a randomized controlled trial (RCT). When using a composite definition of treatment failure for prolapse incorporating both anatomical and symptom definitions, this study reported prolapse failure rates considerably higher than previously published. The estimated probability of failure at 7 years for the urethropexy group was 34% and that of the no urethropexy group was 48%. Despite this high failure rate, only 5% of women underwent surgical correction of the recurrent prolapse. This study highlights the need for long-term reporting of efficacy of prolapse repair procedures, as failure rates appear to increase over time.

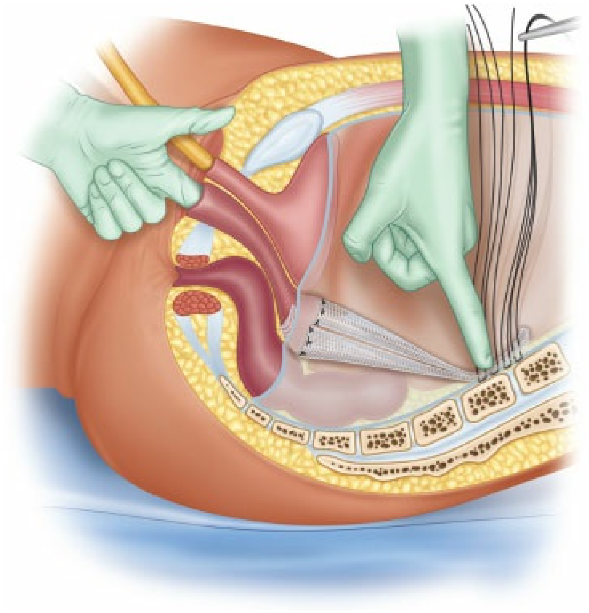
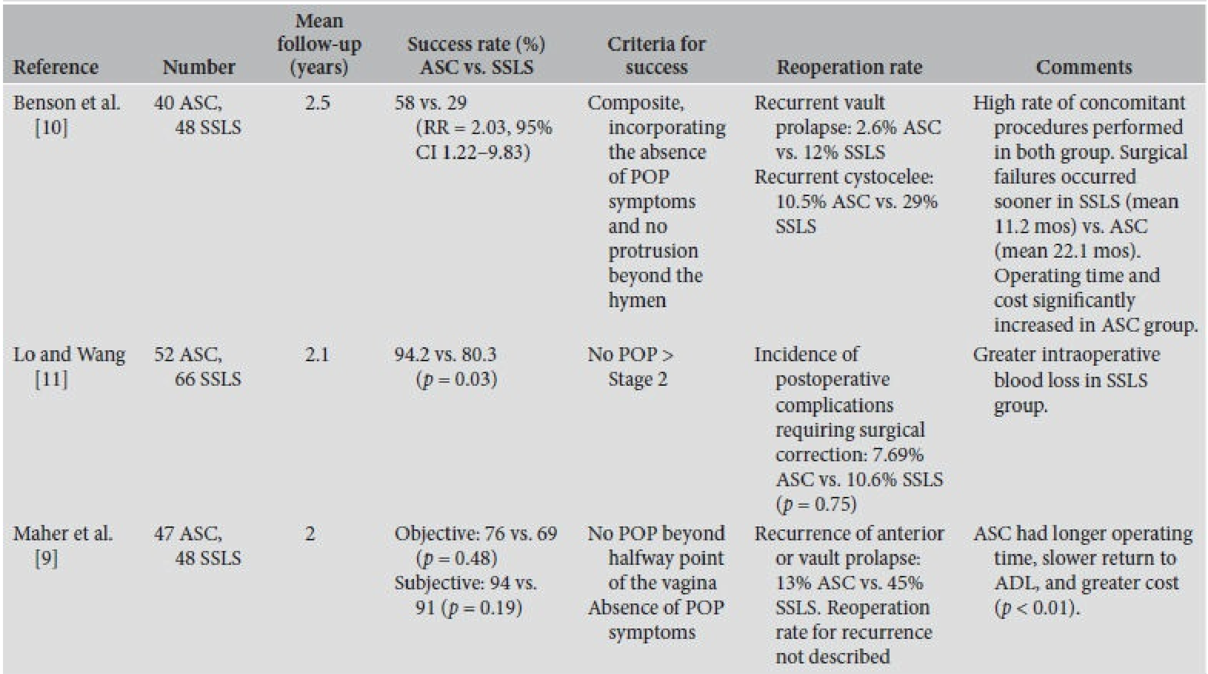


Figure 86.1 Abdominal sacrocolpopexy technique. (Reprinted from Cvach K et al., *Female Pelvic Med Reconstr Surg*, 18, 286, 2012. With permission from Wolters Kluwer Health.)

ASC compares favorably to other apical suspension procedures. Maher et al. reported on 2-year follow-up of an RCT in 95 women comparing ASC to sacrospinous ligament suspension (SSLS) [9]. The subjective success rate in ASC and SSLS was 94% and 91% (p = 0.19), respectively. Anatomic successes in ASC and SSLS were 76% and 69% (p = 0.48), respectively. Both groups showed significant improvement in the quality of life (Table 86.1). Despite these equivalent findings, the most recent Cochrane review on surgical management of prolapse has shown the superiority of ASC when compared to SSLS [6]. Analyzing the Maher et al. study with similar studies by Benson et al. [10] and Lo and Wang [11] showed ASC had a lower all compartment failure rate (RR 0.29, 95% CI 0.09–0.97), a lower rate of recurrent vault prolapse (RR 0.23, 95% CI 0.07–0.77), and a lower rate of postoperative dyspareunia (RR 0.39, 95% CI 0.18–0.86).

Comparisons to other vaginal apical suspension procedures in the literature are lacking. Braun et al. [12] published a small study comparing total abdominal hysterectomy (TAH) and ASC to vaginal hysterectomy (VH) and Mayo McCall culdoplasty with a mean follow-up of 33 months, which showed anatomical failure rates of 0% for TAH/ASC compared to 17% for VH/McCall. Rondini et al. [13] randomly allocated women to ASC or high uterosacral vault suspension (HUSLS) with follow-up to 1 year and showed anatomical success (point C less than −1 cm) in 100% of ASC compared to 83% HUSLS. Recurrent anterior or posterior compartment prolapse was 5.5% in ASC compared to 33.9% in HUSLS with corresponding lower rates of reoperation in ASC (5%) compared to HUSLS (17.8%). Lim et al. reported on an RCT comparing ASC to extraperitoneal vaginal uterosacral ligament suspension (VEULS) with anterior mesh reinforcement [14]. Objective success was 76.5% for ASC and 70% for VEULS ($p = 0.38$). There were no between-group differences for subjective outcomes based on changes in symptoms (Pelvic Floor Distress Inventory [PFDI-20]), prolapse quality of life (Pelvic Floor Impact Questionnaire [PFIQ-7]), and sexual health (Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire [PISQ-12]). ME occurred in three women in the ASC group and in two women in the VEULS group. A further retrospective study by Sanses et al. [15] compared vaginal mesh procedures (VMP) to uterosacral ligament suspensions (USLS) and ASC. This study was based on short-term follow-up (3–6 months) and showed equivalent apical success rates for all procedures of >98%; however, VMP showed a significant reduction in total vaginal length.

Table 86.1 Randomized Controlled Trial Results Comparing Abdominal Sacrocolpopexy to Sacrospinous Vaginal Vault Suspension



Reference	Number	Mean follow-up (years)	Success rate (%) ASC vs. SSLS	Criteria for success	Reoperation rate	Comments
Benson et al. [10]	40 ASC, 48 SSLS	2.5	58 vs. 29 (RR = 2.03, 95% CI 1.22–9.83)	Composite, incorporating the absence of POP symptoms and no protrusion beyond the hymen	Recurrent vault prolapse: 2.6% ASC vs. 12% SSLS Recurrent cystocelee: 10.5% ASC vs. 29% SSLS	High rate of concomitant procedures performed in both group. Surgical failures occurred sooner in SSLS (mean 11.2 mos) vs. ASC (mean 22.1 mos). Operating time and cost significantly increased in ASC group.
Lo and Wang [11]	52 ASC, 66 SSLS	2.1	94.2 vs. 80.3 ($p = 0.03$)	No POP > Stage 2	Incidence of postoperative complications requiring surgical correction: 7.69% ASC vs. 10.6% SSLS ($p = 0.75$)	Greater intraoperative blood loss in SSLS group.
Maher et al. [9]	47 ASC, 48 SSLS	2	Objective: 76 vs. 69 ($p = 0.48$) Subjective: 94 vs. 91 ($p = 0.19$)	No POP beyond halfway point of the vagina Absence of POP symptoms	Recurrence of anterior or vault prolapse: 13% ASC vs. 45% SSLS. Reoperation rate for recurrence not described	ASC had longer operating time, slower return to ADL, and greater cost ($p < 0.01$).

Source: Reprinted from Cardozo L and Staskin D, Chapter 80: Abdominal approach to supporting the vaginal apex, in *Textbook of Female Urology and Urogynecology*, 3rd ed., Informa Healthcare, p. 827. With permission.

Abbreviations:RCT, randomized controlled trial; POP, pelvic organ prolapse; RR, relative risk; CI, confidence interval; mos, months.

The choice of graft material, synthetic versus biologic, has not been extensively studied. Tate et al. have reported on 5-year follow-up of an RCT of ASC with polypropylene mesh versus cadaveric fascia lata [16]. Objective results at 5 years reflected 1 year data, with superior results in the polypropylene group (93% vs. 62%, $p = 0.02$). Subjective results, however, did not reach statistical significance (97% vs. 90%, $p = 0.61$). Reoperation for recurrent prolapse occurred in two patients, one in each group. There were two MEs in the mesh group and one in the fascia lata group.

All studies, comparing ASC to vaginal procedures, show that ASC does have higher intraoperative morbidity with longer operating time, higher blood loss, longer hospital stay, and slower return to activities of daily living. These results have driven the development of new procedures using laparoscopy and robotics to potentially mitigate the negative aspects of what is an anatomically superior approach to apical prolapse repair. Freeman et al. published an RCT assessing the clinical equivalence of ASC and laparoscopic sacrocolpopexy (LSC) in 53 women with follow-up at 1 year [17]. Anatomical outcomes for point C showed equivalence (−6.63 ASC vs. −6.65 LSC), as did subjective assessment of improvement (90% ASC vs. 80% LSC), and change in quality of life outcomes. Reoperation occurred in 2 ASC and 3 LSC. LSC had less blood loss, less narcotic use, and shorter length of stay (4.1 days ASC vs. 3.2 days LSC). Paraiso et al. published an RCT of LSC and robotic sacrocolpopexy (RSC) with follow-up at 1 year [18]. The primary outcome was total operating time, with RSC taking significantly longer (+67 minute difference, 95% CI 43–89; $p < 0.001$). Women in the RSC group also had significantly higher pain and longer use of nonsteroidal anti-inflammatory drugs. Not surprisingly, RSC incurred a higher cost than LSC (+$1936, 95% CI $417–$3454; $p = 0.008$). There were no differences in anatomical or subjective outcomes between groups, with significant improvements from baseline in both LSC and RSC. While the laparoscopic approaches to sacrocolpopexy appear to have some advantages over the open approach, they do require a different skill set. There is a definite learning curve for both techniques, and the surgeon embarking on these must undergo the appropriate training.

SACROHYSTEROPEXY

Technique

Abdominal sacrohysteropexy (ASH) is a uterine-conserving procedure for women with uterovaginal prolapse. Current cervical or uterine pathology is excluded prior to this procedure, and women at high risk of developing endometrial carcinoma should not undergo uterine conservation. Women need to continue to have their cervical screening following the procedure and are counseled about the potential difficulties of future pelvic surgery in the presence of pericervical mesh. While preservation of fertility is one of the reasons women may wish to avoid hysterectomy, there are few published cases of pregnancy and prolapse outcomes following ASH [19–21], and, in general, it is preferable that women have completed their childbearing prior to prolapse surgery. In those contemplating future pregnancy, there is little evidence to guide the discussion regarding mode of delivery, and it is conceivable that pregnancy per se, as well as vaginal delivery, increases the risk of recurrent uterine prolapse following ASH.

After entry into the abdomen, the sacral, paracolic, and posterior vaginal dissections are carried out as per ASC. Synthetic mesh may be attached over the upper posterior vagina and cervix and suspended to the anterior sacrum. If there is significant anterior compartment prolapse, synthetic mesh can also be attached over the anterior vaginal wall. An incision is made in the anterior leaf of the broad ligament bilaterally, inferior to the fallopian tubes, and extended down to the uterovesical fold. The bladder is mobilized off the cervix to expose 3–4 cm of the underlying anterior vaginal wall. Windows are made in the broad ligament bilaterally at the level of the cervicouterine junction, lateral to the uterine artery. Two mesh strips are then fashioned; one is bisected to produce a Y-configuration for the anterior mesh. The anterior mesh arms are passed through the broad ligament windows. Both the anterior and posterior mesh strips are attached to the vagina using permanent or delayed absorbable sutures (Figure 86.2). Other authors attach the broad end of the anterior Y mesh to the vagina and pass the arms of the Y through the broad ligament, attaching these to the posterior mesh [20,22,23], or have reported on the use of a single mesh strip attached only posteriorly [24]. Irrespective of the mesh strip configuration, the proximal end(s) is attached to the anterior longitudinal ligament and the peritoneum closed over the mesh as per the ASC.

Efficacy

Most studies assessing the efficacy of ASH are case series of 12–55 subjects with variable follow-up of up to 5 years (Table 86.2). Barranger et al. reported on a series of 30 women undergoing ASH with concomitant Burch colposuspension and posterior vaginal repair [20]. With a mean objective follow-up of 44 months and mean subjective follow-up of 94 months, failure rates were 6.6% (2/30) and 3.3% (1/30), respectively. Demirci et al. published a series of 20 cases of ASH with concomitant anti-incontinence surgery and posterior vaginal repair, with follow-up of 25 months [24]. One patient (5%) developed early recurrence with Stage 2 anterior and posterior prolapse within 1 month of surgery. Subjective improvement based on a prolapse-specific symptom inventory and quality of life questionnaire showed significant reduction in total scores, signifying improvement in prolapse symptoms postoperatively. Costantini et al. reported on their 5-year follow-up of 52/55 women undergoing sacrohysteropexy [23]. There were no cases of recurrent uterine prolapse. Stage 2 or more anterior recurrence occurred in 4/52 (7.7%) and posterior recurrence in 3/52 (5.7%); however, these recurrences were asymptomatic and did not require further surgical intervention. Both Urinary Distress Inventory (short form) and Incontinence Impact Questionnaire (short form) scores were significantly reduced postoperatively showing improvement in both urinary symptoms and quality of life. Satisfaction with prolapse surgery was measured on a 10-point visual analogue scale, with a mean score of 8.6, suggesting high satisfaction. No cervical or uterine abnormalities were detected with annual screening postoperatively.

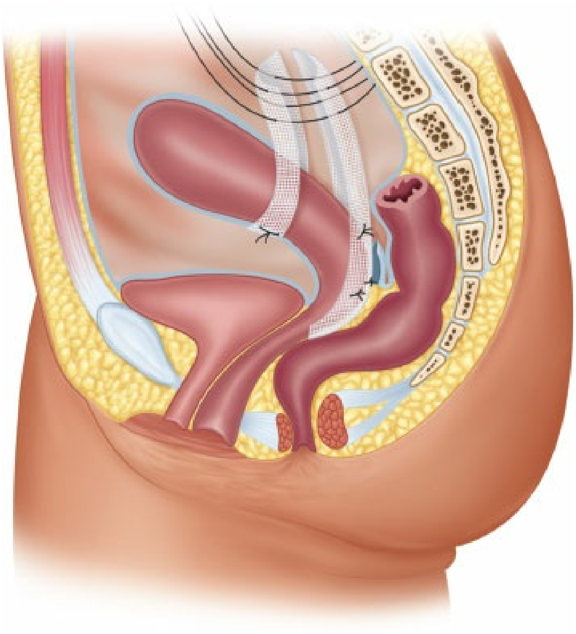


Figure 86.2 Abdominal sacrohysteropexy technique. (Reprinted from Cvach K et al., *Female Pelvic Med Reconstr Surg*, 18, 286, 2012. With permission from Wolters Kluwer Health.)

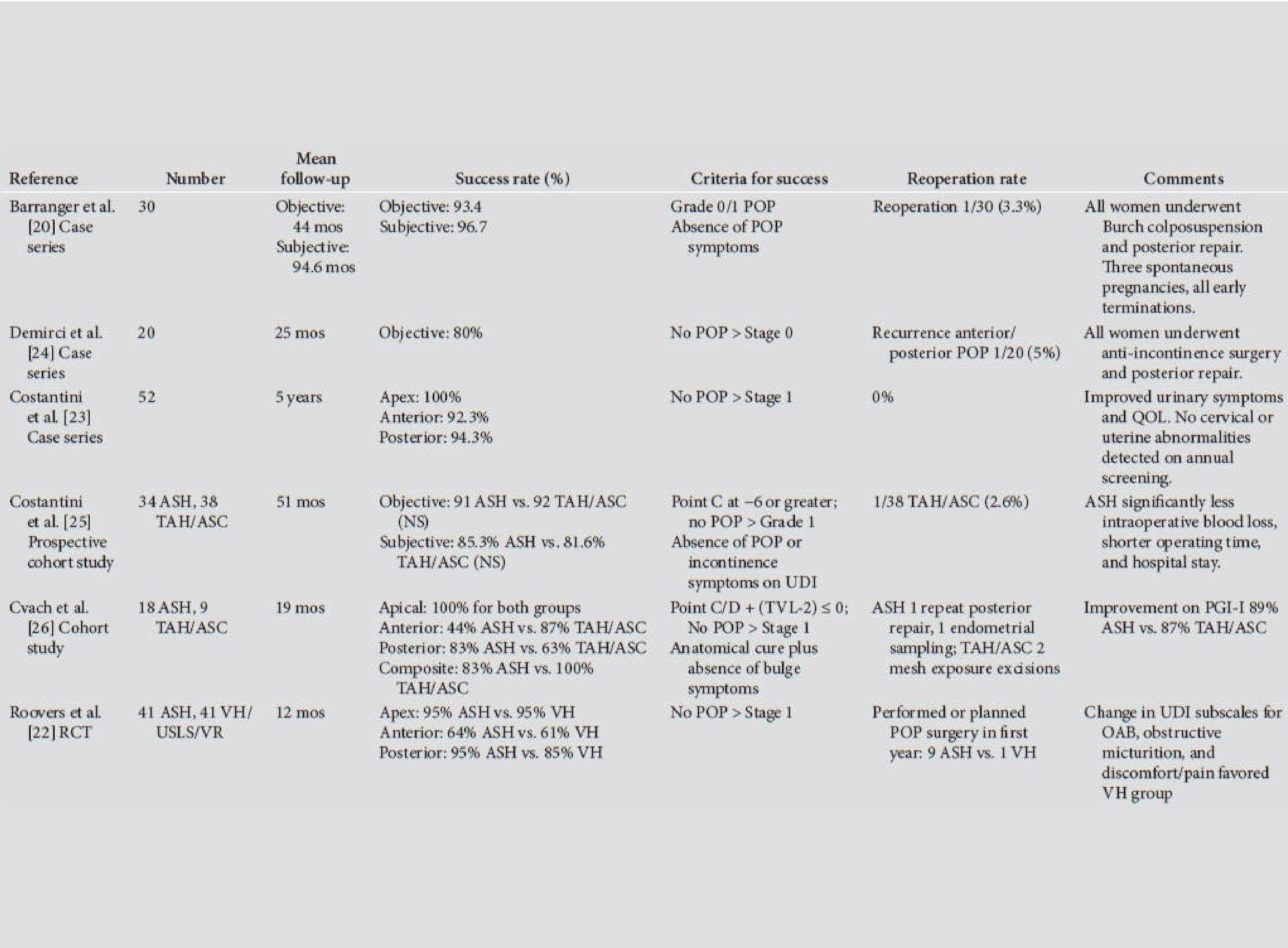
There are few comparative studies of ASH. Costantini et al. published a prospective cohort study comparing 34 women undergoing ASH to 38 undergoing TAH/ASC with mean follow-up of 51 months (range 12–115 months) [25]. Objective successes were 91% (31/34) in the ASH group (3 had recurrent anterior prolapse) and 92% (35/38) in the TAH/ASC group (3 had recurrent posterior prolapse, 1 required repeat prolapse surgery). Subjective successes based on the absence of prolapse or incontinence symptoms using the Urogenital Distress Inventory (UDI) were 85.3% in the ASH group and 81.6% in the TAH/ASC group (not significant). Satisfaction rates were also not statistically different between the groups (ASH 91%, TAH/ASC 86.8%). Cvach et al. have published a similar comparative study of 18 ASH and 9 TAH/ASC patients with a mean follow-up of 19 months [26]. There were no apical recurrences in either group. Objective success for the anterior compartment was 44% (8/18) in the ASH group and 87% (7/8) in the TAH/ASC group and, in the posterior compartment, 83% (15/18) in the ASH group and 63% (5/8) in the TAH/ASC group. One patient in the ASH group required repeat posterior vaginal prolapse surgery. Subjective success based on change in Pelvic Floor Distress Inventory and Pelvic Floor Impact Questionnaire scores was seen in both groups postoperatively with no statistical difference between surgical groups. Patient satisfaction was high; 89% in the ASH and 87% in the TAH/ASC group (NS). If a composite measure of success was used (based on anatomical cure plus absence of bulge symptoms), then 83% of ASH and 100% TAH/ASC were considered cured.

Roovers et al. published an RCT comparing ASH (with no concomitant vaginal surgery) to VH, USLS, and vaginal repair (VH) in 82 women with 12 months of follow-up [22]. Primary outcome was based on change in UDI scores. While both groups showed significant changes in all UDI subscales, there was a significant difference in the changes of the overactive bladder, obstructive micturition, and discomfort/pain subscales, favoring the VH group. Objective success in the apical compartment was 95% for both the ASH and VH groups, in the anterior compartment 64% for the ASH group and 61%

for the VH group, and in the posterior compartment 95% for the ASH group and 85% in the VH group. Performed or planned prolapse surgery within the first year of the original prolapse surgery occurred in 9 women in the ASH group (5 anterior, 4 uterine) and 1 women in the VH group (vault). There are currently no studies comparing abdominal to vaginal uterine preservation techniques.

Overall, studies assessing the efficacy of ASH have shown excellent results for the apical compartment. Anterior and posterior compartment results are variable and may reflect differences in configuration of the mesh (use of posterior mesh only), the anchoring of the anterior mesh (broad end or mesh arms), and whether concomitant anterior or posterior vaginal repairs are performed. There may be an advantage in intraoperative and short-term postoperative morbidity in avoiding hysterectomy at time of uterine prolapse surgery. In Costantini's study of ASH versus TAH/ASC discussed earlier, uterine conservation was associated with a shorter operating time (89 vs. 115 minutes; $p < 0.001$), less intraoperative blood loss less (325 vs. 200 mL; $p < 0.001$), and shorter hospital stay ($p < 0.05$).

Table 86.2 Abdominal Sacrohysteropexy Studies



Reference	Number	Mean follow-up	Success rate (%)	Criteria for success	Reoperation rate	Comments
Barranger et al. [20] Case series	30	Objective: 44 mos Subjective: 94.6 mos	Objective: 93.4 Subjective: 96.7	Grade 0/1 POP Absence of POP symptoms	Reoperation 1/30 (3.3%)	All women underwent Burch colposuspension and posterior repair. Three spontaneous pregnancies, all early terminations.
Demirci et al. [24] Case series	20	25 mos	Objective: 80%	No POP > Stage 0	Recurrence anterior/ posterior POP 1/20 (5%)	All women underwent anti-incontinence surgery and posterior repair.
Costantini et al. [23] Case series	52	5 years	Apex: 100% Anterior: 92.3% Posterior: 94.3%	No POP > Stage 1	0%	Improved urinary symptoms and QOL. No cervical or uterine abnormalities detected on annual screening.
Costantini et al. [25] Prospective cohort study	34 ASH, 38 TAH/ASC	51 mos	Objective: 91 ASH vs. 92 TAH/ASC (NS) Subjective: 85.3% ASH vs. 81.6% TAH/ASC (NS)	Point C at −6 or greater; no POP > Grade 1 Absence of POP or incontinence symptoms on UDI	1/38 TAH/ASC (2.6%)	ASH significantly less intraoperative blood loss, shorter operating time, and hospital stay.
Cvach et al. [26] Cohort study	18 ASH, 9 TAH/ASC	19 mos	Apical: 100% for both groups Anterior: 44% ASH vs. 87% TAH/ASC Posterior: 83% ASH vs. 63% TAH/ASC Composite: 83% ASH vs. 100% TAH/ASC	Point C/D + (TVL-2) ≤ 0; No POP > Stage 1 Anatomical cure plus absence of bulge symptoms	ASH 1 repeat posterior repair, 1 endometrial sampling; TAH/ASC 2 mesh exposure excisions	Improvement on PGI-I 89% ASH vs. 87% TAH/ASC
Roovers et al. [22] RCT	41 ASH, 41 VH/ USLS/VR	12 mos	Apex: 95% ASH vs. 95% VH Anterior: 64% ASH vs. 61% VH Posterior: 95% ASH vs. 85% VH	No POP > Stage 1	Performed or planned POP surgery in first year: 9 ASH vs. 1 VH	Change in UDI subscales for OAB, obstructive micturition, and discomfort/pain favored VH group

Abbreviations:POP, pelvic organ prolapse; mos, months; ASH, abdominal sacrohysteropexy; TAH/ASC, total abdominal hysterectomy/abdominal sacrocolpopexy; VH/USLS/VR, vaginal hysterectomy/uterosacral ligament suspension/vaginal repair; UDI, Urogenital Distress Inventory; QOL, quality of life; TVL, total vaginal length; PGI-I, Patient global impression-improvement.

COMPLICATIONS

Complications following ASC/ASH can be divided into those occurring intraoperatively or postoperatively.

Intraoperative Complications

These are similar to those of any open abdominal procedure. In Nygaard's review of ASC [7], median rates of complications were cystotomy 3.1%, ureteric injury 1%, enterotomy/proctotomy 1.6%, and hemorrhage requiring transfusion at a rate of 2.6%–4.4% [7,10]. Specific to ASC/ASH is hemorrhage occurring during the presacral dissection due to injury to the presacral vascular plexus. Bleeding from these vessels can be difficult to control as they retract into the bony surface of the sacrum and often require the use of bone wax or sterile thumb tacks to achieve hemostasis.

Postoperative Complications

Urinary tract infection is the commonest postoperative complication (10.9%), followed by wound problems (4.6%), ileus (3.6%), deep vein thrombosis or pulmonary embolism (3.3%), operation for small bowel obstruction (1.1%), and incisional hernia repair (5%) [7].

Mesh Complications

ME is a recognized complication of ASC/ASH and can occur at any time point following surgery. ME rates vary according to the synthetic material used with the overall ME rate reported by Nygaard et al. at 3.4% [7]. It is thought that the Amid classification of the material with regard to pore size and weave has a bearing on the risk of ME, with macroporous, monofilament meshes having lower ME rates compared with those having a microporous, multifilament design (Table 86.3). Currently, polypropylene mesh is the most commonly used mesh in prolapse surgery. For published ME rates to be meaningful, long-term follow-up of women with reporting of these data is crucial. The 7-year follow-up of the CARE trial reported a 10% probability of ME, much higher than previously reported [8]. It is important to note that 48% of women in this trial had Mersilene or Gortex mesh, both of which are recognized to have higher rates of ME than polypropylene.

ME may be affected by other factors. Concomitant hysterectomy may increase the risk of ME, with an ancillary study of the CARE trial reporting an OR of 4.9 [5]. The same study showed current smoking increased ME with an odds ratio (OR) of 5.2.

Management of ME requires thorough counseling of the patient. Rarely does conservative management with application of topical estrogen rectify the problem. Most women will require surgical revision of the mesh with an initial vaginal approach to excise the exposed mesh. Complete excision of the mesh may be required if the initial partial excision fails. Quiroz et al. reported on a series of women undergoing mesh revision surgery, with only 48% success with initial vaginal surgery. Most women required more than one mesh revision, often through an abdominal approach [27].

Multiple case reports of small bowel obstruction related to abdominal mesh or scar tissue occurring up to 14 years following ASC have been published, highlighting the need for ongoing follow-up of any women undergoing these procedures [20,28–30].

A small number of case reports of discitis and osteomyelitis occurring 2 months to 8 years after ASC have been published [31–34]. All required open exploration and removal of the mesh, with debridement of the L5–S1 disc.

CONCLUSION

The abdominal sacrocolpopexy or sacrohysteropexy is an effective procedure for the treatment of apical vaginal prolapse. However, the significant morbidity associated with the abdominal approach must be carefully weighed against potential benefits when considering this option. There are advantages and disadvantages of all techniques, and the decision should be based on the patient's needs and wishes once sensible discussion has occurred. Relevant clinical factors in making this decision are the patient's age and general health, whether further pregnancies are desired, sexual activity, presence of dyspareunia, and vaginal size. The abdominal approach will be preferable in the presence of other abdominal pathology requiring treatment such as an ovarian cyst or when vaginal capacity is already reduced from previous surgery in a sexually active woman. In most cases, further vaginal surgery is more likely to decrease vaginal capacity and cause coital difficulty than the abdominal approach.

However, the vaginal approach may be preferable in the presence of severe adhesions increasing the difficulty and risk of an abdominal approach. Older women with medical comorbidity will be better served by shorter operations with a lower risk profile performed vaginally. The risk of recurrence may influence the decision in favor of the abdominal approach and the use of synthetic mesh. However, poor publicity and outcomes with vaginal mesh have also impacted on patient's perceptions with the ASC and rectopexy procedures. Surgical training and experience will and should have an influence on surgical choice so that the procedure can be completed safely. Finally, pelvic floor dysfunction is frequently caused by multiple defect sites. Apical prolapse may be associated with rectoceles, perineal defects, and stress or fecal incontinence that may require concomitant correction and surgical repair. In many cases, these are best performed vaginally, so a combined abdominovaginal approach may be required.

Table 86.3 Comparison of Mesh Type and Mean Exposure Rate

Mesh type	**Manufacturer**	**Mean exposure rates**
Autologous or cadaveric fascia		0% (0/88)
Polypropylene	Prolene, Ethicon[a]	0.5% (1/211)
Polyethylene terephthalate	Mersilene, Ethicon[b]	3% (25/811)
Polytetrafluoroethylene	GORE-TEX, W.L. Gore[c]	3.4% (12/350)
Polyethylene	Marlex, Phillips Sumika[d]	5% (20/402)
Polytetrafluoroethylene	Teflon, EI Dupont[e]	5.5% (6/119)

[a] Prolene, Ethicon Endosurgery Inc., Blue Ash, OH.

[b] Mersilene, Ethicon Endosurgery Inc., Blue Ash, OH.

[c] W.L. Gore & Associates Inc., Flagstaff, AZ.

[d] Marlex, Phillips Sumika Polypropylene Co., Houston, TX.

[e] EI Dupont de nemours and Co., Wilmington, DE.

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87 Laparoscopic and Robotic Approaches to Apical and Vaginal Vault Suspension

Vaneesha Vallabh-Patel and Patrick J. Culligan

INTRODUCTION

Pelvic organ prolapse (POP) is often described as a herniation of the pelvic organs toward the vaginal walls. It is further divided into different categories based on the anatomical location of the herniation to include anterior, apical, and posterior prolapse. Apical prolapse is further described as the descent of the uterus and cervix or vaginal vault in posthysterectomy cases toward the hymen. This chapter will focus on the treatment of apical prolapse using laparoscopic techniques with or without robotic assistance. The two techniques specifically discussed are high uterosacral ligament suspension (HUSLS) and sacrocolpopexy.

ETIOLOGY

Although there are little data about the epidemiology of POP, there is no dispute that it is a growing problem in the United States as the population of elderly Americans rises. A recent study performed by Wu et al. extrapolating data from the U.S. Claims and encounters database estimated the lifetime risk for females 18 years and older to develop pelvic floor dysfunction and need for surgical management to be as high as 20% in the United States [1].

Presently, there are at least 300,000 operations performed annually in the United States for symptoms of POP [2]. Several studies have shown that of these patients, up to 30% will require an additional surgery for recurrence of prolapse [3,4].

The most notable risk factors associated with POP include vaginal delivery, advancing age, obesity, history of prior hysterectomy, chronic constipation, and other repetitive increases in abdominal pressure. Caucasian and Latina females have a fourfold to fivefold increase when compared to African-American females [4].

Clinical manifestations associated with POP include vaginal bulging, pelvic heaviness, constipation, incomplete bladder and bowel emptying, the need to perform evacuation techniques, or simply having discomfort with intercourse [5].

HIGH UTEROSACRAL LIGAMENT SUSPENSION

In 1927, Miller first described “lifting sutures” when suspending the uterosacral ligaments to the apex of the vaginal vault [6]. A similar technique was again described by Milton L. McCall in 1957 using the culdoplasty technique that revealed the importance of this suspension at the time of a vaginal hysterectomy to prevent an enterocele and posthysterectomy vaginal vault prolapse [7]. Richardson later modified this approach in 1976, introducing the HUSLS [8,9].

Now nearly 60 years after McCall described his technique, the same attachment points and surgical principles are used via laparoscopic approaches.

Laparoscopic Approach for High Uterosacral Ligament Suspension

Laparoscopic Port Placement

Traditionally, three laparoscopic ports are placed in the abdomen. The first is the camera port placed in the umbilicus or up to 2 cm caudal to the umbilicus depending on the patient’s habitus. The second and third ports are 5 mm ports placed suprapubically and at the right paramedian [10] (Figures 87.1 and 87.2).

Technique

A 0° laparoscope is placed through the epigastric/umbilical port. The patient is transitioned into steep Trendelenburg to assist with bowel retraction and to better visualize the pelvic sidewalls. To further assist with visualization of the uterosacral ligaments, a probe is placed in the vagina to hold the ligaments on tension. This will assist the surgeon in tracing the ligaments back to their proximal origin [10]. Next, the ureters should be identified lateral to the uterosacral ligaments. The bladder peritoneum anteriorly and posteriorly should be dissected free. This is performed so that the pubocervical fascia and the rectovaginal fascia can be visualized. Next, a figure-eight suture is then placed approximately two-thirds cephalad to the proximal origin of the ligament and 1 cm caudal to the most anterior palpable margin of the sacrum [11]. The suture is then connected to the ipsilateral portion of the vaginal apex. We recommend using a delayed absorbable or permanent suture cut to a length of 36–48 in. Additionally, when first performing this technique, it is recommended to use the extracorporeal approach with a closed knot pusher to secure knot placement, as this is the easiest method to both learn and teach. After knots are secured in place, the ureters should be inspected on each side, and an intraoperative cystoscopy should be performed. It is important that cystoscopy is performed prior to the removal of the laparoscopic ports, so that any ureteral compromise can be addressed prior to the completion of the case.

Robotic-Assisted Laparoscopic Approach for High Uterosacral Ligament Suspension

Robotic Port Placement

At our institution, robotic-assisted laparoscopic HUSLSs are performed in selected patients who are not candidates for a sacrocolpopexy or have an objection to mesh utilization.

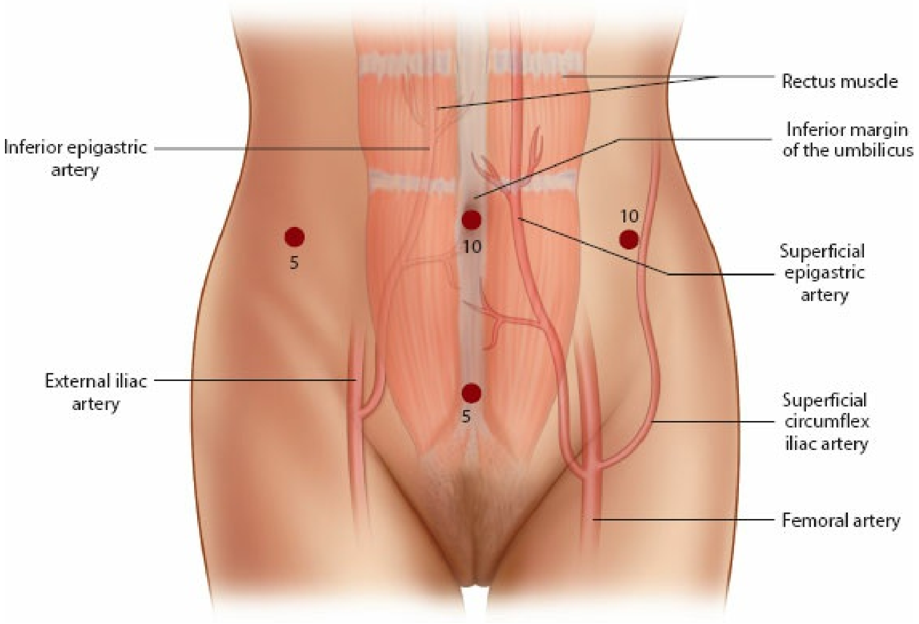
Rectus muscle
Inferior margin of the umbilicus
Inferior epigastric artery
10
10
5
Superficial epigastric artery
External iliac artery
5
Superficial circumflex iliac artery
Femoral artery

Figure 87.1 Trocar placement with anatomical boundaries. (Courtesy of Drs. Miklos and Moore, 2015.)

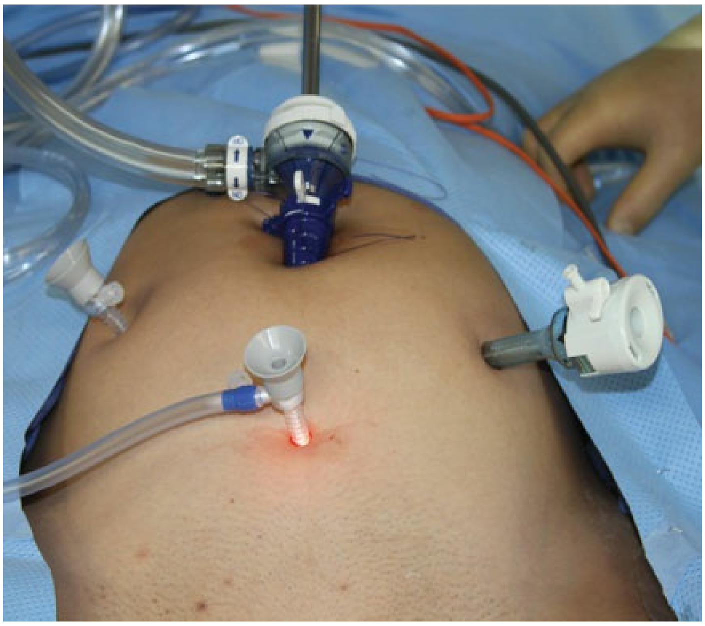

Figure 87.2 Laparoscopic trocar placement. (Courtesy of Drs. Miklos and Moore, 2015.)

The camera port is 12 mm in diameter and is placed in the umbilicus. For the main operative ports, a line is marked 16 cm cephalad to the inferior margin of the symphysis pubis. A left and right port are then placed 9 cm lateral to this mark once the abdomen has been insufflated. This is to prevent the robot arms from colliding with each other during the procedure. The third arm port is then placed on the left side, 4 cm superior and 3 cm lateral to the camera port. An assistant 5 mm diameter port is placed 5 cm lateral to the camera port [12] (Figure 87.3).

Technique

Once the patient is placed in steep Trendelenburg, the robot patient side cart is positioned either between the patient's legs to align the center of the cart with the patient's midline (central docking) or aligned alongside the patient for parallel docking. Docking position is based on surgeon preference. A 0° laparoscope is then placed through the camera port. The remainder of the robotic arms is then connected to the already placed ports.

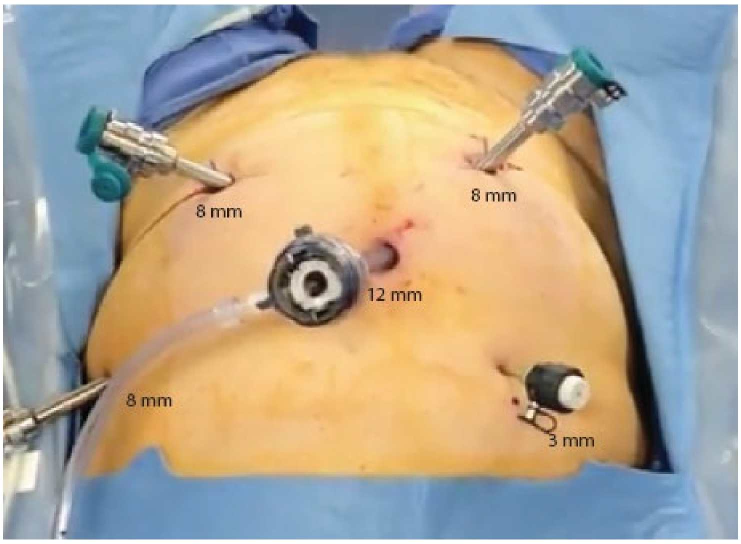

Figure 87.3 Trocar placements for robotic-assisted laparoscopic techniques.

Identification of the uterosacral ligaments can be achieved by placing traction on the vaginal apex with a probe in the vagina when the uterus is not present or by using a uterine manipulator when the uterus is present. If the later method is indicated, after the uterus has been completely devitalized and prior to colpotomy, upward pressure is placed on the uterine manipulator to help with the identification of the uterosacral ligaments. The complete pelvic course of the ureter is then identified prior to placing sutures. 2 CV-2 polytetrafluoroethylene sutures are passed on each side in the upper portion of the uterosacral ligament (Figure 87.4a, b), lateral to the rectosigmoid. At this level, the uterosacral ligaments are the furthest from the ureters as they are heading toward S3 and the ureters are clearing the pelvic brim. The distal end of the sutures are then passed through the pubocervical and rectovaginal fascia and then incorporated into the vaginal cuff. The vaginal cuff is then tied down after the completion of the cuff closure with polyglactin sutures. A third row of sutures can be used in the instance of elongated uterosacral ligaments. It is important to note that the vaginal cuff closure is completed prior to the HUSL sutures being tied down (Figure 87.5). Again as stated in the laparoscopic section, an intraoperative cystoscopy should be performed prior to removal of the ports.

The goal of both procedures is to restore normal anatomical support by suspending the apex of the vagina above the level of the ischial spines toward the level of the sacrum without causing any significant distortion to the vaginal axis [13].

Complications

The most common complication associated with the HUSLS is obstruction or kinking of the ureters, which occurs at a rate up to 11% making the performance of intraoperative cystoscopy to determine ureteral patency an important step. In most cases, removing the offending suture(s) will alleviate any obstruction without consequence as long as the surgeon finds the problem intraoperatively [14,15]. Other potential complications include bowel injury, pelvic abscess, dyspareunia, hemorrhage and in rare cases bladder injury, and exposure of permanent sutures into the vaginal lumen [16].

Outcomes

Although multiple studies and meta-analyses have been performed evaluating the long-term success of uterosacral ligament suspension when approached vaginally, there are few studies describing the long-term outcomes associated with the laparoscopic and robotic-assisted approach. In 2005, Diwan and colleagues reported that when comparing postoperative pelvic organ prolapse quantification (POP-Q) scores in 50 patients between the vaginal and laparoscopic approaches, point C was better improved with the laparoscopic approach. However, in this study, the uterus was conserved in the laparoscopic approach [17].

A study performed by Carter et al. in 2001 presented a series of eight patients who underwent laparoscopic vaginal vault suspension. In this series, at 6 months follow-up, there was a 100% objective success rate [18,19]. Another study performed by Seman et al. followed 73 females after laparoscopic apical pelvic floor repair demonstrating a 100% objective success rate at 12 months and a 90% objective success rate at 24 months follow-up [20].

Finally, a cadaveric study performed in 2003 by Culligan et al. comparing the tensile strength of uterosacral ligament sutures between the vaginal and laparoscopic approach revealed that the average peak tension required to break a laparoscopic suture was 26.2 psi compared to 22.5 psi with vaginally placed sutures [21]. Contrary to many previous studies, this further suggests that the laparoscopic approach is as effective as the traditional vaginal approach.

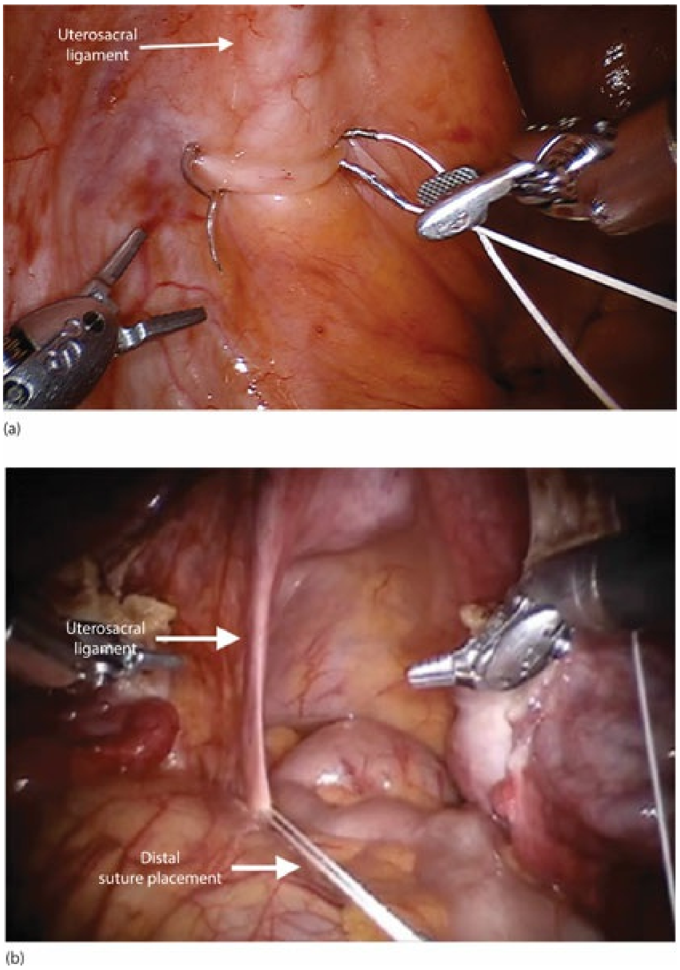

Figure 87.4 (a) Initial step of identification and suture placement for high uterosacral ligament suspension. (b) Final suture placement for high uterosacral ligament suspension.

The laparoscopic and robotic approach to performing uterosacral ligament suspension allows the surgeon to have a more global view to inspect the pelvic cavity. Other advantages include the ability to use pneumoperitoneum to access better surgical planes and the also the accuracy of suture placement to achieve an optimal result [18]. The postoperative advantages of this approach are less blood loss, shorter hospital stays, decreased postoperative pain, and the ability to perform adhesiolysis when necessary to obtain a better anatomical result [20].

SACROCOLPOPEXY

In 1962, Lane was the first to describe sacrocolpopexy using an abdominal approach utilizing grafts to anchor the vaginal apex to the sacral promontory. Although the procedure has been modified through the years, the same principles of using multiple interrupted permanent sutures to attach mesh to the vagina and elevating this up to the anterior longitudinal ligament at the level of the sacrum are still important today. Lane also describes the importance of reapproximating the peritoneum over the synthetic material to avoid interaction of the graft with other pelvic structures. He further emphasized the importance of using mesh to replace the inadequately supported structures that contribute to prolapse as a disorder [22].

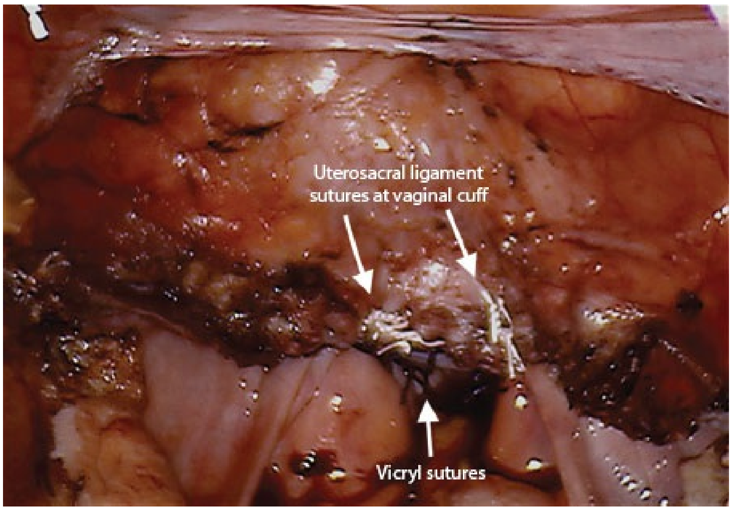

Figure 87.5 Post supracervical hysterectomy with completion of high uterosacral ligament sutures anchored to the vaginal cuff.

Although the gold standard for treatment of apical prolapse is the abdominal sacrocolpopexy due to its effectiveness and availability around the world, many institutions have adopted the more minimally invasive approaches of laparoscopy and robotic-assisted techniques [17,23,24].

Nezhat in 1994 first introduced the laparoscopic sacrocolpopexy, showing its decrease in operative blood loss and, most importantly, patient recovery time while still producing high success rates [23]. In 2006, Elliot et al. and multiple others described the introduction of the robotic-assisted laparoscopic sacrocolpopexy and its importance in negating the technical difficulties associated with straight stick laparoscopy, improvement in visualizing anatomical planes, and decreasing recovery time, while still maintaining a high success rate [25–28].

Although there is no strict definition of success for this procedure, we and many other authors define a successful procedure based on both the "clinical cure" and "objective anatomic cure" rates [12,29]. Clinical cure rate is defined as the patient meeting all of the following criteria: (1) no symptoms of vaginal bulge as measured by the Pelvic Floor Distress Inventory-20 (PFDI-20), (2) no reoperation for POP since the initial surgery, (3) POP-Q point C less than or equal to −5, (4) no POP-Q points greater than 0, and (5) an answer of "satisfied" or "very satisfied" on the Surgical Satisfaction Questionnaire-8. Objective anatomic cure rate is defined as (1) POP-Q point C less than or equal to −5, (2) overall POP-Q stage of 0 or 1, and (3) no reoperation for POP [30].

Laparoscopic Approach for Sacrocolpopexy

Port Placement

Traditionally, four laparoscopic ports are placed in the abdomen. The first is a 5 mm camera port placed intra-umbilically. A 10 mm suturing port is placed in the left paramedian region, and two additional 5 mm ports are placed. The first accessory port is placed suprapubically, and the second is placed in the right paramedian region [24] (Figures 87.1 and 87.2).

Technique

To assist with clearly visualizing the vaginal apex, a probe is placed in the vagina. Next, the peritoneum is dissected away from the vaginal apex anteriorly, exposing the full thickness of the vaginal wall. The dissection is continued one-third down the anterior wall and the space between the rectovaginal fascias. The dissection is continued down to the level of the rectal reflection or further down to the level of the perineal body [31]. If an enterocele is encountered, it should be repaired in a site-specific fashion to avoid suture placement near the area of the graft.

The peritoneum overlying the sacral promontory is then incised in a longitudinal fashion and extended down to the right paracolic gutter between the ureter and the colon. The presacral adipose tissue can then be carefully dissected away to reveal the anterior longitudinal ligament. The peritoneum on the sidewalls should be freed enough so that the mesh can be easily retroperitonealized at the end of the procedure [32].

Mesh is introduced through the 10 mm port. The Y-shaped mesh can usually be cut 5–7 cm anteriorly and 8–10 cm posteriorly. The anterior leaf of the mesh is sutured using approximately six to ten 2-0 permanent, evenly placed sutures beginning distally toward the vaginal apex. The posterior leaf is sutured in a similar fashion through the rectovaginal fascia. Knots can be tied using the extracorporeal method. As previously discussed in the high uterosacral section, the choice of suture should be a monofilament suture such as ePTFE, polypropylene, or polydioxanone. Braided sutures have an increased risk of bacterial colonization, biological tissue response with cellular ingrowth, high tissue reactivity, and suture and mesh erosion [33].

A vaginal probe or Breisky® vaginal retractor (Novosurgical, Oak Brook, IL) is used to place tension on the vaginal apex to delineate its natural position in the pelvic cavity. Our institution uses the manual tension approach, where a probe is placed in the vagina to assist with the tensioning of the sacral arm of the mesh. The probe is then removed half way out of the vaginal canal for the placement of the sacral promontory sutures. The surgeon can then tie the free end of the mesh to the anterior longitudinal ligament using two #0 permanent sutures. An assistant then palpates the anterior and posterior wall of the vagina to insure that appropriate tension is used prior to the final sutures being placed. It is important to note that the mesh is not placed on increased tension to prevent postoperative pelvic pain and dyspareunia [29]. The peritoneum is then reapproximated to cover the mesh to prevent adhesion or entrapment of the bowel to the mesh. At this time, an intraoperative cystoscopy should be performed to ensure no bladder or ureteral injury [32].

Robotic-Assisted Laparoscopic Approach for Sacrocolpopexy

In 2005, our institution transitioned from performing laparoscopic sacrocolpopexy to utilizing the robotic-assisted approach [29]. We felt that the robotic-assisted approach offered better visualization of the anatomical planes, decreased operative time, and allowed us to further dissect the pubocervical and rectovaginal fascial planes to offer more optimal anatomical results [29,31]. If a concomitant hysterectomy procedure is performed, we have found that performing a supracervical hysterectomy decreases the patient’s predisposition to graft erosion at the level of the vaginal cuff [12].

Port Placement

Port placements are the same as previously described in the robotic-assisted HUSLS section.

Technique When Uterus Is Present

After a supracervical hysterectomy is performed, the anterior cervix may be grasped with a robotic single tooth tenaculum on the third robotic arm. The cervix is then tensioned anterior and cephalad toward the sacral promontory. This technique with the tenaculum eliminates the need to place any instrumentation in the vagina for the first part of the procedure (Figure 87.6). The peritoneum is then dissected from the anterior portion of the vaginal apex. A manual grasper is introduced through the assistant port to grasp the bladder peritoneum to assist with countertraction while dissecting the anterior portion to further expose the vesicovaginal plane. The boundaries of this dissection includes the bladder neck distally and the vaginal sulcus laterally [12,29] (Figure 87.7).

For the posterior dissection, the rectal reflection is identified along with the insertion of the uterosacral ligaments to the cervix. The posterior portion of the cervix is grasped with the tenaculum and pulled anterior toward the symphysis pubis. The dissection is started at the level of the cervical stump to avoid bleeding. The peritoneum is then incised in a horizontal fashion between the uterosacral ligaments. Using a combination of sharp and blunt dissection with the monopolar scissors, the posterior vaginal wall is exposed. The distal boundary of the dissection is the rectal reflection or perineal body and the posterior boundary in the rectum. Once the space is exposed, a robotic double fenestrated grasper can be used to assist with traction and countertraction to further dissect the space [12,29].

At the level of the sacral promontory, the peritoneum is lifted and hot CO_2 from the cautery is allowed to infiltrate the space in order to better expose the areolar tissue, which assists in identifying an avascular plane to dissect. At this stage of the procedure, the location of the common iliac vein, middle sacral, and hypogastric vessels should be visualized. Any small vessels that are identified should be cauterized as hemostasis is of the upmost importance to fully visualize the correct planes (Figure 87.8).

Approximately 2 cm of the anterior longitudinal ligament is then exposed with blunt dissection, and the peritoneum is extended down to the right paracolic gutter between the ureter and the colon [12,29].

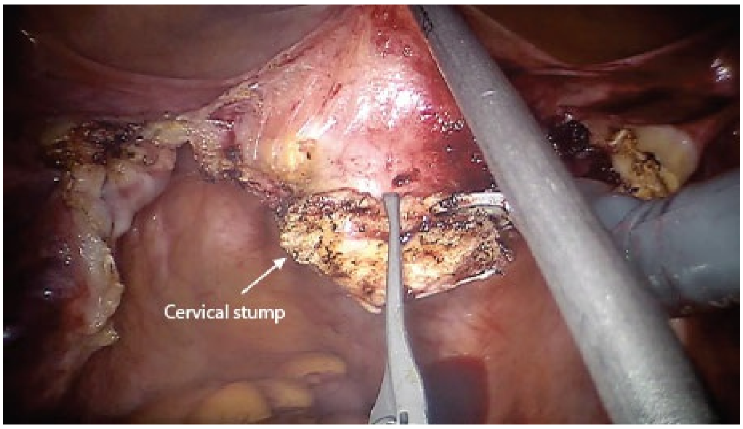

Figure 87.6 Demonstrating tensioning of the cervical stump anterior and cephalad toward the sacral promontory to assist in anterior vaginal wall dissection.

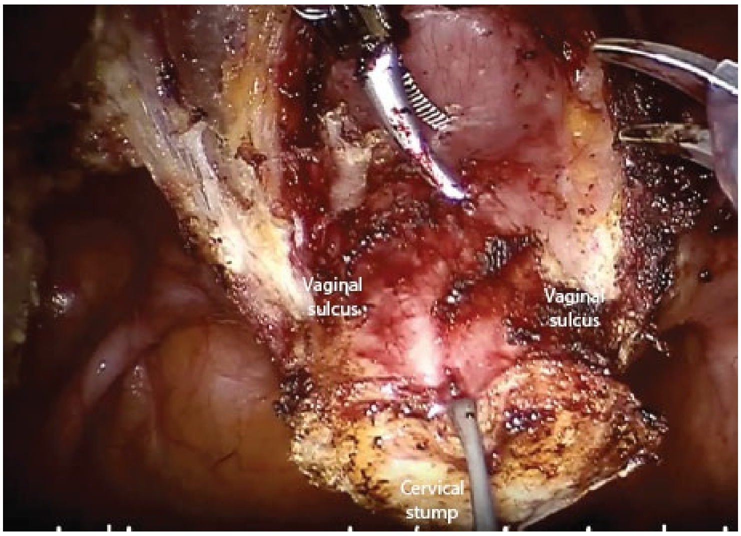

Figure 87.7 Completion of anterior vaginal wall dissection in robotic-assisted laparoscopic sacrocolpopexy.

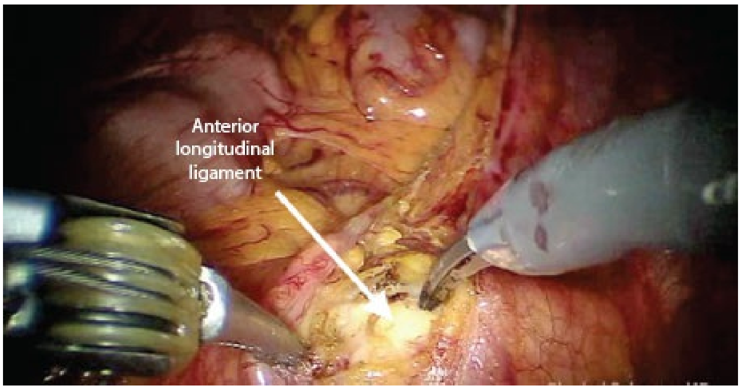

Figure 87.8 Dissection of the anterior longitudinal ligament.

A lightweight Y mesh is used with the anterior arm of the mesh cut between 6 and 8 cm and the posterior arm between 8 and 11 cm. The arms are cut longer than reported in most literature to accommodate for the 2 cm cervical stump (Figure 87.9). The anterior mesh is then loosely tied to the sacral arm and passed through the camera port, along with six 8 in. CV-4 GORE-TEX sutures on a TH-26 needle, and one 10 in. 0 monocryl (Ethicon^{TM}) suture on an SH needle [12,29].

The posterior arm of the mesh is placed on the posterior vaginal wall with traction applied on the cervix from the tenaculum attached to the third robotic arm. The sutures are then placed so the knots lie flat between the vagina and the mesh. Three sutures are placed at the distal end of the posterior dissection, being careful to avoid placing sutures at the junction of the vagina and the rectum. Next, two sutures are placed in the midline 2 cm proximal to the most distal sutures, and two additional sutures are placed 2 cm proximal to the midline sutures at the lateral boundary of the dissection. This is continued until the level of the cervix or uterosacral ligaments. The knot previously attaching the anterior arm to the sacral arm is released and removed by the assistant. The tenaculum is adjusted to the anterior portion of the cervical stump providing tension superiorly and cephalad toward the sacrum. The bladder peritoneum is tractioned in a similar manner by the assistant grasper. The anterior arm of the mesh is then placed into the already dissected space with the first three sutures placed at the distal end of the dissection at the level of the bladder neck. The knots will now lie anterior to the mesh and lateral sutures are then placed every 2 cm cephalad until the level of the cervix [12,29].

The peritoneum overlying the vaginal portion of the mesh is covered by approximating the peritoneum using 0 monocryl (Ethicon). This technique can be accomplished with the first stitch being placed in the middle of the bladder peritoneum and continuing out to the left round ligament and then toward the rectovaginal peritoneal edge. The suture is then taken over the mesh and the middle portion of the bladder peritoneum is reapproached. The suture is continued toward the right round ligament and down to the cut edge of the pelvis peritoneum to include the right uterosacral ligament. The posterior rectal peritoneum is attached to the anterior peritoneum through a previously made loop at the end of the suture (Figure 87.10). The suture is temporarily placed on the anterior abdominal wall while the assistant performs manual vaginal tensioning [12,29].

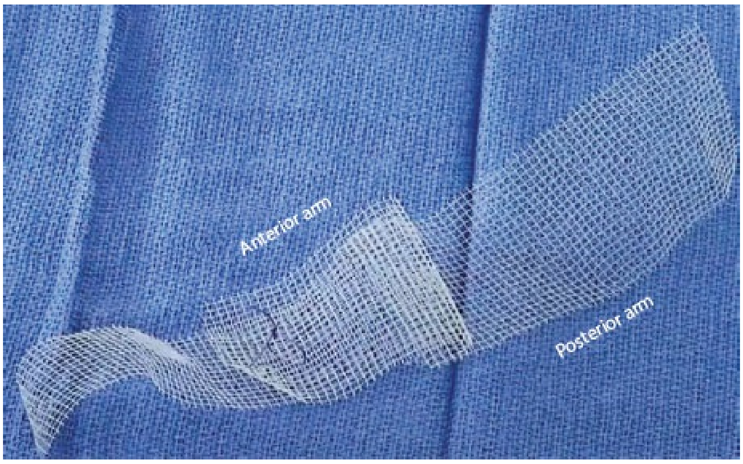

Figure 87.9 Preparation of Y-mesh with the anterior arm sutured to the sacrum arm of the mesh to assist with posterior arm mesh placement and suturing.

Once the appropriate tension is achieved, the excess sacral arm mesh is cut either using the robotic suture-cut or manually with scissors through the assistant port. CV-4 Gore-Tex sutures on a TH-26 needle are used to place two sutures perpendicular through the anterior longitudinal ligament and back through the mesh. Vaginal tension is further verified and the sutures are tied down (Figure 87.11). Next, using the already attached 0 monocryl suture, the remaining peritoneum is reapproximated to cover the mesh up to the level of the sacral promontory (Figure 87.12) [12,29].

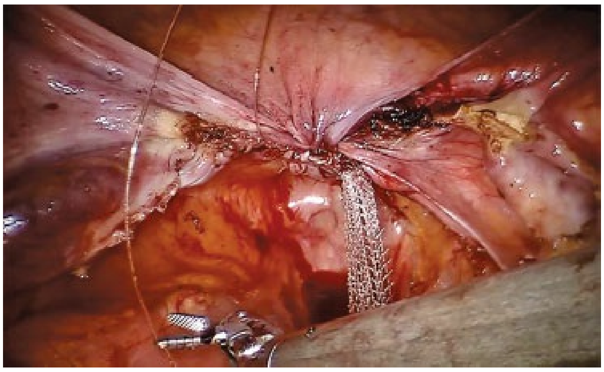

Figure 87.10 Completion of purse string suture in robotic-assisted laparoscopic sacrocolpopexy.

In posthysterectomy cases, the addition of a Breisky vaginal retractor is placed into the vagina to further delineate the anterior and posterior vaginal wall at the level of the vaginal cuff and apex. The remainder of the procedure is performed in the same fashion.

As with laparoscopic approach, a cystoscopy is performed at the end of the procedure.

Complications

The most common complications associated with these two approaches are the same as the complications sited for an abdominal sacrocolpopexy. Complications include injury to the ureter and bladder and injury to the bowel and rectum during lysis of adhesions and dissection. Overall risk for bleeding is quite low; however, when it does occur, it can be life threatening. There is also the risk of hematomas, pelvic abscesses, injury to the vertebral disc, infection in the sacrum periosteum due to suture placement, and potential mesh erosion [34–36].

Outcomes

Rozet et al. performed the largest case series of laparoscopic sacrocolpopexy during 1996–2002, which included 363 females. The authors concluded after 14-month follow-up, there was a 4% recurrence rate of POP and 1% vaginal erosion rate and reported a 96% satisfaction rate by the patient [35,37].

Claerhout et al. reported the largest prospective series of laparoscopic sacrocolpopexy including 132 patients. During the study, mean follow-up rate was 12 months and reported 98% objective cure rate. However, there was an 18% failure rate with recurrence of posterior prolapse and mesh erosion was seen in 4.5% of patients within 1 year of surgery [35,38].

Salamon et al. performed a single arm prospective study of 120 women with stage II or greater POP, undergoing robotic-assisted sacrocolpopexy. With interval follow-up at 6 and 12 months, the group reported an 89% anatomical success rate and 94% clinical cure rate. This study was able to accomplish a 98% follow-up rate at 1 year. Mean operative time for the procedure was 161 ± 29 minutes [39].

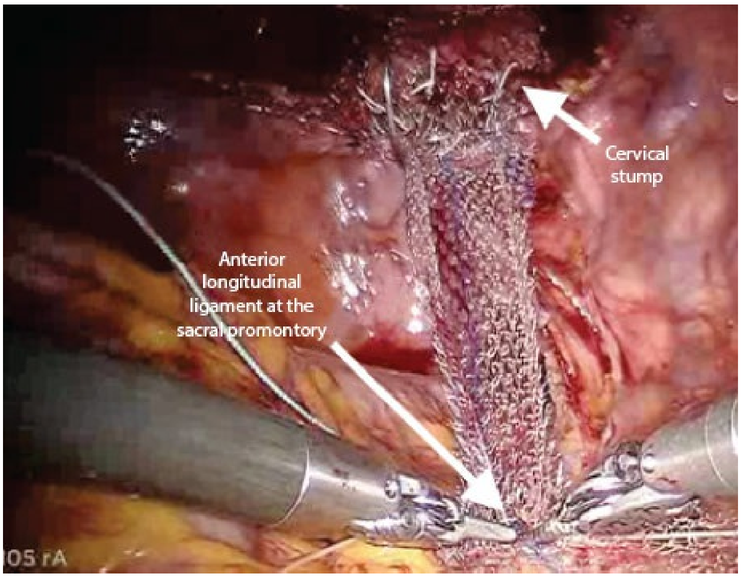

Figure 87.11 Tensioning of mesh prior to suturing down mesh onto the anterior longitudinal ligament.

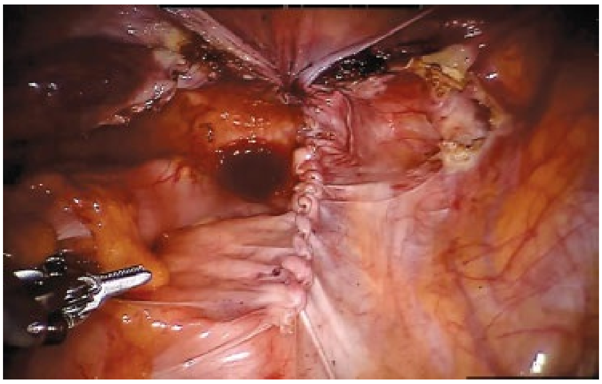

Figure 87.12 Completed robotic-assisted laparoscopic sacrocolpopexy with reapproximation of the peritoneum over the mesh.

Culligan et al. in 2014 performed a single-arm prospective study of 150 women with symptomatic POP who were scheduled to undergo robotic-assisted sacrocolpopexy. This study evaluated cure rates at 12 months postoperatively. They reported a clinical cure rate of 95% and an objective anatomy cure rate of 84% with no cases of mesh erosion or exposures. This study was also able to accomplish a 95% follow-up rate at 1 year. Mean operative for the procedure was 148 ± 27.6 minutes [30].

When comparing the two different approaches, Lee et al. performed a review encompassing 17 patient series between 1966 and 2013, which included 11 laparoscopic approach studies with a total of 1221 patients. The authors found the mean operative time was 124 minutes with a 3% conversion rate to an abdominal approach. The objective cure rate was 91% and a patient satisfaction rate of 92%. Additionally, 6 robotic-assisted sacrocolpopexy studies with a total of 363 patients were reviewed. They found the mean operative time to be 202 minutes; however, this ranged greatly by surgeon experience. They reported a 1% conversion rate to an abdominal approach, and the objective cure rate was reported to be 94% and a 95% subjective cure rate [35].

In 2014, Anger et al. performed a randomized controlled trial comparing the two minimally invasive approaches. This study included 78 randomized patients with stage II or greater POP. They reported, after deducting the initial cost of the robot at the facility, there was no significant difference in the cost between the two procedures. They also reported longer surgical times with the robot-assisted approach at 202 minutes compared to 178 minutes with laparoscopic surgery but no group differences in symptoms both in the PFDI-20 and POP-Q staging, or rate of adverse events [40].

MESH

In 2010, Osterguard discussed the importance of different mesh properties to include density, pore size, elasticity, filament size, surface area, and overall mesh load (Table 87.1) [41,42].

He also discussed potential mesh-related complications to include erosion and exposure, dyspareunia, and pelvic pain. Due to these basic mesh-related principles and complications, multiple studies have been performed focusing on mesh load, durability, and complications associated with mesh placement. Multiple studies have also been performed comparing native tissue mesh and the traditional polypropylene mesh outcomes.

The majority of studies examining mesh complications to date have been performed using Marlex (95 g/m^2) (C.R. Bard, Cranston, RI), as this was previously the gold standard. Kohli et al. performed a retrospective study over an 8-year period examining vaginal mesh erosions complicating abdominal sacrocolpopexy. They revealed an erosion rate of 8% when following patients up to 24 months postoperatively [43]. Recently, prospective studies using lighter mesh (18 g/m^2) have reported the same or better success rates with no mesh complications or erosion [39,44].

Table 87.1 Y-Mesh Products Available for Sacrocolpopexy

Brand Name	**Pore size (mm^2)**	**Density (g/m^2)**	**Thickness (μm)**
Restorelle Y	1.8	18	305
ALYTE® Y-Mesh Graft Vaginal flaps (CR Bard)	2.9	17	287
ALYTE Y-Mesh Graft Sacral flap (CR Bard)	2.9	34	400
Artisyn (Ethicon)	3.9	28	533
Upsylon (Boston Scientific)	2.8	25	200
IntePro (AMS)	1.6	52	527
Vertessa (Caldera)	1.4	22	325

Culligan et al. performed a study comparing the surgical outcomes using porcine dermis mesh and the current gold standard polypropylene mesh. In the 115 patients studied at 12 months follow-up, patients had an anatomic cure rate of 80% with porcine mesh and 86% with polypropylene mesh. The clinical cure rate was 84% and 89%, respectively [45]. However, a similar study performed by this group in 2005 comparing fascia lata and synthetic mesh in 100 patients demonstrated that polypropylene mesh was superior in postoperative POP-Q points, POP-Q stage, and objective and anatomic failure rates [46].

Due to the current media exposure associated with mesh erosions, multiple changes in surgical techniques have been explored to prevent such complications. Limited retrospective data have shown that a total hysterectomy at the time of sacrocolpopexy regardless of the approach relates to a 14%–23% erosion rate [47,48]. With the cervical stump left in place, there is the theoretical benefit of a buffer between the mesh and the vaginal apex, preventing both ascending infection and erosion into the vaginal wall [49]. This technique is controversial because the benefit of a supracervical hysterectomy versus the future challenges of trachelectomy due to pelvic pain or premenopausal cycle cervical bleeding and continued cervical screening has not been well studied.

CONCLUSION

Worldwide abdominal sacrocolpopexy continues to be the gold standard for the treatment of apical prolapse. However, with the evolving technology of laparoscopy and robotic-assisted techniques, we now have the opportunity to perform HUSLSs and sacrocolpopexy for our patients with the prospect of higher surgical success rates while also minimizing postoperative complications. This ultimately will improve both patient safety and satisfaction.

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88 Uterine Prolapse

Miriam Seitz and Roger P. Goldberg

Uterine prolapse results from the descent of the vaginal apex, cervix, and surrounding connective tissue supports. It is a common problem that can significantly impair a woman's quality of life [1]. Women across the age spectrum are prone to this disorder, particularly those who have undergone vaginal delivery. Beyond meeting the technical challenge of reducing the prolapse bulge with successful long-term results, it is also important for the pelvic reconstructive surgeon to bear in mind that for many women, the uterus represents a valued symbol of sexual and reproductive identity. In this respect, uterine prolapse stands apart from other "hernias" that may occur throughout the body. Rather than adopting a uniform treatment approach for all uterine prolapse cases, surgeons should gain familiarity with a range of strategies, including the use of pessaries and traditional operative techniques that incorporate hysterectomy, and also uterine-preserving repairs.

PRINCIPLES OF NORMAL UTERINE SUPPORT

Based on our current understanding of normal pelvic anatomy, key anatomic elements contributing to uterovaginal support are (1) connective tissue supports at the vaginal apex including the cardinal–uterosacral complex and paracolpium (DeLancey level I) [2] and (2) the levator ani musculature, including a horizontally positioned levator plate. The levator plate extends from the sacrum to the anorectal junction and receives components of both the iliococcygeus and puborectalis muscles. The levator ani complex provides a foundation of pelvic support, which, with respect to the uterus, includes the critical upper vaginal/cervical region. The levator ani muscles, when well toned and anatomically intact, maintain closure of the urogenital hiatus and actively promote reflex hiatal closure during physical activity. The levator ani musculature is exposed to substantial risk of injury during vaginal birth, and levator defects are commonly found afterward due to avulsion injuries and denervation [3]. If the cervix and upper vagina remain well supported by an intact and horizontally oriented levator plate providing a base of support during physical exertion, then the development of prolapse is believed to be less likely [4], and the amount of strain on secondary and tertiary support structures (i.e., uterosacral ligaments) is decreased.

On the connective tissue level, a well-suspended and intact cervix serves as a central fusion point for the vaginal endopelvic connective tissues, an area of insertion referred to as the paracervical ring. When these anatomic connections are compromised, an enterocele and/or proximal rectocele and cystocele defects may occur. Whereas the pelvic floor musculature cannot be repaired with existing surgical techniques, restoring or preserving the connective tissue architecture of the upper vagina should represent an overarching goal when addressing uterine prolapse of any degree. These principles are illustrated in Figure 88.1.

The upper third of the vagina (level I) is suspended from the pelvic walls by vertical fibers of the paracolpium, which is a continuation of the cardinal ligament. In the middle third of the vagina (level II), the paracolpium attaches the vagina laterally to the arcus tendineus and the fascia of the levator ani muscles [5]. The cervix and vaginal apex should be regarded as central structures receiving numerous important connective tissue insertions including the proximal components of the pubocervical and rectovaginal septae and cardinal–uterosacral ligaments laterally and posteriorly. The overall architecture of the vagina largely relies on the integrity of these attachments and on a tethering of the vaginal apex and cervix to approximately the level of the ischial spines.

EPIDEMIOLOGY AND ETIOLOGY OF UTERINE PROLAPSE

Defining the rate of uterine prolapse in the general population, and its natural progression, is challenging due to varying ways to define and grade the condition, and differences observed across populations. According to the women's health initiative study of over 16,000 women with a uterus, prolapse of the uterus (of any degree) was recorded in 14.2%. Another study, by Nygaard et al. [6], recorded a 25.6% overall rate of prolapse among women with an intact uterus. Swift et al. [7] identified a twofold increased incidence of severe pelvic organ prolapse (POP) with each additional decade of life. A Swedish study including gynecological examination of 487 women aged 20–59 years found the prevalence of any degree of prolapse to be 31%; however, only 2% had a prolapse bulge reaching the vaginal introitus. Age, parity, pelvic muscle strength, and, among parous subjects, maximum birth weight were significantly associated with the presence of prolapse [8]. Nygaard et al. [9] published a cross-sectional analysis of 1961 nonpregnant women >20 years old who participated in the 2005–2006 national health and nutrition examination survey, including standardized physical examinations in a mobile examination center. The weighted prevalence estimates included 2.9% of women experiencing POP. Another study [10] of over 1800 women from a single small Dutch city identified an 11.4% rate of self-reported prolapse symptoms with a total population-attributable risk of 46%. Independent risk factors for prolapse symptoms included pregnancy, a maternal history of prolapse, and heavy physical labor. In the developed world, parity and childbirth represent the primary risk factors associated with uterovaginal prolapse. Samuelsson et al. [8] reported a 44% versus 6% prevalence of genital prolapse among parous and nonparous women, respectively. Another population-based study [11] found that prolapse risk was significantly increased in women with one (odds ratio [OR] 2.8), two (OR 4.1), and three or more (OR 5.3) vaginal deliveries compared with nulliparous women.

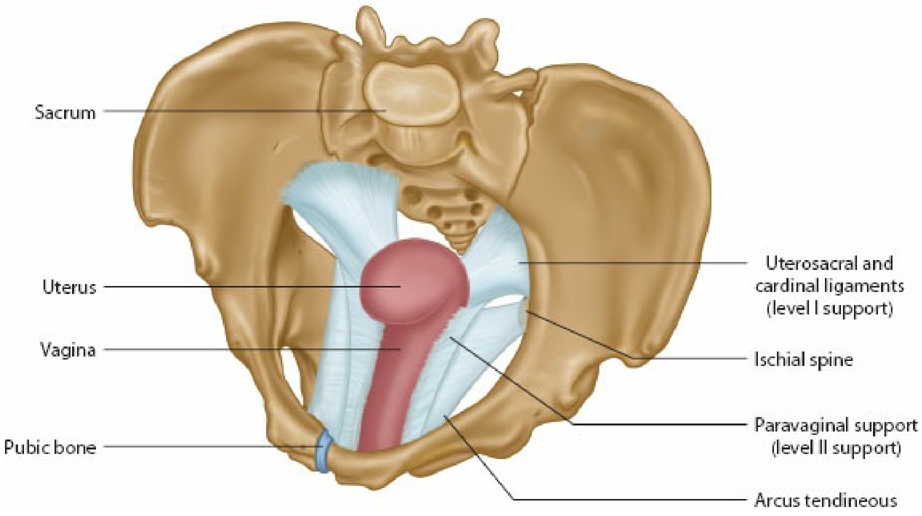
Sacrum
Uterus
Vagina
Pubic bone
Uterosacral and cardinal ligaments (level I support)
Ischial spine
Paravaginal support (level II support)
Arcus tendineous

Figure 88.1 Uterus and surrounding support structures.

One analysis of 1.4 million women from a Swedish hospital registry identified an adjusted OR of 0.18 (0.16–2.0) when comparing the odds of a recorded prolapse diagnosis after cesarean versus vaginal birth [12]. Among nulliparous women, up to 99% demonstrate no appreciable prolapse (stage 0 or 1) when undergoing systematic gynecological exam [13]. Nonobstetrical risk factors for uterine prolapse include advancing age, obesity, chronic heavy lifting, straining due to constipation, chronic obstructive pulmonary disease, connective tissue disorders [14], including Marfan or Ehlers–Danlos, and neurological or spinal cord injury. Some research has indicated that Caucasian and Hispanic women have the highest rate of prolapse, while Asian women have lower rates and black women were reported to have symptomatic prolapse at less than half the rate of Caucasian women (OR 0.4, 95% CI 0.2–0.8) [11]. One population-based study of 1137 women included quantitative prolapse examinations (POP-Q) and concluded that white women had 1.4-fold higher risk of objective prolapse with the leading edge of prolapse at or beyond the hymen [15].

Although symptomatic uterine prolapse cases among nulliparous women appear to be rare in the developed world, in some developing countries, nonobstetrical risk factors including prolonged lifting from a young age, smoking, chronic obstructive pulmonary disease, and malnutrition appear to play a more important contributory role. As many women in the developing world then proceed to undergo childbirth at a young age, the impact of unattended deliveries and traumatic childbirth contributes to the development of uterine prolapse, leading to social isolation. For instance, in Nepal, uterine prolapse represents a women's health crisis, reflecting deep gender inequalities [16].

UTERINE PROLAPSE SYMPTOMS

Symptoms of uterine prolapse may include an external vaginal bulge, pelvic heaviness, and incomplete urinary emptying. Rates of symptomatic prolapse increase with advancing age, increasing from an estimated 6.6% among women aged 20–29 to 56% among those aged 50–59 [8]. Urinary retention may accompany uterine prolapse due to concomitant prolapse of the anterior vaginal wall and anatomic kinking of the urethra or obstruction of the bladder neck by the prolapsing cervix. Many women with uterine prolapse report no symptoms until the prolapse approaches the vaginal introitus and beyond. At this stage, common complaints include a palpable bulge, sensation of vaginal pressure or fullness, low back pain, and voiding difficulties. Low back pain has not been associated with POP [17]. Abnormal bleeding is not associated with uterine prolapse with the occasional exception of advanced prolapse causing cervical ulceration.

EVALUATION OF UTERINE PROLAPSE

Examination in the standing position, during maximal Valsalva or repetitive coughing, is often required to fully appreciate the degree of uterine descent. Cervical elongation, which may occur in up to one-third of women with pelvic prolapse [18], should be assessed with a bimanual examination to palpate the length of cervix protruding, while the apical vagina is maximally elevated with the examining fingers suspending each lateral fornix and then visually by using a full bivalve speculum to elevate the vaginal apex to the level of the ischial spines. If the cervix extends to the midvagina or beyond even with support of the apex, this suggests cervical elongation—the implication being that uterine-sparing surgery may be at higher risk for failing to relieve symptoms, even if the apex has been successfully resuspended (Figure 88.2).

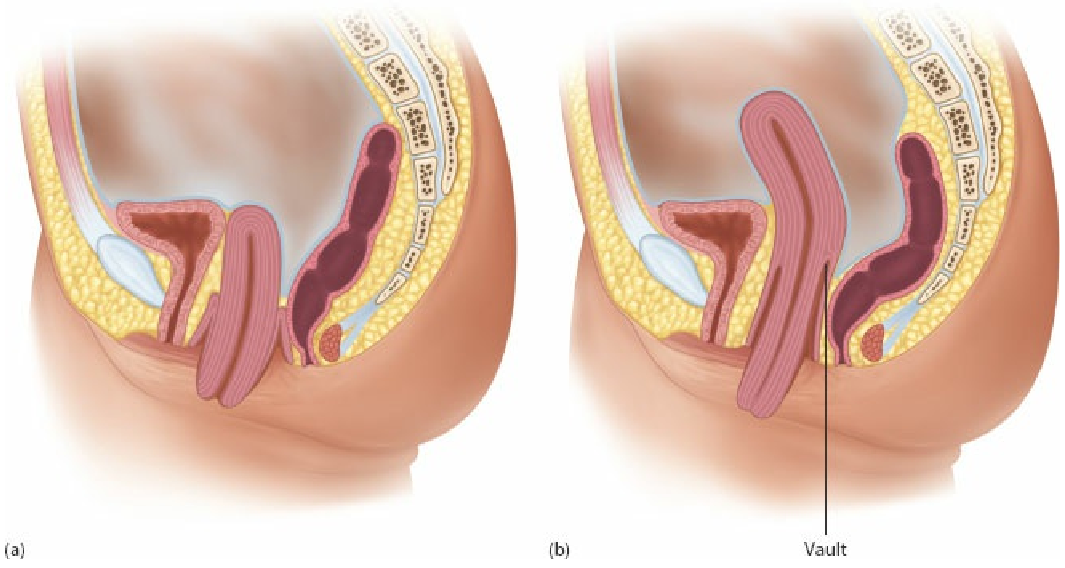

Figure 88.2 Example of cervical elongation versus uterine prolapse: (a) uterine prolapse, (b) cervical elongation.

The anterior and posterior vaginal compartments should be separately and carefully assessed using the posterior blade of a bivalve speculum or Sims speculum to retract the opposite vaginal wall while visualizing the prolapse during straining efforts. In particular, prolapse in the apical and anterior compartments tend to often occur concomitantly, thus achieving satisfactory anterior compartment support that requires attention to the apex, and vice versa. It is increasingly appreciated that apical support defects represent an important factor underlying cystoceles and also rectoceles [19].

The international continence society's pelvic organ prolapse quantitative (POP-Q) staging system [20], which creates a vaginal profile utilizing nine designated points along the anterior, posterior, and apical vaginal compartments, is covered elsewhere in more detail and can be utilized to describe the degree of uterine prolapse, with point C (cervix) describing the maximal prolapsed position of the most distal edge of the cervix during a straining effort. The POP-Q system provides a useful means for recording, comparing, and exchanging clinical findings, with acceptable intra- and interobserver reliability [21]. Alternatively, the Baden–Walker "halfway" system [22] may be used to describe the position of the cervix relative to the hymenal ring. Using this scale, second-degree uterine prolapse involves a cervix extending to the hymenal ring, third-degree prolapse extends beyond the hymenal ring, and fourth-degree prolapse represents complete procidentia with no appreciable support remaining. The most severe cases, referred to as complete procidentia, involve the uterus fully protruding through the genital hiatus.

TREATMENTS OF UTERINE PROLAPSE

Along with aging of the female population, the number of individuals requiring treatment for uterine prolapse is expected to substantially increase in the decades ahead [23]. As surgical treatments become less invasive and thus more appealing, demand for prolapse operations will most likely continue to increase. Wu et al. (2014) studied a U.S. population and published a lifetime risk of POP surgery of 12.6% (95% CI 12.4–2.7) by the age of 80 years [24]. Luber et al. [25] projected a 45% increase in demand over the next 30 years for treatment of female pelvic floor disorders including POP.

Pessary management remains an option that should be offered in almost all cases, although clearly, the percentage of women selecting this modality has declined in the recent decades as surgical procedures have become less invasive and more widely popularized. It is important for surgeons treating uterine prolapse to remain skilled in pessary management, to provide symptom relief for women with uterine prolapse who are poor surgical candidates or who wish to avoid or delay surgery.

Pessaries for uterine prolapse need to provide adequate drainage of cervical secretions and may cause ulceration, vaginitis, bleeding, and, if left unattended, more serious complications such as fistula formation with erosion into the bladder or rectum. Typically, the two most common "first-line" pessaries for uterine prolapse are the ring pessary with support and the Gellhorn pessary (Figure 88.3), with the latter being especially useful for women with advanced uterine prolapse and reduced introital and perineal support. For uterine prolapse during early pregnancy requiring symptom relief, the Smith–Hodge pessary is the most commonly cited; by 20 weeks gestation, however, uterine prolapse rarely persists as the gravid uterus elevates above the pelvic brim. Although nearly any pessary can be tried for uterine prolapse if monitored closely, cube and donut pessaries should be avoided with rare exception due to their tendency to trap secretions and cause ulcerations. Topical estrogen is commonly prescribed to postmenopausal women wearing a pessary to mitigate some of these risks. In addition to a benign leukorrhea that often occurs with pessary use, bacterial vaginosis is also relatively common and may occasionally require removal of the pessary. Most of the more serious complications result from pessaries that have been inadequately monitored [26,27]. Especially patients unable to remove the device on their own need to be prepared for periodic office visits in the range of every 6–12 weeks. Most complications can be avoided if the patient removes the pessary overnight, every night, or several times a week. Vaginal and cervical cancers associated with pessary use have been reported but are exceptionally rare [28].

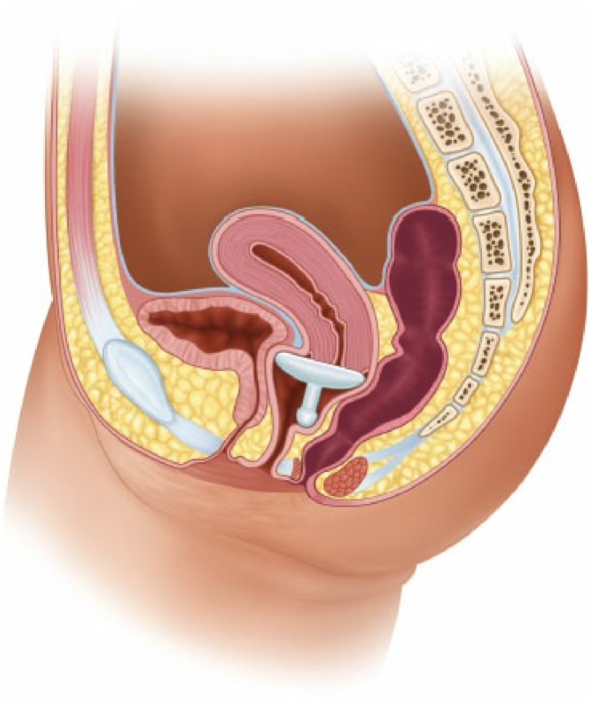

Figure 88.3 Gellhorn pessary in place, for the treatment of uterine prolapse.

Several surgical approaches are available, and each should be judged according to how effectively they achieve a successful anatomic outcome and an improved quality of life. There is no single "gold standard" surgical approach for the treatment of uterine prolapse. Vaginal surgery carries the advantage of its relative safety and efficiency, shorter recuperation times, and also the ability to efficiently address concomitant prolapse defects and stress urinary incontinence. Factors to be considered include perioperative risk, present and planned reproductive and coital activity, previous pelvic reconstructive surgery, and general health status. As the overall safety of a variety of surgical approaches has improved, age itself appears to play a lesser role in surgical decision-making. All techniques worth considering should achieve an effective suspension of the vaginal apex; this can be accomplished with or without removal of the uterus. This raises a key question: does hysterectomy tend to help, hinder, or not significantly impact our efforts to achieve a successful and long-lasting anatomic result and improved quality of life? This question should be considered from both patient and physician perspectives. On the one hand, uterine prolapse does not result from any abnormality of the uterus itself, but rather from relaxation or detachments involving the cardinal–uterosacral ligament complex and nearby vaginal apical supports. Moreover, hysterectomy involves purposeful detachment of what remains of these connective tissue supports and structures. In up to 12% of cases, hysterectomy performed for prolapse is associated with vaginal vault prolapse and enteroceles later on [22] and also may increase the susceptibility of the anterior compartment to subsequent prolapse defects [29]. An epidemiological study from Oxford [30] found that the risk of prolapse following hysterectomy was 5.5 times higher in women whose initial hysterectomy was performed for POP, as opposed to other reasons. Often, the repair of posthysterectomy prolapse may be even more challenging than the primary surgery, due to an absence of normal connective tissue structure and strength. On the other hand, vaginal hysterectomy is associated with a known track record and excellent success. Furthermore, removing the uterus eliminates the risk of future interventions for new pathology such as fibroids, cervical dysplasia, or endometrial hyperplasia. And aside from specific medical reasons, some women personally feel that they "want it out." We believe that if surgeons have the ability to offer both extirpative and uterine-sparing approaches, then satisfaction will be achieved for the largest number of patients.

Hysterectomy with Vaginal Vault Suspension

The most common surgical treatment for uterine prolapse is vaginal hysterectomy followed by vault suspension, along with repairing any significant concomitant defects of the vagina in the anterior, posterior, and lateral compartments. It is crucial to emphasize that the vault suspension and restoration of anterior and posterior compartment support are the components of this repair that restore pelvic support. In other words, at the moment the hysterectomy is completed and the uterine specimen is removed, the prolapse operation has just begun. The decision to perform hysterectomy is often more the result of surgical habit and residency training patterns than any scientific evidence. For most practitioners, uterine prolapse is considered an automatic indication for hysterectomy even for cases involving no intrauterine pathology, and this translates into roughly 17% of hysterectomy procedures being performed for the primary indication of prolapse [31].

Apical suspension at the time of hysterectomy is a critical step, as roughly 12% of women after hysterectomy may develop subsequent vaginal vault prolapse. The procedures most commonly performed during hysterectomy include uterosacral vaginal vault fixation, sacrospinous or iliococcygeus suspension, and McCall culdoplasty [32].

Uterosacral ligament suspension tends to be performed with varying techniques among surgeons, with fixation strengths and results varying accordingly. However, in our experience, a fixation stitch on the upper one-third of the ligament, near the ischial spine, provides consistent support and excellent restoration of vaginal length when each suture is passed through the ipsilateral vaginal cuff corner. Barber et al. reported success in 90% of women after high uterosacral ligament suspension at a median follow-up of 15 months, although some subjects had been followed for as little as 3.4 months in this cohort, and the technique was associated with a concerning 11% intraoperative ureteral injury rate. Shull et al. [33] reported good anatomic success among 89% of subjects at last follow-up, with only a 1% rate of ureteral kinking (a risk profile, which is reflective of our experience). Karram et al. [34] evaluated 168 of 202 women undergoing high uterosacral ligament suspension after 6 months to 3 years follow-up. Eighty-nine percent of this cohort expressed satisfaction with the procedure. Figure 88.4 illustrates a typical high uterosacral vaginal fixation. Rardin et al. reported that laparoscopic uterosacral ligament suspension achieved similar results to the transvaginal technique.

The McCall culdoplasty is a variation of the uterosacral ligament suspension, wherein the detached uterosacral ligaments are shortened and fixed to the vaginal cuff; this operation usually includes closure of the peritoneal cavity by reefing a suture across the posterior peritoneum at the rectal reflection. This operation utilizes the uterosacral ligaments at a somewhat more distal location—where they are mobile and closer to the ureters. When performing any uterosacral ligament suspension technique, intraoperative cystoscopy is necessary to demonstrate ureteral patency.

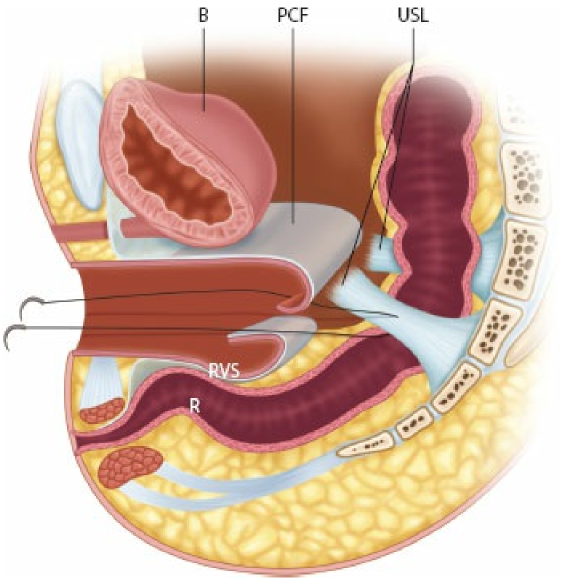

Figure 88.4 Uterosacral vaginal vault fixation following hysterectomy. *Abbreviations*: PCF, pubocervical facia; USL, uterosacral ligament; PS, pubic symphysis; B, bladder; RVF, rectovaginal fascia; R, rectum.

Sacrospinous colposuspension has traditionally been described as a unilateral fixation of the vaginal apex, performed by a posterior (rectocele) approach. As detailed by Richter, Nichols [35], Morley and

DeLancey [36], and others, the vagina is usually suspended to the patient's right side to avoid the rectosigmoid anatomy. The vaginal apex is attached, using either permanent or absorbable sutures, to the midportion of the sacrospinous ligament with care, as the most serious complications from this repair are traumas to the pudendal neurovascular structures and inferior gluteal vessels. At our center, although self-limited peripheral nerve injuries have been encountered, pudendal vascular injuries have been completely avoided by adhering to one simple principle: suture into, never over, the ligament. This translates into a fixation point located one to two fingerbreadths directly medial to the ischial spine. Excellent results have been reported for the classical sacrospinous suspension, but the operation also has clear limitations. First, the vagina deviates to one side, creating an esthetic but not usually functional disadvantage. Second, the traditional sacrospinous fixation technique appears to confer a significant risk of recurrent anterior vaginal wall relaxation [37]. Colombo et al. concluded that unilateral sacrospinous fixation did not offer an advantage over McCall culdoplasty when performed at the time of vaginal hysterectomy [38].

For the past 15 years, our center has utilized an approach whereby the sacrospinous ligaments are accessed through the anterior (cystocele) rather than posterior (rectocele) dissection, and the vagina is affixed bilaterally. For the vast majority of cases, fixation into the sacrospinous ligament is performed with no vaginal retractors, utilizing a push-and-catch suturing device. We have found the bilateral anterior approach to anchoring the vaginal apex to the sacrospinous ligament allows the surgeon to address the anterior compartment with the same dissection, hopefully decreasing the higher rates of cystocele recurrence associated with the traditional technique utilizing native tissues. For larger cystoceles, this may include augmenting the anterior compartment with a biograft or polypropylene mesh, a topic beyond the scope of this chapter.

The iliococcygeus fascial suspension is similar to the sacrospinous suspension; however, here the apex is attached to the prespinous musculature (iliococcygeus or obturator internus fascia). Because the operation utilizes a fixation point that is less cephalad, it may achieve slightly less vaginal depth; however, it carries less risk of neurovascular injury than the sacrospinous repair and has demonstrated good anatomic success. There are no major vascular structures of concern in the high iliococcygeus area, and so it can be considered an excellent secondary choice for surgeons not fully comfortable with placing a fixation suture at the sacrospinous level, or for cases involving distorted or challenging anatomy in and around the ischial spine and sacrospinous ligament.

All cases of uterine prolapse are inherently associated with an enterocele, which may occur because of the descent of the posterior peritoneal cul-de-sac along with the prolapsed uterus ("traction" enterocele) and/or because of separation of the pubocervical and rectovaginal connective tissue at the vaginal apex away from the pubocervical "ring." Past teaching tended to emphasize the surgical separation of the peritoneal sac from the vagina and ligation and excision of this redundant tissue. However, many surgeons, ourselves included, have found that ligation or purse-string closure of the peritoneum may be unnecessary, as long as the operation restores continuity of the anterior (pubocervical) and posterior (rectovaginal) connective tissue planes to the pubocervical ring at the vaginal apex and suspension of this apex to a reliable source of apical support.

Uterine prolapse may also be treated with an abdominal approach, although this is less commonly performed for the nonenlarged prolapsed uterus. Proper fixation of the vaginal vault is no less essential when operating abdominally, but it appears to be emphasized less during abdominal cases. High uterosacral ligament suspension and abdominal sacral colpopexy with sutures through the presacral fascia are appropriate techniques, as they reinforce the vaginal apex to an appropriate cephalad-anchoring point. Nygaard et al. [39] published a 7-year follow-up of the Pelvic Floor Disorders Network multicenter randomized masked trial (Colpopexy and Urinary Reduction Efforts trial). By year 7, the estimated probability of failure was 0.27 (abdominal sacrocolpopexy [ASC] and urethropexy) and 0.22 (ASC alone) of anatomic failure (treatment difference of 0.050; 95% CI −0.161 to 0.271). Mesh erosion at 7 years was 10.5% (95% CI 6.8%–16.1%).

Some authors have identified higher rates of mesh erosion when abdominal sacral colpopexy is performed at the time of hysterectomy for uterine prolapse, leading some surgeons to perform a supracervical hysterectomy followed by sacral cervicopexy. However, other studies have indicated no excess risk from a baseline mesh erosion rate of approximately 3.4%–4.2%, even when the operation is performed by experienced subspecialists [40,41].

Laparoscopic sacral colpopexy or uterosacral ligament suspension may be performed following laparoscopic hysterectomy. The scientific evidence regarding the outcomes of these vault suspension procedures is limited but growing more robust with the introduction of robotic-assisted techniques, which may offer a greater number of surgeons to truly replicate the open abdominal repair.

Uterine-Sparing Techniques

Uterine-sparing prolapse repairs have been described as far back as the 1880s, and for years, influential gynecological surgeons have suggested that the uterus plays a passive, rather than an active role, in uterovaginal prolapse [42].

Alwin Mackendrot (1859–1925) provided an early description of prolapse and an accurate description of the cardinal and uterosacral ligaments. Thomas Watkins (1898) described an interposition operation for postmenopausal women, involving cervical amputation and fixation of the bladder against the posterior uterine wall, thereby elevating the lower uterine segment. Dr. Watkins advised against uterine removal for prolapse, unless the organ was diseased. By the end of the nineteenth century, several techniques had been proposed for ventral fixation of the uterine fundus to the abdominal wall by surgeons including Harris, Murphy, and Kocher, and in the early twentieth century, a combined vaginal and abdominal procedure included dilatation and curettage, trachelorrhaphy, anterior and posterior colporrhaphy, and abdominal uterosacral plication with uterine suspension. Dr. David Nichols, in his classic textbook on *Vaginal Surgery*, described the uterus as an innocent bystander, "…the result of genital prolapse and not the primary cause of the symptomatology" [43]. Diwan et al. [44], in reviewing the subject of uterine preservation, concluded that hysterectomy has not been proven to improve durability of the repair and may carry several disadvantages including increased morbidity, blood loss, operative and recovery times, and increased pelvic neuropathy and disruption of natural support structures. The authors cited a potential risk for new-onset urinary incontinence, bladder dysfunction, prolapse, and possibly adverse effects on sexual identity. Altman et al. [45] compared 162,488 Swedish women with hysterectomy to 470,519 matched controls and found that 3.2% (n = 5270) of women after hysterectomy needed to undergo prolapse surgery versus 2.0% of the controls (n = 9437), with the highest risks observed in women having had vaginal hysterectomy (hazard ratio 3.8; 95% CI 3.1–4.8). The authors concluded that hysterectomy was associated with increased risk of subsequent prolapse surgery. Likewise, Blandon et al. [46] studied a cohort of 8220 women with prior hysterectomy and found that a cumulative incidence of subsequent prolapse surgery was 5.1% by 30 years (study period 1965–2002). Prolapse surgery was more likely among women with an original diagnosis of prolapse, who underwent vaginal hysterectomy (hazard ratio 4.3; 95% CI 2.5–7.3). With respect to bowel function, Karasick et al. [47] studied 354 women undergoing defecography and concluded that hysterectomy was associated with a higher risk of enterocele (40% vs. 25%, $p = 0.009$) and pelvic floor descent (25% vs. 15%, $p = 0.04$) and may contribute to the development of defecation disorders.

Patient choice is often the driving factor leading to uterine preservation. For younger women, this decision may be fueled by a general desire to feel young, intact, and fertile; it is certainly understandable that many women—younger women in particular—have a psychological attachment to this reproductive organ. For the advanced elderly, a desire to avoid hysterectomy may relate to fear over the perceived invasiveness of the operation, surgical risks, and/or length of recuperation. In theory, effective hysteropexy procedures may preserve the architecture of the vaginal apex better than hysterectomy, *suspending rather than transecting* the cardinal–uterosacral ligament complex and envelope of connective tissue attachments surrounding the paracervical ring. Before performing a hysteropexy, abnormal bleeding patterns and/or undiagnosed gynecologic symptoms should be addressed. Additionally, the presence of cervical or uterine pathology (i.e., dysplasia and undiagnosed bleeding) would serve as contraindications to uterine preservation, and up-to-date cervical cytology must be confirmed.

Uterine preservation operations fall into two major categories: (1) *hysteropexy procedures* that attempt to reconstruct normal anatomy and (2) *obliterative procedures* designed to resolve the prolapse bulge and not preserve the normal anatomy of the vagina.

Hysteropexy Procedures

Sacrospinous Hysteropexy

It is interesting to note that uterine-sparing techniques were promoted well before hysterectomy was popularized as a procedure of choice for prolapse. In the modern gynecologic literature, open abdominal, vaginal, and laparoscopic techniques have been described. Hysteropexy techniques vary significantly among the scattered centers that have taken an interest in uterine preservation and published their technique and results.

The feasibility of sacrospinous hysteropexy was suggested by several early case series [48,49], all of them involving a posterior approach and unilateral fixation of the apex, suggesting short operative time and encouraging rates of success. Cruikshank et al. reported successful long-term support even among four of five younger women who reported a subsequent pregnancy and childbirth. Maher et al. [50] compared 70 women aged 23–87 years old, who underwent either sacrospinous hysteropexy (*n* = 34) or vaginal hysterectomy" (*n* = 36). Standardized questionnaires and blinded postoperative examinations were performed at a mean follow-up of 33 months. Recurrence rate after hysteropexy was 3.6%, no higher than what was observed in the vaginal hysterectomy group. Additionally, uterine preservation was associated with shorter operative time (59 vs. 91 minutes) and less estimated blood loss (198 vs. 402 mL). Rates of patient satisfaction were high for both groups (85% for hysteropexy and 86% for vaginal hysterectomy).

Other comparative studies include Hefni et al. [51], who compared 61 sacrospinous hysteropexy cases to 48 hysterectomies and reported 95% versus 95% success, respectively. van Brummen et al. [52] compared 54 sacrospinous hysteropexy cases to 49 vaginal hysterectomies and found equivalent anatomic results for the two operations with quicker recuperation after hysteropexy. Interestingly, vaginal hysterectomy was associated with up to threefold higher rates of urge incontinence and overactive bladder symptoms, raising speculation as to whether the dissection of bladder base during hysterectomy may increase the likelihood of denervation injury and subsequent lower urinary tract dysfunction.

Dietz et al. [53] evaluated 133 women after sacrospinous hysteropexy at a mean follow-up of 22 months; 99 completed questionnaire, but only 60 followed up for the postoperative exam. Eighty-four percent of respondents were highly satisfied. The authors recorded only a 2.3% recurrence rate for uterine descent; however, 35% of subjects developed a subsequent cystocele. A separate analysis [54] on functional outcome among 72 of these subjects, 1 year after sacrospinous hysteropexy, included validated symptom and quality-of-life questionnaires. Scores on all domains of urogenital symptoms and defecatory symptoms, except for the pain and fecal incontinence domain, improved significantly. Self-reported quality of life was improved for all domains, and no major complications were encountered in this cohort.

The same authors performed a separate randomized trial including 71 subjects undergoing either sacrospinous hysteropexy or vaginal hysterectomy for stage 2 to 4 uterine descent [55]. With respect to subjective outcomes, sacrospinous hysteropexy and vaginal hysterectomy were equally effective in improving urogenital/defecatory symptoms. No differences were found in quality-of-life scores and self-reported urogenital/defecatory symptoms at 1-year follow-up between the two procedures. Sacrospinous hysteropexy was associated with better mean apical support than vaginal hysterectomy as measured by C and D points on POP-Q testing at 1 year. However, among women presenting with stage >2 uterine prolapse, the risk of apical recurrence was 17% lower after vaginal hysterectomy compared with those undergoing sacrospinous hysteropexy. Women who had presented preoperatively with advanced stage uterine prolapse were especially prone to objective recurrent prolapse 1 year after sacrospinous hysteropexy in this study. Repeat surgery for prolapse was performed in 11% of women after sacrospinous hysteropexy versus 7% after vaginal hysterectomy. Alshaikh recently compared sacrospinous hysteropexy and uterosacral ligament suspension at the time of hysterectomy and found similar subjective results although there was a trend toward more objective recurrences in the hysteropexy group [56].

Mesh-augmented sacrospinous hysteropexy procedures have been utilized as a means to simplify the technical steps of the surgery and also to concurrently address both the anterior and apical compartments. Vu et al. (2012) published 1-year recurrence rate of 1.89% (no anterior and one apical [C ≥ 1]) when mesh was used to augment sacrospinous hysteropexy, defining recurrence as POP-Q stage ≥2 in the anterior and/or apical compartments. Pelvic Floor Distress Inventory (PFDI) scores were improved in all domains postoperatively [57]. There were no surgeries performed for recurrence, and when patients were asked if they would choose the surgery again, 93% said they would. Additionally, the risk of vaginal mesh erosion associated with this repair was 1.9%, consistent with previous reports suggesting that uterine-preserving prolapse repairs may be associated with low rates of mesh complications [58]. The use of mesh has triggered substantial controversy in recent years, and at the present time, large multicenter trials are in progress to better delineate the risks and benefits of mesh-augmented hysteropexy in comparison with the alternative of vaginal hysterectomy (Figure 88.5).

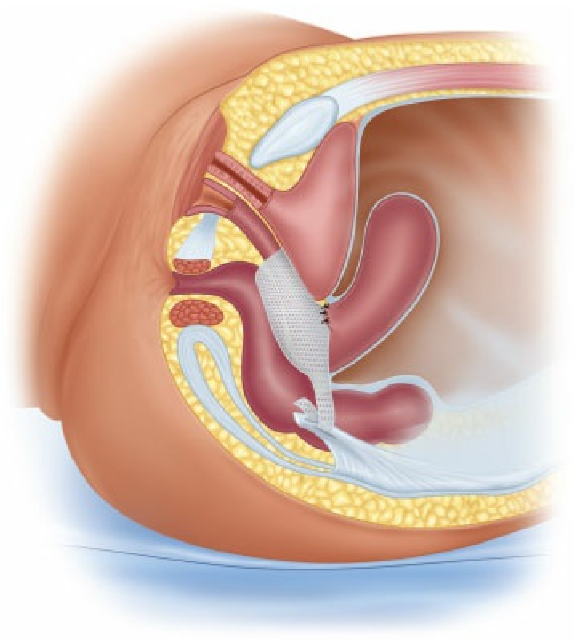

Figure 88.5 Mesh-augmented sacrospinous hysteropexy for uterine prolapse and combined cystocele.

Abdominal and Laparoscopic Sacrohysteropexy

Open abdominal sacrohysteropexy involves suturing the uterus to the anterior longitudinal ligament with a graft and more recently polypropylene mesh. Studies have demonstrated favorable anatomical cure rates and improved quality of life and sexual function. Abdominal hysteropexy is an approach that has been established by both observational series showing long-term (0 > 1 year) apical failure rates in the range of only 1%–7% [59–61].

Roovers et al. [62] performed the only randomized controlled trial (RCT)-comparing abdominal sacrohysteropexy and Burch ($n = 31$) to vaginal hysterectomy, uterosacral ligament suspension, anterior and posterior colporrhaphy, and needle suspension ($n = 31$). Anatomical outcomes were similar with regard to apical (95%) and posterior (85%–95%) success, but anterior defects recurred in 61% and 64% of women. There were more physician visits and more reoperations in the abdominal sacrohysteropexy group.

Costantini et al. [63] performed a prospective, cohort study on 72 consecutive subjects undergoing repair of uterovaginal prolapse by the abdominal approach; 34 were treated with abdominal hysteropexy and 38 with abdominal hysterectomy, followed by sacrocolpopexy. The sacrocolpopexy was performed with two pieces of rectangular mesh, and hysteropexy was performed with one posterior rectangular and one anterior Y-shaped mesh. Mean operative time, estimated blood loss, and hospital stay were significantly lower in the hysteropexy group ($p < 0.001$). At a mean follow-up of 51 (12–115) months, success rates were similar for uterine and vaginal apical support (100%). Recurrent low-grade cystoceles were observed in 1/38 (2.6%) after sacral colpopexy and 3/34 (8.8%) after hysteropexy (p = NS). There were no surgeries performed for recurrent vault or uterine prolapse, and the majority of subjects in each group (91% after hysteropexy, 87% after hysterectomy) were “satisfied and would do (this) again.”

Uterosacral and Round Ligament Hysteropexy

Hysteropexy techniques involving the uterosacral ligaments have also been described, including one by Maher et al. [64] in which laparoscopic suture hysteropexy was performed on 43 women. The Moschcowitz closure of the posterior cul-de-sac was combined with uterosacral shortening and fixation of the ligaments into the posterior cervix and then fixation to the contralateral uterosacral. At a mean interval of 12 ± 7 months, 81% remained symptom-free, and objective prolapse cure was achieved in 79%. Eventually, 16% underwent repeat surgery, all performed for uterine prolapse. Bedford et al. [65] compared hysterectomy with laparoscopic uterosacral colpopexy to laparoscopic hysteropexy and found with a median follow-up of 2.5 years that the failures at the apex were 27% for the hysteropexy group and 11% for the hysterectomy group ($p < 0.2$). It appears that the uterosacral approach has not matched the efficacy of sacrospinous and sacral hysteropexy techniques.

Likewise, varieties of “round ligament” uterine suspensions have been proposed and have performed rather poorly in comparison with the alternatives. These have included laparoscopic [66,67] techniques and also open techniques including that reported by O’Brien and Ibrahim [68] who observed uterine prolapse recurrence in eight of nine postmenopausal patients after 3 months. The round ligament is generally not regarded as a pelvic support structure or a reliable anatomic anchoring point for uterine prolapse surgery.

In summary, preserving the prolapsed uterus is a strategy receiving increased attention as we face an expanding “toolbox” of surgical options including mesh-augmented repairs and tissue fixation systems offering alternatives to standard suture-based approaches. New techniques appear to provide greater operative ease and show highly promising results in both the apical and anterior compartments. In particular, sacrospinous hysteropexy and abdominal sacrohysteropexy have established credible track records from the standpoints of anatomic outcomes, morbidity, and patient satisfaction. Uterine preservation now plays a more central role in the treatment of symptomatic uterovaginal prolapse.

Obliterative Procedures: Lefort Colpocleisis and the Manchester Operation

The Manchester/Fothergill procedure was described in 1888 by Archibald Donald of Manchester, England. The Manchester procedure involves shortening and reattachment of the uterosacral and cardinal ligaments, combined with either partial or complete cervical amputation. Up to 20% recurrence rates have been described within the first few months, and additionally, functional concerns including dyspareunia and dysmenorrhea have been cited. A recent retrospective observational study evaluated 204 younger women (mean age 34.68 ± 4.24 years) with grade 2–3 uterine prolapse; 95.1% had associated cystoceles and 51.3% had associated rectoceles. Postoperatively, 27 patients (13.2%) had febrile morbidity, urinary retention occurred in 45 patients (22.0%), and cervical stenosis occurred in 23 patients (11.3%). Within the first year, one patient underwent abdominal hysterectomy because of unsuccessful cervical dilatation, and at a mean of 3.6 years following the operation, eight patients had undergone a vaginal hysterectomy for recurrent uterine prolapse. The authors noted a mean satisfaction/acceptance score for the operation of 8.52 ± 2.13 (range, 2–10).

The Manchester operation is no longer used widely but may still represent a consideration for select cases of prolapse in women wishing to retain their uterus.

Lefort Colpocleisis

Colpocleisis represents an excellent alternative for a select group of older, nonsexually active women with severe prolapse who wish to undergo a low-morbidity repair with extremely quick recuperative times. The Lefort (partial colpocleisis) operation, first described by its namesake in 1877, results in closure of the vagina, leaving small (pencil-width) lateral channels on each side, and therefore is only appropriate for women who are completely certain they do not ever want to have penetrative sexual intercourse again.

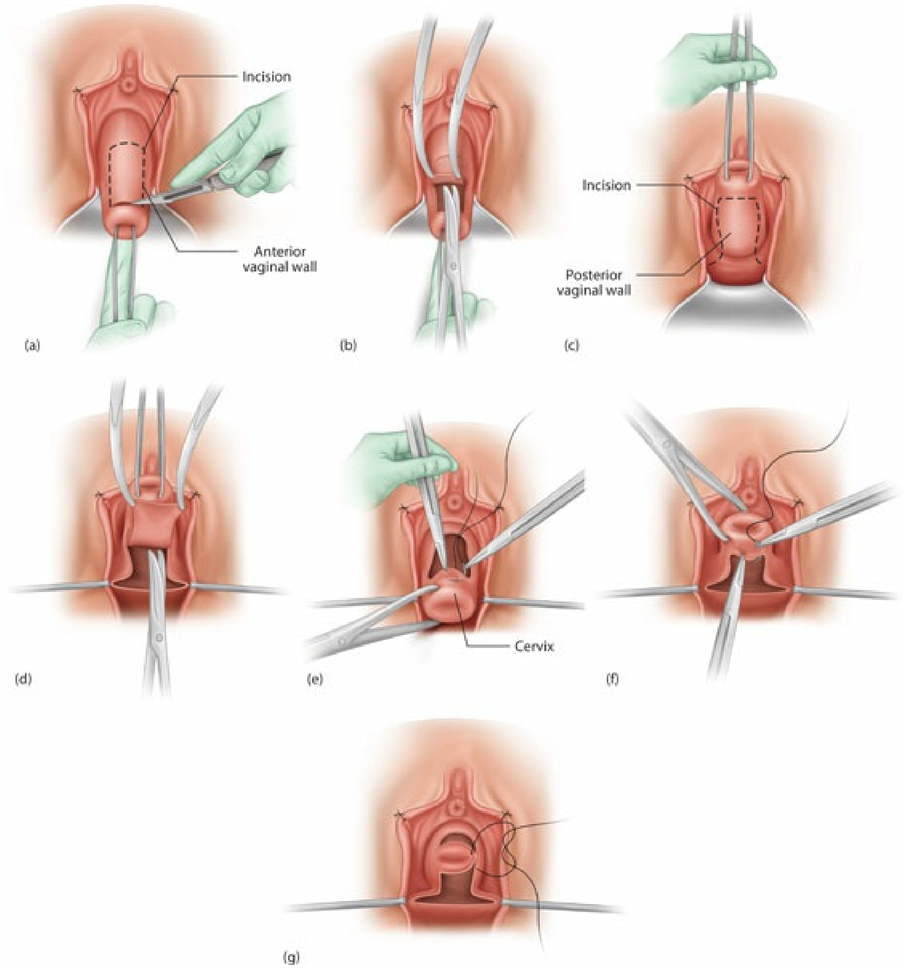

Figure 88.6 (a) anterior vaginal incisions, (b) anterior dissection, (c) posterior incision, (d) posterior dissection, (e) anterior suture placement, (f) posterior suture placement, (g) sutures tied, creating lateral tunnels.

The operation can be performed under local anesthesia if desired and is associated with minimal postoperative pain, high rates of patient satisfaction, and exceptionally low rates of failure [69,70]. With this technique, trapezoidal patches of vaginal epithelium are removed from both anterior and posterior vaginal walls, followed by placement of interrupted absorbable sutures approximating the anterior and posterior edges of the retained vaginal epithelium “strips” running along each lateral side of the prolapse. As the sutures are sequentially tied, the effect is to fold the pubocervical and rectovaginal connective tissue surfaces onto each other, which reduces the cervix and vaginal apex and eventually inverts the entire prolapse bulge, while obliterating the vaginal canal. The repair should include a robust perineorrhaphy to significantly narrow the vaginal introitus. Although the operation retains epithelialized “tunnels” allowing for cervical and uterine secretions to discharge, there is a risk of future difficulty sampling the cervix and endometrium should vaginal bleeding later occur, and patients need to be counseled about this. Cases of cancer and hematocolpos have been reported [71], and these cases may introduce difficult diagnostic and treatment challenges.

Before performing this operation, normal cervical cytology screening should be verified according to age-appropriate guidelines, and either ultrasonography or endometrial sampling may be a consideration in some cases (Figure 88.6).

CONCLUSIONS

Uterine prolapse is common among our patients and remains a challenging surgical condition even in experienced hands. Pessary management remains an important and often effective strategy that should be offered as an alternative to surgical repair. Vaginal hysterectomy followed by apical suspension remains a surgical mainstay, although the scientific evidence suggests that the removal of the uterus, in anatomic terms, may contribute no structural benefit to a prolapse repair in many cases. Hysterectomy is still commonly performed with prolapse repairs, but it is important to emphasize that uterine prolapse is most often a result of the disease process rather than its cause—in other words, an "innocent bystander." Hysteropexy repairs are an alternative whose efficacy has been established by an increasing amount of research, although one recent comparative trial found hysteropexy to be associated with higher rates of objective failure than hysterectomy for the treatment of advanced prolapse cases; the same trial, however, found rates of patient satisfaction to be identical. Although numerous questions remain open for future research, the current evidence suggests that favorable results can be achieved using both the "traditional" hysterectomy-based approach and the uterine-preserving surgery. As new and improved minimally invasive hysteropexy techniques emerge, uterine preservation may have the potential for increased appeal among both surgeons and patients.

Choosing the "right" treatment strategy for uterine prolapse, whether surgical or nonsurgical, should take into consideration the individual patient's sexual and reproductive activity, personal feelings, sites and degrees of pelvic prolapse, concurrent pelvic pathology, and overall health status. By offering several treatment alternatives, clinicians can help to ensure that the largest number of symptomatic women achieves their personal goals.

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89 Biological Grafts in Reconstructive Pelvic Surgery

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Successful repair of pelvic floor defects remains one of the greatest challenges facing pelvic reconstructive surgeons. The recognized high rate of recurrence following anterior vaginal wall repairs has led pelvic floor surgeons to augment these repairs with various materials. A variety of prostheses have been used: allografts, xenografts, and absorbable and permanent synthetic mesh. Among the most important advances in this field has been the utilization of new lightweight synthetic mesh and biological grafts into the surgical armamentarium. One of the arguments for using a biological graft versus a synthetic mesh is to theoretically minimize the risk of graft exposure, extrusion, infection, or new-onset dyspareunia. A recent American Urogynecologic Society (AUGS) survey reported that transvaginal mesh use decreased from 90% in AUGS survey responders to 61% after the FDA safety update in 2011 [1]. Biological grafts represent an important option in transvaginal pelvic reconstruction, especially following heightened public and governmental scrutiny of synthetic materials and the subsequent declining utilization of transvaginal permanent mesh.

BASIC SCIENCE OF BIOLOGICAL GRAFTS

The purported function of biologics is to provide a regenerative framework for extracellular matrix and remodeling with new collagen deposition, resulting in new tissue formation with eventual replacement of the graft.

The initial reaction after implantation is adsorption of host proteins to the implant creating a biofilm. This process does not require a cellular response and is initiated within seconds of implantation. After this initial response, low-molecular-weight proteins such as albumin and fibrinogen, immunoglobulins, and extracellular matrix molecules are adsorbed to incorporate the implant within the host tissue. Once the proteins undergo conformational changes, the host-implant complex becomes immunogenic and sets off an inflammatory response including the complementary system.

A cascade of events follows graft implantation. First, an acute inflammatory response occurs. This is the same foreign body response that occurs in wound healing after any insult. Mononuclear cells (macrophages, mast cells) populate and penetrate the graft scaffold. The following typical sequence of wound healing follows this with mononuclear cells secreting signaling factors such as cytokines and growth factors. Fibroblasts are attracted to the site to initiate synthesis of collagen, predominated by type 3 collagen initially. Eventually, matrix proteins are produced, which begin the remodeling process. Early cellular and vascular infiltration of a graft scaffold is critical for fibroblast proliferation and new collagen deposition. In the absence of angiogenesis, tissue remodeling does not occur and instead scar formation results. In a rodent animal model, neocellularity was seen at 3 months after alloderm implantation [2]. This was also observed in a primate model 1 month after human dermal graft implantation [3].

The initial inflammatory response can promote either graft integration, excessive scarring, graft encapsulation, or graft degradation. This balance between normal wound healing and a disproportionate inflammatory response is largely controlled by the action of chemical signaling molecules at the host/graft interface. In vitro studies demonstrated alloderm (acellular cadaveric dermis) inducing a smaller cytokine response than non-cross-linked porcine dermal grafts and porcine intestinal submucosa [4,5]. Animal models have also showed that cross-linked porcine dermal grafts are associated with a heightened foreign body response and pronounced early inflammatory response. Similar tissue response has been observed in humans. Our histopathological analysis of cross-linked, nonperforated, porcine dermal grafts used as transvaginal suburethral slings in recurrent stress incontinent patients demonstrated an increased lymphocytic cell reaction and multinucleated giant cells infiltrating the specimen at 42 weeks post graft implantation with no graft material detected thereafter. The consequences of eventual loss of the graft on the structural and functional integrity of the surgical repair in pelvic reconstructive procedures need to be determined [6] (Figure 89.1).

When scaffold degradation of the graft is accompanied by cellular infiltration, extracellular matrix deposition, and neovascularization, tissue remodeling occurs [7]. If this process fails to take place in the host, the graft, instead of being replaced by new regenerated tissue, is replaced by a scar. Vaginally, this can result in unwanted outcomes such as vaginal shortening, constriction, or dyspareunia. It has been suggested that rapid degradation of the graft scaffold without deposition of new collagen can predispose to implant failure. The biomechanical properties (strength, elasticity, stiffness, and strain) and histopathological characteristics of a graft in vivo have been studied largely in vitro with animal models.

In the New Zealand white rabbit model, the histopathology and biomechanical properties of four biological grafts: human dermis, porcine dermis, porcine collagen–coated polypropylene mesh, and autologous fascia at two anatomical sites were investigated. Elastic modulus and ultimate strength decreased in dermal collagen grafts. Vaginal site graft implantation was associated variably with decreased strength, with more shrinkage, and with less stiffness and erosions. Histologically, cadaveric and xenograft dermal grafts promoted more inflammation and demonstrated less collagen ingrowth than autologous fascia or porcine collagen–coated synthetic material. Longer-term outcomes (9 months) in this model demonstrated cross-linked porcine dermal graft–induced variable host tissue responses. Some grafts demonstrated encapsulation with minimal host tissue infiltration into the graft. Others showed a severe foreign body reaction [8,7].

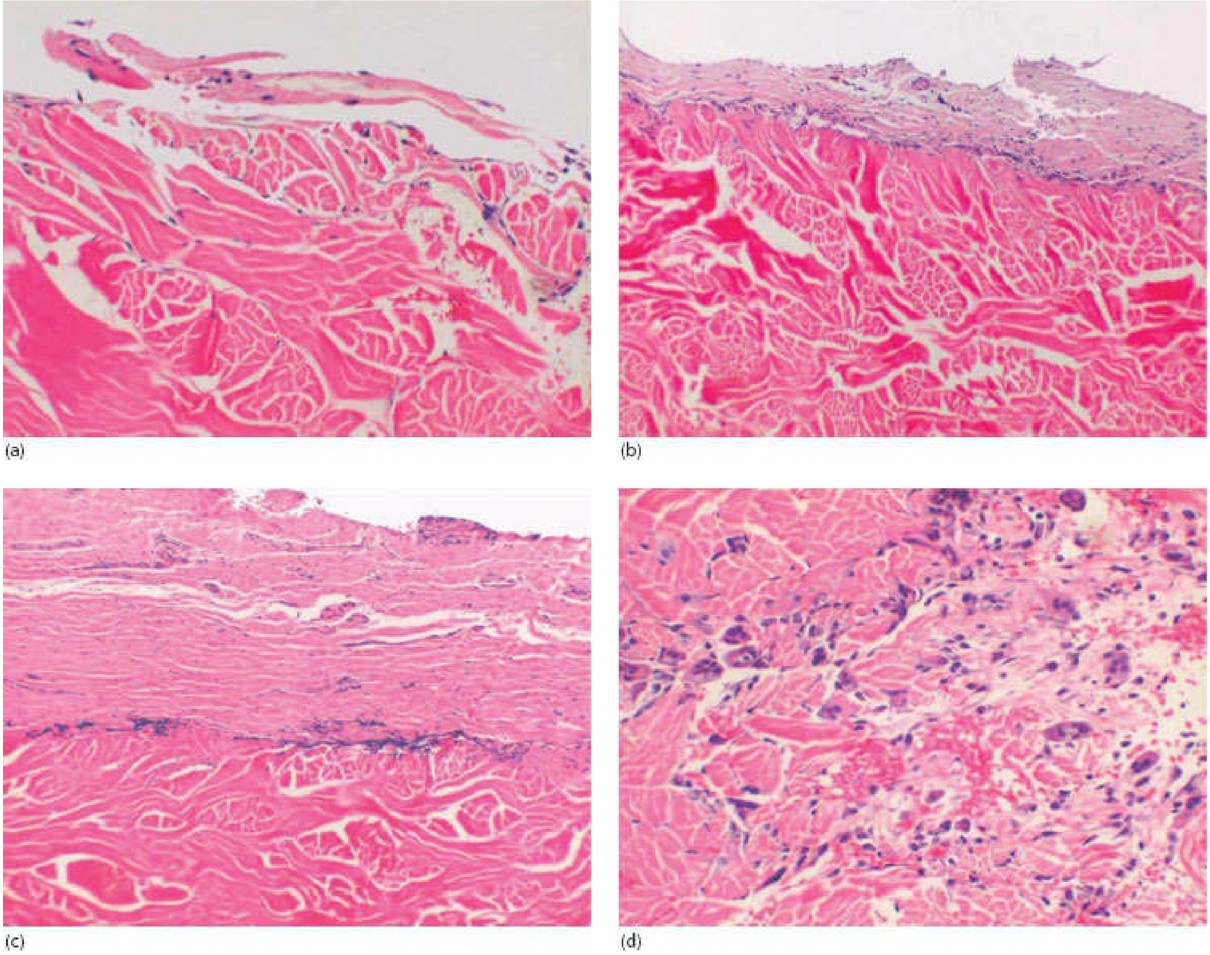

Figure 89.1 Hexamethylene diisocyanate cross-linked porcine dermal implants may integrate or encapsulate and undergo degradation and not be incorporated into host tissue. (a) Suburethral graft 15 weeks after implantation. The periphery of the graft demonstrates a thin layer of new collagen formation with minimal fibroblast infiltration. (b) Suburethral graft 19 weeks after implantation. Graft demonstrates mild fibroblast proliferation with neovascularization at its periphery. There is a mild lymphocytic reaction at the interface of the graft and new collagen formation. (c) Suburethral graft 21 weeks after implantation. Graft demonstrates moderate fibroblastic proliferation and collagen formation with a more prominent lymphocytic reaction at the

interface. (d) Suburethral graft 42 weeks after implantation. Graft demonstrates histiocytes and multinucleated giant cells infiltrating the thickness of the specimen (a, d, hematoxylin and eosin, 20× magnification; b, c, hematoxylin and eosin, 10× magnification). (From Gandhi S et al., *Am J Obstet Gynecol*, 192, 1643, 2005. With permission.)

The mechanical properties of grafts changed after implantation.

Preimplantation graft properties did not predict postimplantation biomechanical graft behavior. Human dermal graft displayed more strength and stiffness at the start, but these properties diminished with time. The investigators concluded that in this animal model the dermal graft did not offer more mechanical support than autologous fascia or synthetic mesh.

As shown in both animal models and clinical studies, porcine dermis cross-linked grafts induce inconsistent long-term response in different hosts. Some behave more as a resorbable material with degradation and total loss of mechanical strength at the graft site during remodeling, and some behave more as a synthetic implant without any tissue ingrowth. Suburethral tissue specimens in patients with recurrent SUI after sling surgery with hexamethylene diisocyanate (HMDI) cross-linked porcine dermis showed some specimens with limited collagen remodeling and minimal inflammation, while others induced a strong foreign body response. Gandhi et al. reported unpredictable tissue reactions with this adjuvant graft in stress urinary incontinence surgery [6,7].

In animal models, we have seen that vaginal site implantation displays different behaviors than abdominal site implantation of prosthetic grafts. Vaginal grafts underwent degradation at a more rapid rate. Erosion rates were minimized by decreasing graft size.

GRAFT TYPES

The use of biological grafts dates back to 1917 in anti-incontinence procedures [9]. These consisted of autologous grafts. Allografts were the first biological mesh type to be introduced to North America in the 1990s. Dermis is the most common tissue due to the size of the graft, which may be obtained. These dominated the market and literature until the introduction of xenografts. Xenografts quickly gained popularity as a result of its reduced cost, improved availability, and reduced regulatory restrictions.

In female pelvic reconstruction, biological grafts consist of three types: autologous grafts, and allograft and xenografts [10]. Autologous grafts consist of fascia lata, dura mater, split-thickness skin grafts, or rectus fascia harvested from the host recipient. Allografts consist of cadaveric sources of dermis or fascia lata. Xenografts consist of porcine dermis, small intestinal submucosa (SIS), bovine dermis, and pericardium and xenograft synthetic composites (acellular cross-linked porcine dermis with polypropylene mesh) (Table 89.1).

The differences observed in graft behaviors are likely a result of the host response, tissue types, and processing methods. Tissue processing can alter the immunogenic and foreign body response to these grafts. Perforation of biological grafts has been shown to be beneficial as it promotes angiogenesis and more rapid host infiltration of fibroblasts for collagen deposition. The porosity of the graft material also seems to reduce seroma formation and the risk of infection.

Table 89.1 Commercially Available Biological Grafts for Reconstructive Pelvic Surgery

Tissue	Brand name	Processing
Cadaveric fascia lata	Suspend Tutoplast (Mentor, Santa Barbara, CA)	g irradiated Solvent dehydrated Preserved
	FasLata (C.R. Bard, Covington, GA)	g irradiated Freeze-dried
	ReadiGRAFT (LifeNet, Virginia Beach, VA)	Freeze-dried, Allowash (removes cells, bacteria, virus, fungi, and spores)
Cadaveric dermis	Alloderm (LifeCell Corp., Branchburg, NJ)	Freeze-dried
	Repliform (Boston Scientific, Natick, MA)	Cryopreservation without ice crystal Damage
	Bard Dermal Allograft (C.R. Bard, Murray Hill, NJ)	g irradiated Freeze-dried

	Axis Tutoplast Processed Dermis (Mentor, Santa Barbara, CA)	g irradiated Solvent dehydrated
Porcine dermis	Pelvicol Acellular Collagen Matrix (C.R. Bard, Murray Hill, NJ)	g irradiated Hexamethylene diisocyanate HMDI cross-linked
	PelviSoft Biomesh (C.R. Bard, Murray Hill, NJ)	g irradiated HMDI cross-linked Fenestrated
	PelviLace Biourethral Support System (C.R. Bard, Murray Hill, NJ)	g irradiated HMDI cross-linked
	Intexen (American Medical Systems, Minnetonka, MN)	Freeze-dried
Porcine SIS	Symphysis Smart Remodeling Matrix (Cook Urological, Inc., Bloomington, IN)	Solvent dehydrated Freeze-dried Non-cross-linked
	Surgisis Soft Tissue Graft (Cook Urological, Inc., Bloomington, IN)	Solvent dehydrated Freeze-dried Non-cross-linked
	Stratasis Tension-Free Urethral Sling (Cook Urological, Inc., Bloomington, IN)	Solvent dehydrated Freeze-dried Non-cross-linked
	FortaGen (Organogenesis, Canton, MA)	g irradiated 1-ethyl-3-[(3-dimethylamino)propyl]-carbodiimide hydrochloride cross-linked
Bovine pericardium	Veritas (Synovis Surgical Innovations, St Paul, MN)	Non-cross-linked
Bovine dermis	Xenform Soft Tissue Repair System (Boston Scientific, Natick, MA)	Non-cross-linked

Allografts carry a potential risk of one to two per million for viral transmission and one in eight million for HIV transmission. Xenografts carry a theoretical prion risk although no cases have been reported.

Autologous grafts offer the benefit of avoiding the effects of processing, of graft rejection, and of transmissible infections. Because the patient serves as her own donor, these grafts induce very little foreign body reaction, and there is usually good incorporation of the graft into the native tissue. These grafts, unlike others, may also be used for infected surgical sites.

The harvesting of autologous fascia lata has been described in various pelvic floor reconstructive surgical procedures. With the patient's leg rotated medially in a dorsal lithotomy position, a 4 cm incision is made between a point 2 cm above the lateral epicondyle and directly superior to the medial aspect of the patella. The vertical fibers of the iliotibial tract and the oblique and horizontal fibers of the dorsal fascia lata are exposed with blunt and sharp dissection. A similar 4 cm incision is made 15–20 cm superior to the previous incision in the line of the lateral epicondyle and greater trochanter. With a special stripper, an extended transverse fascial thigh graft is excised. The skin is reapproximated with sutures and the leg is wrapped in an elastic bandage. Leg compression is necessary for hemostasis but may increase the risk of deep venous thrombophlebitis.

Procurement from the patient's own body eliminates the concerns about transmissible infections, but harvesting the tissue may be associated with surgical morbidity. Pain, infection, weakness, and unsatisfactory cosmetic outcomes have all been cited as disadvantages to harvesting autologous grafts. In a retrospective review of 71 patients undergoing either a pubovaginal sling or abdominal sacrocolpopexy using autologous fascia lata, Walter reported one case of a hematoma requiring draining and five cases of incisional cellulitis requiring oral antibiotics. Nineteen percent of patients also reported persistent thigh numbness with a mean follow-up time of 25 months [11].

Since their first use in pelvic reconstruction, the popularity of autologous grafts has been surpassed by the use of other materials as a result of questions regarding the durability of autologous grafts [12]. More recently, a reanalysis of a 5-year data on apical repair with cadaveric fascia lata reported success rates exceeding 90% when a composite score was used to define success [13,14]. This was markedly higher than the 68% success rate at 5 years when only anatomic outcomes were measured. The limitation of this analysis from this randomized controlled trial was that the subjective query of patients was not blinded nor utilized validated instruments. It has been suggested, from in vitro study, that differences in horizontal or vertical graft orientation significantly affects the graft's bursting strength.

Xenografts and allografts must undergo decellularization and sterilization to prevent antigenic responses and infection. Sterilization methods include freeze-drying, solvent dehydration, and irradiation. Each is purported to have an effect on the donor tissue. Previous studies of biological implants used as slings reported that freeze-dried cadaveric fascia lata demonstrated the most diminished biomechanical properties and intratissue consistency after graft implantation [12,15].

Xenografts may also undergo supplemental cross-linking. Possible cross-linking agents are HMDI, carbodiimide, glutaraldehyde, or photooxidizing agents. Although cross-links exist in native collagen present in dermal grafts, additional processing increases the amount of collagen cross-links, resulting in supplemental cross-linking. Supplemental cross-linking is purported to prolong the lifespan of the implant. The 3D structure of the collagen mechanically strengthens the matrix and impedes degradation by enzymatic collagenase.

The effect of supplemental cross-linking on xenograft behaviors appears to play the largest role on host tissue responses. Even though in vitro studies report generally improved graft resistance to enzymatic degradation to host collagenases with increased collagen cross-links, this has not always correlated to clinical efficacy [2]. Long-term tissue reinforcement to serve host tissue regeneration is a purported benefit of cross-linked biological grafts. Cross-linked biologics in the plastic surgery literature were found to behave more as a permanent synthetic. In both translational animal models and in vivo, supplemental cross-links may have a significantly higher immunologic disadvantage, which may result in graft rejection. In the hernia literature, cross-linked dermal grafts were found to be completely degraded in infected wounds. In uninfected implants, no evidence of tissue remodeling was seen. In vivo, cross-linked porcine dermal can behave more as a permanent foreign body or a synthetic due to its lack of integration into host tissue and likely resultant fibrous encapsulation [6]. Non-cross-linked implants facilitate tissue ingrowth without encapsulation and promote tissue remodeling.

The balance between extracellular deposition and scaffold degradation is necessary for effective tissue graft reinforcement during tissue remodeling. While some study investigators have reported deposition of new matrix at the site of biological graft implantation, tissue regeneration within a degrading scaffold can be mimicked by fibrotic scar formation. The distinction between these two states is not always histologically apparent.

One of the major limitations of biological graft research is the common animal models used. Most investigations in the female pelvic medicine and reconstructive surgery literature have used the New Zealand white rabbit model. In the general surgical literature, rodents, guinea pigs, or minipigs have been utilized. Those animals are used due to relative ease of graft implantation and low cost. Tissue responses in different species do not directly compare to humans—especially in the long term. We have shown this in the vaginal rabbit model.

Failure of grafts may be due to a rapid or an unbalanced degradation of the graft scaffold without the necessary time for proper support from the deposition of the components of the extracellular matrix. Gradual tissue remodeling of an implanted tissue graft is essential for success in pelvic reconstructive procedures.

CLINICAL USE OF BIOLOGICAL GRAFTS

Anterior Compartment Defects

Biological graft augmentation in the anterior compartment has been an area of scientific interest as reflected by the largest number of prospective, retrospective, and randomized controlled trials to support its use. This interest is because anterior compartment repairs with native tissue have very high anatomic failure rates in excess of 40% [16]. Studies have shown that anterior compartment defects benefit from graft-reinforced repairs. It is well established that repairs with polypropylene monofilament mesh result in higher long-term anatomic success rates compared to traditional native tissue repairs (46% vs. 14%) [17]. However, the anatomic benefit of synthetic permanent reinforced repair must be balanced against its increased potential risk of mesh erosion, exposure, pelvic pain, and dyspareunia.

To minimize the risk of exposures with synthetic mesh, Sand et al., in a prospective, randomized, controlled trial, used a polyglactin 910 mesh imbricated into an anterior application of the endopelvic connective tissue compared to a native tissue repair with a midline colporrhaphy for vaginal repair of the anterior compartment. Anatomic success (less than grade 2) was significantly increased with absorbable synthetic mesh after 1 year (75% vs. 57%, $p = 0.02$) [16].

Long-term follow-up (greater than 18 months) of prospective work by Clemons et al. demonstrated that when cadaveric dermal grafts were attached adjacent to the arcus tendineus fascia bilaterally, the anatomic recurrence (POP-Q stage ≥ 2) rate was 58.3%. Among these recurrences, only 28.6% were symptomatic. They concluded that alloderm graft has good subjective success despite a moderate rate of objective failure within 24 months of placement [18]. In Clemons' initial study, 33 patients had a 59% objective success rate and a 97% subjective success rate.

Conversely, in a retrospective comparative study, Botros et al. reported a significantly higher success preventing recurrent anterior prolapse (greater than or equal to stage 2) when using a human dermal graft for a paravaginal repair (attached directly to the arcus tendineus fasciae) in addition to standard anterior colporrhaphy when compared to only anterior colporrhaphy alone (19% vs. 43%, $p = 0.004$) [19]. Favorable subjective outcomes were reported, but limited by response. The differences in outcomes between these two trials using barrier grafts of human dermis may be attributed to the surgical technique. While many studies have described tension-free placement of biological grafts or anchoring to sites along the pelvic wall, Botros et al. described the fixation of the graft to the arcus tendineus fasciae pelvis with minimal tensioning.

The 2013 Cochrane meta-analysis of two randomized controlled trials of primary prolapse repair with or without HMDI cross-linked porcine dermis in the anterior compartment concluded that anterior colporrhaphy has a nearly twofold (RR 1.7) risk of recurrence as compared to using an adjuvant acellular porcine dermal implant (CI 1.1–2.6) [20,21].

Two other well-designed randomized controlled trials by Natale et al. and Menefee et al. demonstrated lower recurrence rates with adjuvant synthetic meshes compared to porcine dermis. Natale et al. reported a 72% anatomic success rate (less than or equal to stage 2) with polypropylene vs. a 56% in the porcine dermal graft group. Extrusion was only seen in the synthetic mesh group (6.3%). Both groups reported improvement in QOL [22]. Menefee et al. compared success between polypropylene, porcine dermis, and native tissue anterior colporrhaphy in a randomized controlled trial with blinded postoperative outcomes [23]. They reported the highest success rate with polypropylene (82%) versus porcine dermis (54%) and 42% with native tissue repairs. Extrusion rates were higher in the polypropylene group (14%) versus 4% in the porcine dermal group and with none in the native tissue group. Higher extrusion rates have also been noted in other trials with synthetic grafts [17].

When anterior colporrhaphy with native tissue repair was compared to using an adjuvant porcine dermal graft in three randomized trials, the objective failure was significantly higher in the native tissue group (27%) compared to the porcine dermis group (16%) [20,21,23].

When used in the anterior compartment for vaginal reconstructive surgery, it seems that how allografts are implanted may impact their success of preventing recurrence. In a prospective, randomized, controlled trial, Gandhi et al. reported that a 2 × 4 cm cadaveric fascia lata graft overlay did not reduce the rate of recurrent cystocele. At 13 months, the objective (>stage 2) and subjective failure rates of the anterior colporrhaphy were not statistically significantly different: 29% and 21% from the 10.5% and 10.9% noted in the fascial patch group, respectively [15]. In a study using adjuvant cadaveric fascia lata grafts, which were attached using transvaginal bone anchors, only 2 out of 132 patients at 12 months had recurrent cystoceles of greater than second degree. Only one case of osteitis pubis was reported [24].

A randomized controlled trial of standard native tissue anterior colporrhaphy compared to utilizing adjuvant small intestine submucosa grafts reported a 59.3% anatomic cure rate vs. 86.2%, with the adjuvant small intestine submucosa intestine grafts. No differences were noted in QOL measures or subjective outcomes [25]. No inflammatory complications were reported—as had been reported in single case with porcine small intestine submucosa transobturator slings [26]. Guerette et al. compared native tissue repairs with bovine pericardium graft–reinforced repairs in the anterior compartment. They reported a 78.4% versus 85.7% success rate, respectively at 1 year. At 2 years, the bovine pericardium graft group's success rate dropped to 76.5% vs. 63% with native tissue. Both groups demonstrated improvements in subjective outcomes. No statistically significant differences in subjective or objective outcomes were noted with use of bovine pericardium adjuvant grafts in the anterior compartment [27].

Reanalysis by Barber et al. of the original work suggested that when subjective outcomes are considered, the failure rates of graft-augmented repairs are comparable to native tissue. Surgical success defined as anatomic support proximal to the hymen had the lowest treatment success (19.2%–57.6%).

When surgical success was defined as the absence of bulge symptoms, the cure rate was 92.1%. If success was defined as absence of retreatment then the success rate was 97.2%. These wide variations in reported success were also demonstrated in apical prolapse compartment repairs. Utilization of a composite definition (subjective and objective outcomes) of success may alter the success of various biological adjuvant grafts in anterior compartment repairs. Adjuvant biological grafts have demonstrated superior anatomical outcomes when compared to native tissue repairs in the anterior compartment. However, no change was seen in subjective outcomes compared with native tissue anterior compartment repairs [13].

Posterior Compartment Defects

Posterior vaginal wall prolapse is commonly associated with functional symptoms of vaginal bulging, obstructed defecation, and sexual dysfunction. Repair of posterior compartment defects should theoretically work to restore normal anorectal caliber and support to improve anorectal symptoms. However, studies have reported variable functional responses to anatomic correction [28–30]. Although transvaginal use of biological grafts for posterior compartment defects is proposed to reinforce repairs, there is a paucity of studies to support this hypothesis. When cadaveric dermal grafts were used to augment site-specific defect repairs in the posterior compartment, Kohli reported that 93% of patients had a POP-Q point Ap measurement of <−0.5 at 13 months in his prospective trial [31]. There are three randomized controlled trials evaluating biological graft–augmented repairs in the posterior compartment [16,28,29]. But mostly the literature is limited to retrospective comparative studies [28,29]. Paraiso et al., in a double-blinded, randomized controlled trial, compared posterior colporrhaphy, site-specific repair in the posterior compartment, and site-specific defect repairs augmented by porcine SIS. At 1 year, the authors reported a failure rate (greater than or equal to stage 2) of 14%, 22%, 46%, respectively [28]. In a secondary analysis by Gustilo-Ashby at 1 year, it was determined that although defecatory symptoms improved after posterior repair with and without graft augmentation, they persisted or worsened in up to 35% of patients. No difference was observed in sexual function [30]. Sung et al. also performed a randomized, controlled trial comparing native tissue repairs with small intestine submucosa augmented repairs. At 1 year, there was no difference in anatomic or subjective failures (notice of vaginal bulge symptom or defecatory symptom failure). These authors concluded that small intestine submucosa graft augmentation was not superior to native tissue for either measure at 1 year. The rate of dyspareunia was comparable to the control group (12.5% vs. 7%) [29]. Novi et al., in a prospective cohort trial examining sexual function at 6 months, determined that the porcine dermis–reinforced posterior repair group had a significant improvement in the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire scores vs. the site-specific native tissue posterior repair group (19.9 vs. 6.9, respectively). Interestingly, both groups demonstrated a significant and comparable improvement in dyspareunia (decrease of 8% vs. 10%, respectively) [32].

Based on the available data, biological graft–reinforced repairs in the posterior compartment demonstrate similar or worse anatomic outcomes when compared to native tissue repairs. Mild improvements in functional outcomes were seen; specifically, there was a positive impact on sexual function. This benefit possibly represents the only reported potential benefit of graft-reinforced repairs in the posterior compartment.

Apical Prolapse

Abdominal sacrocolpopexy (ASC) has been considered the gold standard abdominal approach for prolapse of the vaginal apex with variable cure rates that depend on the definition of success employed (19.2% if perfect anatomic support to 97.2% if no reoperation) [13,33,34]. Although most of the long-term studies utilized synthetic mesh with an open approach, there exists a concern about adverse events such as mesh erosion with these grafts [33–35]. The 7-year outcomes from the extended CARE trial estimate the probability of mesh erosion to be 9.9%–10.5%, depending on whether the last censoring time was based on the last clinic visit or the last telephone interview [35]. These authors maintain that these results cannot be extrapolated to estimate outcomes in other surgical approaches for apical prolapse repair. However, the 2012 publication by Siddiqui et al. is promising. They retrospectively compared robotic-assisted laparoscopic sacrocolpopexy (RSC) to the historical abdominal sacrocolpopexy cohort from the CARE trial. They determined that at 1 year, both groups had comparable improvement in pelvic floor outcomes and quality of life measures. As consistent with Nygaard et al., the mesh erosion was higher in the ASC group (5.3% vs. 2.4%). These authors attribute their decreased rate of mesh erosion in the RSC cohort with the advent of lighter polypropylene mesh and performance of supracervical hysterectomy at the time of concomitant hysterectomy [36]. To date, the majority of extant studies support the use of synthetic mesh with the durability outweighing the potential risks. In a double-blinded, randomized, controlled trial comparing the use of cadaveric fascia lata and polypropylene mesh for abdominal sacrocolpopexy, synthetic mesh demonstrated superior durability with sustained support of the anterior and apical segments of the vagina utilizing the pelvic organ prolapse quantification (POP-Q) points Aa and C. The objective failure rate was significantly worse (32%) in the fascial graft cohort versus 9% in the polypropylene mesh cohort. Mesh exposures occurred in 2 of the 54 subjects [37]. Five-year data determined that objective recurrence was higher in the fascial group at 38% vs. 6.8% in the synthetic mesh group for any (POP-q stage greater than or equal to 2) [14]. When a composite score was used to define success, the failure rates were less for both cohorts, 10% vs. 3.4%, respectively.

In our center, Letko et al. retrospectively reported on sacrospinous hysteropexy augmented with an acellular cadaveric dermis versus polypropylene mesh for apical compartment defects in post-hysterectomy patients. The dermal graft group demonstrated an objective recurrence (defined as greater than or equal to stage 2) at 1 year of 27.1% and the recurrence rate was 18.5% when polypropylene mesh was used [38].

Currently, the evidence supports that synthetic mesh is best for transabdominal procedures for pelvic reconstructive surgery, but the ideal choice of graft material for vaginal reconstructive surgery is less clear. The role of the site of graft implantation, size of graft, tension or tension-free placement, variable host responses, variability across graft procedures and anchoring methods, and the effect of graft processing are all aspects of biological adjuvant grafts, which may affect its clinical efficacy after implantation. The ideal graft material would be biocompatible with a minimal inflammatory response and offer long-term stabilization to allow for normal wound healing for the duration of tissue remodeling by the host. These are areas for future study to identify ideal biological grafts for use in reconstructive pelvic surgery. Novel research on the use of engineered biomaterials may herald a new area for biological graft in pelvic reconstructive surgery [39].

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90 Synthetic Grafts in Pelvic Surgery

William Barone and Pamela Moalli

INTRODUCTION

Synthetic meshes, which were originally designed to repair abdominal hernias, have been used since the 1950s to repair pelvic organ prolapse (POP) via sacrocolpopexy and since the 1990s for repair of stress urinary incontinence (SUI) [1,2]. In both applications, the overarching goal of biomaterial use has been to improve the perceived low success rates of native tissue repairs and minimize morbidity associated with harvesting a patient's own tissue. The type of mesh used for urogynecological procedures directly mirrors products introduced into the market for hernia repair, though initially surgeons simply cut the mesh into the desired shape for sacrocolpopexy or suburethral slings. Over time, hernia meshes were designed to have lighter weight with wider pores based on clinical outcomes and the work of Klinge, with the urogynecology community quickly adopting the same materials. For example, Ethicon's Prolene Soft hernia mesh was remarketed for sacrocolpopexy as the prototype prolapse mesh Gynemesh PS (Figure 90.1).

By the time the tension-free vaginal tape (TVT) was introduced into the market in 1996, the use of lighter-weight materials had been widely adopted [3]. The TVT transformed the surgical treatment of SUI into a minimally invasive, highly effective procedure with minimal patient morbidity. Based on its tremendous success and perceived demand for a less invasive approach to prolapse repair, manufacturers introduced transvaginal mesh (TVM) procedures for POP using mesh kits in 2002. TVM kits were developed and aggressively marketed by numerous companies. Surgeons, seeking materials to improve the long-term durability of surgical repair for POP with a less invasive approach relative to sacrocolpopexy, were instructed in TVM procedures, resulting in the rapid escalation of TVM kit use after 2005. Indeed, mesh repair showed improved anatomical success of POP repairs but was also associated with increased reports of complications [4].

Reports of these complications in the Manufacturer and User Facility Device Experience database and in small studies prompted the FDA to issue a public health notification in 2008 warning that complications associated with the use of TVMs had been observed [5]. In 2011, after observing a fivefold increase in POP mesh medical device reports (1503 reports), the FDA revised its warning stating that complications associated with TVMs were not rare [6]. Moreover, long-term follow-up (7 years) from studies of meshes implanted for sacrocolpopexy, a procedure previously thought to be associated with a low rate of mesh-related complications, revealed that mesh complications after these repairs were more common than previously thought (10.5%) and increased with time [7]. As a result, decisions regarding POP surgical management have become complex, as the purported lack of durability of native tissue repairs is weighed against the potential benefits and complications of a mesh-augmented repair, and whether the repair is performed abdominally or vaginally. In this chapter, our current understanding of the importance of textile and mechanical properties of a synthetic mesh in driving the host response to synthetic grafts will be discussed as it relates to our current understanding of the pathogenesis of mesh-related complications. In addition, environmental considerations for application of synthetic grafts will be discussed in regards to the vagina.

MESH COMPLICATIONS

Synthetic mesh complications include mesh erosion, mesh exposure, infection, dyspareunia, and pain. Mesh exposure is identified as the visualization or palpation of mesh through the vaginal epithelium (Figure 90.2), while mesh erosion is defined as the perforation of mesh into adjacent structures (bladder, rectum, etc.). Typical management of mesh-related complications, such as exposure, includes repeat surgery to remove mesh [8–11], though symptoms may persist even after mesh is removed [6,11–13]. While prevous generations of SUI slings were found to have complication rates ranging from 0.3% to

23%, contemporary studies focusing on current lightweight, wide-pore meshes such as TVT report reduced complication rates, with an erosion rate of ~1% [14,15]. However, complication rates for synthetic mesh for prolapse repair remain a cause for concern, highlighted by recent FDA notifications citing complication rates up to 15% and 10.5% for transvaginal procedures and sacrocolpopexy, respectively [16–19]. It was not until just recently that studies began to explore the mechanisms by which these complications arise.

CHARACTERIZING MESH: TEXTILE AND STRUCTURAL PROPERTIES

In order to differentiate their products vendors often promote various textile and structural characteristics (Table 90.1). Textile characteristics refer to physical properties of the product and include filament material and size, weight, pore size, and porosity. Structural properties define the mechanical behavior of meshes and include ultimate load, ultimate elongation, stiffness, and energy absorbed. Prior to discussing synthetic mesh for prolapse repair, the definition or interpretation of these textile and structural properties will be provided.

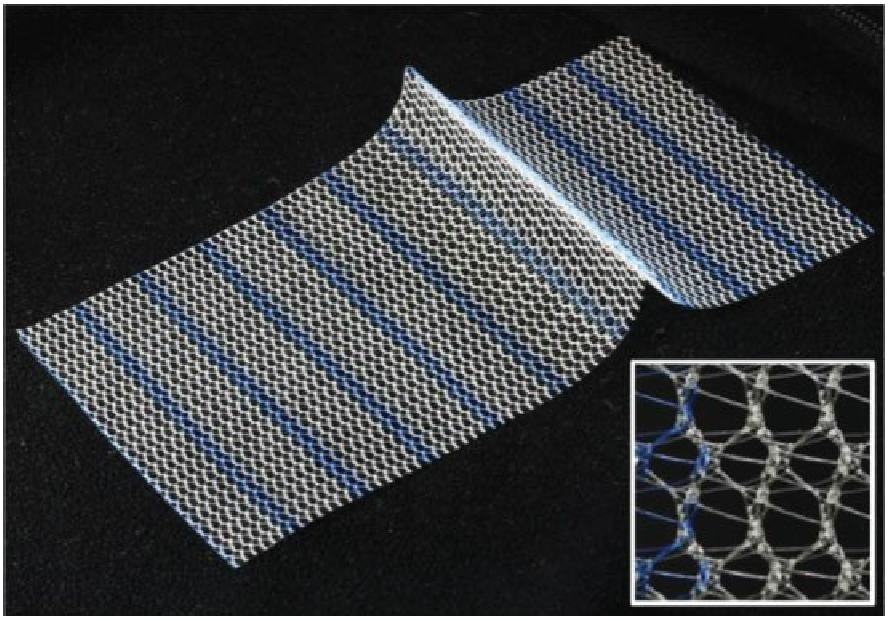


Figure 90.1 Use of synthetic mesh for prolapse repair has drastically increased in recent decades. Following the introduction of the tension-free vaginal tape, nearly all synthetic meshes for urogynecologic applications have been constructed from polypropylene utilizing a knitted, wide-pore, low-weight design. Gynemesh PS (shown here) is the representative of the current generation of products. While the pore geometry (insert) widely varies among contemporary devices, the material and construction techniques are nearly constant.

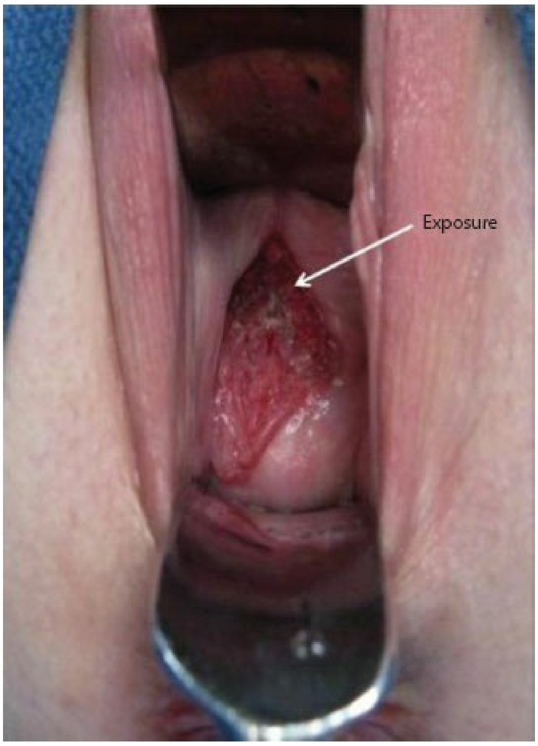


Figure 90.2 One of the most devastating complications following implantation of prolapse mesh is exposure. As shown here in the anterior vaginal wall, exposure occurs when mesh is visible in the vaginal lumen.

Textile Properties

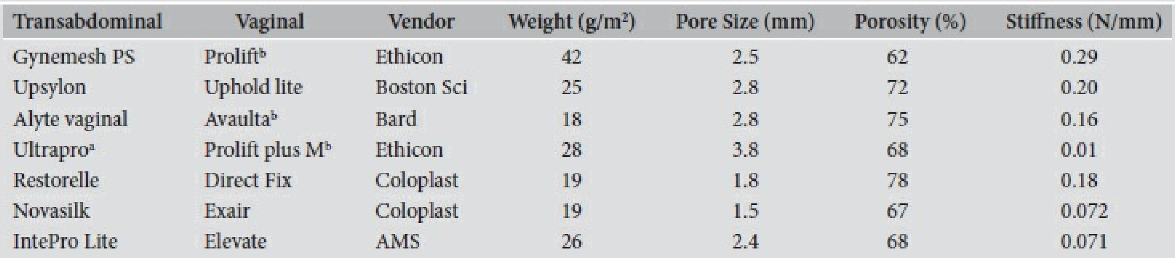
Material: The mesh material refers to the substances from which a mesh is constructed. Mesh materials can be classified as synthetic, biologic, or composite (a combination of synthetic and biological components). Biological materials include autografts and allografts, as well as xenografts. Though biological grafts have been utilized for urogynecological materials, failure rates ranging from 20% to 40% for such devices have significantly limited their use [20,21]. Synthetic meshes are typically comprised of polymeric materials, which have been extruded into thin filaments. Reproducible properties, low morbidity rates, and nondegradable features, in addition to improved anatomical outcomes, have led to the dominance of synthetic materials for urogynecological procedures.

Mesh weight: Mesh weight refers to the area density of the mesh, given in units of g/cm^2. Mesh weight is similar to a measure of density or specific gravity, though given the planar geometry of synthetic meshes, a planar measurement of density is used as opposed to a volumetric measure. More simply, mesh weight provides a measure of the amount of material present in a given area. Given the porous nature of many contemporary synthetic meshes, lower mesh weight is achieved by utilizing greater pore diameters, adding void space to lower the amount of mesh material per unit area.

Pore size: Pore size refers to the maxiumum diameter of the repeating unit pore found in synthetic mesh (Figure 90.1). It must be stressed that mesh vendors typically report the maximum diameter of the largest repeating unit pore, ignoring cross fibers in most cases. In addition, the typical pore geometry is polygonal and thus, a range of diameters may be reported depending on which transverse points are chosen to measure. Further, synthetic meshes often have small pores, which arise from the knit or woven constuction of filaments. However, these smaller pores are generally included in measures of pore size.

Porosity: The porosity of a mesh is defined as the ratio of mesh material to the amount of void space present in a given area, typically constrained to the boundaries of the mesh device. A porosity of 1 refers to a solid “mesh” (i.e. a solid piece of material with no openings), while a porosity of 0 refers to no mesh material present.

Table 90.1 Characteristics of Prolapse Meshes with Names when Applied Transabdominally vs. Vaginally



Transabdominal	Vaginal	Vendor	Weight (g/m^2)	Pore Size (mm)	Porosity (%)	Stiffness (N/mm)
Gynemesh PS	Prolift[b]	Ethicon	42	2.5	62	0.29
Upsylon	Uphold lite	Boston Sci	25	2.8	72	0.20
Alyte vaginal	Avaulta[b]	Bard	18	2.8	75	0.16
Ultrapro[a]	Prolift plus M[b]	Ethicon	28	3.8	68	0.01
Restorelle	Direct Fix	Coloplast	19	1.8	78	0.18
Novasilk	Exair	Coloplast	19	1.5	67	0.072
IntePro Lite	Elevate	AMS	26	2.4	68	0.071

[a] UltraPro (aka Artisyn), measurements made after absorbable component absorbed; stiffness determined in a uniaxial load to failure test.

[b] No longer available on the market.

Structural Properties

In mechanics, structural properties refer to nonnormalized measures of mechanical behavior and describe the load–elongation behavior of structures. Structural properties are dependent on the amount of material present, unlike mechanical properties, which are constant for a given material (Figure 90.3). For instance, a steel rod with a greater diameter will take more force to break relative to a smaller diameter steel rod of equal length. While the structural properties of these rods are different (load and elongation), the mechanical properties (stress and strain) are the same. Due to the porous nature of synthetic mesh, only strucutral properties should be reported. For uniaxial tensile testing, important strucutral properties include ultimate load at failure, ultimate elongation, and stiffness (Figure 90.3). These parameters are defined as follows.

> *Ultimate load*: The load, or force, at which mesh fails (breaks, tears, etc.), reported in Newtons or pounds of force. As a structural property, ultimate load is dependent on the dimensions of the mesh sample tested. Further, this property is dependent on the mechanical test used. The ultimate load is analogous to ultimate stress or tensile strength, where ultimate stress is defined as the ultimate load divided by the specimen's cross-sectional area.
>
> *Ultimate elongation*: The maximum elongation or distension a mesh undergoes until failure occurs, typically reported in units of mm. Similar to the ultimate load, ultimate elongation is dependent on both the dimensions of the tested sample and the mechanical testing protocol used to analyze the mesh. Ultimate elongation is similar to ultimate strain, where ultimate strain is defined as ultimate elongation divided by the initial length of the samples.
>
> *Stiffness*: The slope of the load–elongation curve reported in units of N/mm. Intuitively, stiffness is the resistance of a material to deformation or elongation (i.e., stiffer materials require more force to elongate or deform). Stiffness can be calculated at any point along the load–elongation curve, although often the maximum slope is reported. It is important to note that many mesh products exhibit nonlinear load–elongation behavior; thus, the slope of this line changes along the curve (Figure 90.3). As such, it is best practice to report the elongation at which the slope is calculated. While many different stiffness values can be reported for a mesh, it is ideal that a range of stiffness or the stiffness at the anticipated in-vivo elongation be provided. Whereas stiffness refers to the slope of the load–elongation curve, the slope of a stress–strain curve is referred to as the tangent modulus. Intuitively, the tangent modulus is similar to stiffness but relates the normalized measures of stress and strain rather than load and elongation.

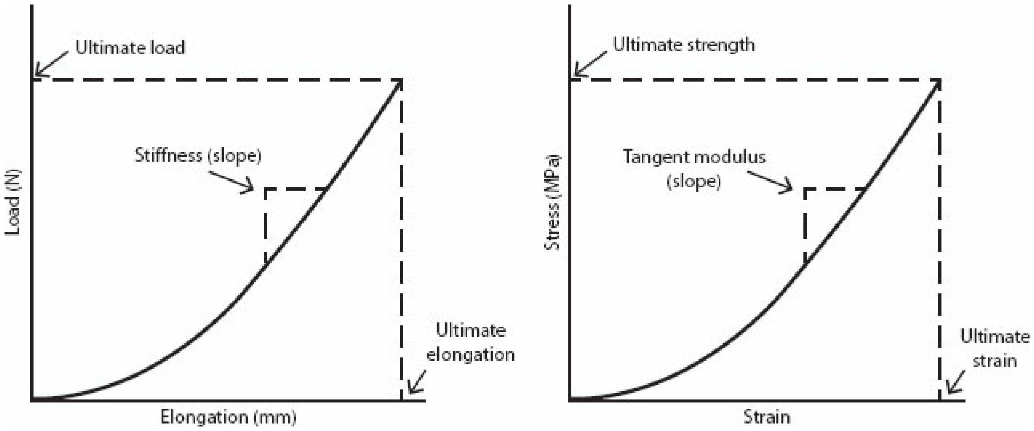


Figure 90.3 Materials testing can be classified as either (a) structural or (b) mechanical. Structural testing measures include ultimate load, ultimate elongation, and stiffness. These parameters are obtained directly from load–elongation curves and do not account for variations in sample dimensions. Mechanical testing properties include ultimate strength, ultimate strain, and tangent modulus. These measures are normalized by specimen dimensions and are used to characterize the mechanical behavior of continuous materials. While materials such as single filament of polypropylene can be characterized using mechanical properties, porous textiles such as synthetic mesh must be characterized by structural properties.

HOST RESPONSE TO SYNTHETIC GRAFTS IN THE VAGINA

To date, few have considered the role of the host tissue response as a significant or causative variable in prolapse mesh outcomes, despite the host response playing a key role in patient outcomes in virtually all other biomaterial applications. In addition, the lack of knowledge concerning the cause of mesh-related complications (erosion, exposure, infection, dyspareunia, and pain) highlights the necessity for examining the host response to grafts in the vagina. Such an understanding is imperative to improve patient outcomes following mesh implantation.

Recent studies have begun to enhance our understanding of the impact of mesh implantation on the morphology, composition, and biomechanical behavior of the vagina. In a rhesus macaque model, Liang et al. compared the host response of the heavier-weight, lower-porosity, high-stiffness prototype prolapse mesh, Gynemesh PS (Ethicon) to two lower-weight, higher-porosity, lower-stiffness meshes, UltraPro (aka Prolift plus M or Artisyn, Ethicon) and Restorelle (Coloplast), following implantation by sacrocolpopexy after a hysterectomy. After 3 months, Gynemesh PS, the stiffest mesh, dramatically altered the histological appearance and functional behavior of the vagina. While all meshes examined were found to disrupt the organization of the vaginal tissue, Gynemesh PS had the greatest negative impact Specifically, Gynemesh PS resulted in atrophy of the smooth muscle layer, with a 55% decrease in the thickness of the muscularis relative to sham-operated controls (Figure 90.4) [22]. Further, Gynemesh significantly increased the number of apoptotic cells in the subepithelium and adventitia layers, rising from 0.43% and 1.56% of cells to 7.22% and 32.49% compared to sham. Overall the impact of mesh was apparent, as a majority of apoptotic cells were located around the individual mesh fibers. Interestingly, changes in vaginal morphology and apoptosis were less pronounced following the lower-stiffness UltraPro and Restorelle implantation.

Gynemesh also negatively impacted the composition of the extracellular matrix, decreasing collagen and elastin content by 20% and 43%, respectively. While UltraPro and Restorelle were not detrimental to collagen content, UltraPro induced a decrease in elastin content by as much as 49%. Finally, sulfated glycosaminoglycan (GAG) content, a marker of tissue injury, was increased by 20% relative to sham samples, while collagenase activity increased by 135% following Gynemesh PS implantation [22]. Overall, these results clearly demonstrate that the vagina undergoes a maladaptive remodeling response following mesh implantation with heavier-weight, lower-porosity, and higher-stiffness meshes elicite the most detrimental changes. The degenerative response was the most consistent with a phenomenon referred to as stress shielding, a mechanosensitive phenomenon in biological tissues, which results in thinning of the tissues associated with a prosthesis. Alternatively, degradation could be the end result of chronic inflammation associated with a foreign body response. Indeed, the increase in sulfated GAG content following synthetic mesh implantation is consistent with acute soft tissue injury and tissue turnover [23]. Regardless of the mechanism, these findings are consistent with processes that result in degradation of the vagina, predisposing vaginal tissue to mesh exposure.

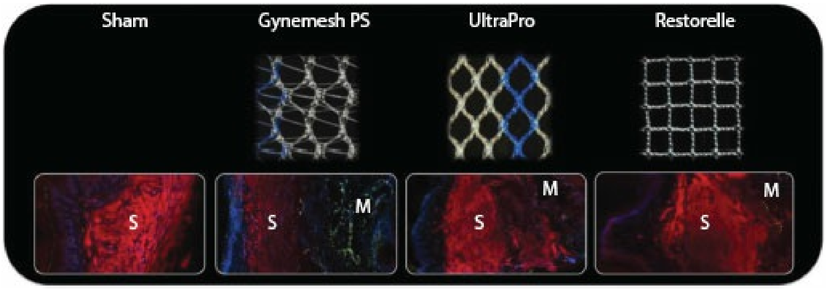


Figure 90.4 Immunofluorescent labeling (bottom) demonstrates the effect of various synthetic mesh products (top) on the vaginal tissue. Here, the red signal represents positive staining of alpha-smooth muscle actin, the green signal represents apoptotic cells, and the blue signal represents nuclei. Gynemesh, the stiffest of all meshes implanted by Liang et al., found to significantly reduce the thickness of the smooth muscle layer (layer designated by S). Further, increased apoptosis was observed surrounding the mesh (mesh designated by M). (From Liang R et al., *Br J Obstet Gynaecol*, 120(2), 233, 2013.)

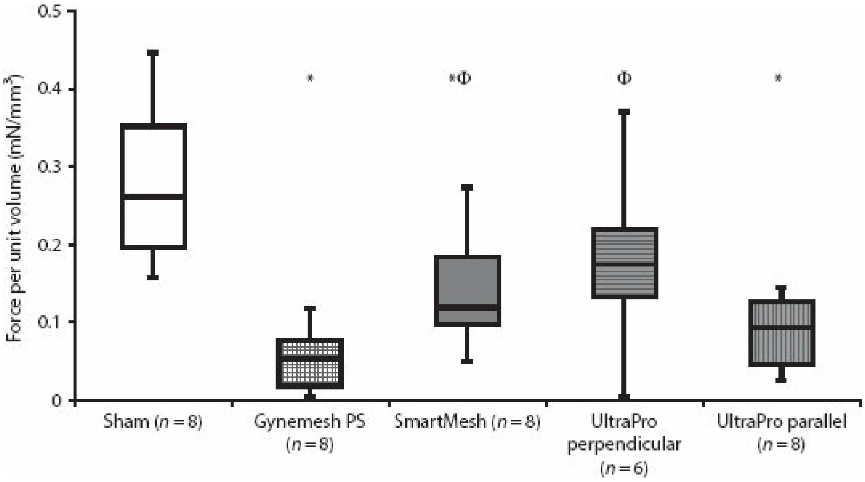


Figure 90.5 Using biomechanical assays to examine smooth muscle contractility, Feola et al. found that synthetic mesh implantation dramatically reduces the active properties of the vagina. Nearly all meshes groups tested reduced smooth muscle contractility relative to sham samples. Significant difference relative to sham is indicated by*. Φ indicates significant differences relative to Gynemesh PS. (From Feola A et al., *Br J Obstet Gynaecol*, 120(2), 224, 2013.)

Functionally, mesh implantation has been found to deteriorate both the active and passive mechanical properties of the underlying and associated vagina (Figure 90.5) [24]. In agreement with morphological findings, Feola et al. reported that Gynemesh eliminated nearly all smooth muscle contractility relative to sham [22,24]. UltraPro and Restorelle also interfered with smooth muscle contractility; however, such negative effects were much less than that observed with Gynemesh. Passive properties, typically representing the mechanical integrity of fibrillar extracellular matrix proteins (collagen and elastin), were evaluated via ball burst testing, as typical planar mechanical tests are invalid for composite mesh–tissue structures of these dimensions. Accounting for the combined stiffness of both mesh and tissue, Gynemesh significantly reduced the passive mechanical integrity of the tissue, decreasing the estimated stiffness of the vagina to almost 0 N/mm, nearly a 10-fold reduction [24]. This result suggests that Gynemesh implantation nearly abolishes the mechanical integrity of underlying and associated vagina in agreement with reports of decreased total collagen and elastin content following mesh implantation [22]. Overall, mesh implantation appears to be detrimental to the mechanical properties of the vagina, particularly with the heavier-weight, lower-porosity, and higher-stiffness devices. This is concerning as degradation of the vaginal smooth muscle, collagen, and elastin (key constituents of vaginal tissue) are already thought to be compromised in women with prolapse [25]. Ideally, mesh implantation would enhance or, at minimum, maintain the supportive capabilities of the vagina, though synthetic mesh, as currently utilized, has the potential to damage native vaginal tissue.

FACTORS INFLUENCING THE HOST RESPONSE TO SYNTHETIC MESH

To date, much of our understanding of urogynecologic mesh products has been derived from the hernia mesh literature, which is not surprising given that the design of current prolapse meshes were originally developed for hernia repair [20]. Thus, the majority of current data in the literature, as well as vendor marketing pamphlets, use legacy methods to demonstrate biocompatibility of prolapse mesh products, by implanting synthetic mesh in the abdominal wall. While there is great utility in such studies, namely, verifying a lack of outright host rejection, the abdominal wall and pelvic floor are quite dissimilar in regard to the biologic environment and the mechanical demands placed on a mesh implant. Because the current generation of synthetic mesh is based on the technology developed for abdominal hernia repair, it is deemed compatible for prolapse repair based on premarket characterization, yet the transfer of this technology from abdominal use to reconstruction of the pelvic organ support leaves much room for optimization. As such, current urogynecologic mesh is largely a prototype solution rather than an optimal one, as evident by the complications associated with mesh implantation. Despite the distinct differences between the abdominal wall and the vagina, many of the design changes responsible for recent reductions in prolapse mesh complications have directly resulted from findings in the abdominal wall. Perhaps the most important concepts shown to impact the host response to synthetic meshes in urogynecologic applications are material type, filament type, and pore size.

Material Type

Since the introduction of the first synthetic nylon sling in the 1950s, urogynecological grafts have been constructed from a variety of materials, resulting in a wide range of outcomes [2]. These materials include polyethylene terephthalate (Mersilene), polypropylene (Marlex), polytetrafluoroethylene (Teflon), and expanded polytetrafluoroethylene (Gore-Tex) [20]. Ex vivo and in vitro studies have shown that these materials are nontoxic and have a high tensile strength, demonstrating their ability to be used in reconstructive pelvic surgeries. Though the material chosen for mesh construction likely plays a role in dictating the host response, additional structural features of a mesh design have confounded the impact of many graft materials.

For instance, Teflon and Gore-Tex experienced disastrous results as prolapse meshes. The distinctive trait for these materials was poor integration with host tissues, and while the ease of removal was initially touted as a benefit, Gore-Tex was plagued with numerous complications of alarming severity [21]. Gore-Tex slings were reported to have a removal rate of at least 35%, with a significant number of sinus tract formations (10%), in addition to infections and reports of vaginal exposures [26]. Similarly, in a large prospective multicenter trial, Gore-Tex was found to be a significant risk factor for mesh exposure into the vagina following sacrocolpopexy [19,27]. Still, the failure of Gore-Tex is likely due to the small pore size (<10 μm) used in this product rather than the polymer itself. Discussion of pore size is included later in this chapter.

Another material that has been linked to poor clinical outcomes is polyethylene terephthalate, a polyester polymer. This polymer was used to construct a graft using a woven, multifilament construction technique and manufactured as Mersilene. Although Mersilene was associated with increased rates of exposure and infection relative to other meshes, surgeons continued to use this material until recently. Interestingly, Mersilene slings also had numerous complications including infection, exposure, erosion, and fistula formation, though manufacturers and surgeons failed to appreciate the problems associated with the use of polyester attempting to overcome the problem by coating it with silicone (marketed as the Protegen sling) [28]. As more data was published on the problems associated with this material, it was gradually been pushed out of the market. Our current understanding of host response to mesh suggests that the adverse host response to Mersilene is likely due to interstices as small as 1 μm that arise from the woven textile construction, rather than the use of polyethylene terephthalate per se. It is thought that such small spaces harbor bacteria because immune cells cannot easily pass into these areas, leading to chronic infection, inflammation, mesh exposure, erosion, and fistula formation.

In the recent decades, polypropylene has become the primary material for synthetic mesh used in incontinence and prolapse surgeries. Unlike the woven construction used for polyethylene terephthalate, polypropylene mesh is most often knitted. Initial studies found polypropylene to elicit a strong inflammatory response including fibrotic tissue formation and multinucleated giant cells (i.e., foreign body response) around mesh filaments [29]. In addition, polypropylene mesh was found to encourage tissue ingrowth, providing a scaffold for tissue penetration. Clinically, polypropylene grafts were found to have relatively low complication rates relative to other material types; however, it was not until the overwhelming success of the TVT that polypropylene became the dominant material for mesh construction [3]. Still, polypropylene's success may be attributed to structural features such as knit construction and large pore sizes, rather than specific properties of polypropylene. However, the publication of large case series and other clinical trials (eCARE) highlights the significant rate of complications associated with both the transvaginal and transabdominal insertion of polypropylene grafts [7]. Given that current mesh products are almost exclusively comprised of polypropylene, the variable success of synthetic grafts suggests that factors other than material selection are responsible dictating the host response.

Filament Type

Often, materials selected for mesh construction are extremely stiff and rigid making them unsuitable for implantation on soft, low-stiffness tissues such as the vagina. For instance, the tangent modulus for polypropylene is 1.5–2 GPa, which is 1000 times greater than that of most soft tissues in the body. In order to reduce the overall product stiffness and provide flexibility to synthetic grafts, materials such as polypropylene are extruded into a thin diameter thread, known as a filament. The structure of the filament has also been linked to the host response of a mesh, specifically its impact on infection. Filaments are classified as either mono- or multifilament, where multifilament fibers are braided or interwoven. Studies have found significantly higher bacterial presence in multifilament meshes, which is believed to result from an increased surface area of ~1.57 for multi-filament fibers, relative to monofilament fibers [30]. The increased amount of surface area is thought to provide more space for bacteria adhesion and, in turn, greater bacterial proliferation [30]. In addition, multifilament structures have inherent spaces between the filaments, which are typically less than 10 μm in diameter. Such diameters allow for the passage of bacteria, yet macrophages are unable to infiltrate these areas, providing a harbor for bacterial proliferation [20].

Fiber Pattern

Individual fibers, whether monofilament or multifilament, provide the basic unit of construction for mesh, yet the manner in which filaments are arranged greatly impacts the behavior of synthetic materials. The two common methods for constructing synthetic grafts are knitting and weaving. Weaving utilizes a simple interlacing technique, with two perpendicular filament orientations. Styles of weaving include plain, twill, and satin. Woven meshes provide superior mechanical strength and shape memory; however, these devices fray when cut and conform poorly to boundaries [31]. In addition to high infection rates (Mersilene), woven mesh is not suitable for the complex geometries of the vagina and its supportive tissues. Unlike woven mesh, knit mesh is constructed by looping of a single fiber. Types of knit structures include warp-lock, interlock, and circular knit, though the latter is uncommon for urogynecologic meshes. Knitted meshes are flexible devices and can easily be manipulated or conformed to the adjacent anatomical structures. Notably, woven mesh has a significantly greater number of mesh-related complications relative to knitted mesh. The impact of construction method is easily illustrated by comparing Marlex, a woven, heavyweight polypropylene mesh, and Prolene, a knitted, heavyweight polypropylene mesh. When first used to treat abdominal hernias, Marlex exposure rates were nearly 44%, while Prolene exposure rates were minimal (<5%), despite similar mesh weights (Prolene ~85 g/m^2 and Marlex ~95, ~85 g/m^2) and identical material selection [31].

In addition to filament type, the fiber pattern, or pore geometry, greatly impacts the mechanical behavior of mesh, highlighted by the wide range of mechanical behaviors (characterized by structural properties in mechanics literature) for type I meshes [32–34]. The importance of mechanical deformation of pores is highlighted by the significance of pore dimensions, which is discussed in the following section. While woven mesh is generally stiff due to high filament alignment and little filament translation with loading, knitting allows for filament rotation and variable behavior along differing axes. Alterations in knit patterns allow for type I polypropylene devices to have a wide range of mechanical behaviors, including manipulation of stiffness and anisotropy. As such, the geometric differences greatly impact the load–elongation behavior of contemporary mesh products [32].

Pore Size

Another characteristic of mesh believed to impact the host response is porosity. Porosity is defined as a ratio of void or empty space in a mesh to the amount of mesh material. A porosity of 0 signifies a solid piece of material (no pores), while a porosity of 1 indicates that no material is present. It is generally accepted that high-porosity meshes reduce complication rates, a belief that is reflected in the movement toward lower-weight meshes. Porosity provides a simple, two-dimensional measure of the amount of mesh in a given area; however, this value is subject to change with mechanical loading, as will be discussed in the succeeding text.

Though recent products have sought to increase mesh porosity, studies suggest that pore size, not porosity, is the most important factor for improving the host response to mesh. In the hernia literature, the impact of pore size has been well characterized, specifically for polypropylene mesh. Larger pores have been shown to improve the mechanical integrity of the resulting mesh–tissue complex, increasing both strength and collagen deposition relative to complexes following implantation of grafts with smaller pore dimensions. Smaller pores restrict and reduce tissue ingrowth relative to larger pore structures, yielding mesh–tissue constructs with limited vascular growth and less mature collagen [35,36]. In addition, the foreign body response is greatly reduced with increasing pore size [37–39]. Importantly, pores with dimensions less than 10 μm allow for the passage of bacteria yet are too small for macrophages and neutrophils to pass through, providing regions for bacterial proliferation and persistent infection [40].

While bacterial proliferation is dependent on the dimensions of openings in a mesh, each individual mesh fiber elicits a foreign body response surrounded by cells and fibrous tissue (granuloma) regardless of size (Figure 90.6) [41–43]. Decreasing pore size reduces the distance between these perifiber inflammatory reactions, and once sufficiently close, adjacent foreign body reactions can overlap with neighboring fibrous granulations, leading to a phenomenon referred to as “bridging fibrosis.” Bridging fibrosis results in the formation of a continuous scar plate or encapsulation, sealing the graft from the body and preventing tissue ingrowth [37,44]. Further, Klinge et al. have found that the foreign body response to fibers is dependent on the hydrophobicity of the polymer used to extrude the filaments [45]. As such, differing materials have dissimilar pore dimensions at which bridging fibrosis will occur. Specifically, it has been shown that effective tissue ingrowth for polypropylene mesh occurs in mesh pores with a diameter of 1000 μm or greater [46], where effective tissue ingrowth is defined by the quality of the tissue, which forms around mesh fibers, with no bridging fibrosis. For polypropylene grafts, pore sizes less than 1000 μm elicit greatly enhanced inflammatory and fibrotic responses [47,48]. It should be noted that studies regarding pore size were performed in an abdominal wall model. While these findings have proven useful in guiding synthetic graft design for abdominal wall and vaginal meshes, extrapolation of such data requires the assumption that the environmental conditions between these sites are similar. The appropriateness of this assumption is questionable and will be highlighted later in this section. Still, there is likely a critical pore diameter for urogynecologic meshes that minimizes scar plate formation, though it may be distinct from that found in abdominal wall studies even for the same material.

Given the importance of pore size, it is not surprising that this design feature is often considered the primary method for mesh characterization, originally outlined by Amid et al. in the late 1990s [40]. The Amid classification divides meshes into four classes [10]:

Type I: Macroporous, with pore sizes greater than 75 μm in diameter
Type II: Microporous, with pore sizes less than 75 μm
Type III: Predominately macroporous with microporous components (e.g., Mersilene and polytetrafluoroethylene)
Type IV: Submicroscopic pore size (<1 μm)

In light of the previous discussion on pore diameter, it is not surprising that type II, type III, and type IV meshes have been met with poor clinical outcomes citing little tissue formation and no adhesion to surrounding tissues, in addition to high infection rates [10,21,26]. While the Amid classification was useful for past mesh devices, nearly all contemporary products are characterized as type I rendering this characterization ineffective for distinguishing products. With nearly all contemporary meshes classified as type I, the Amid classification must be supplemented to guide mesh selection and graft design.

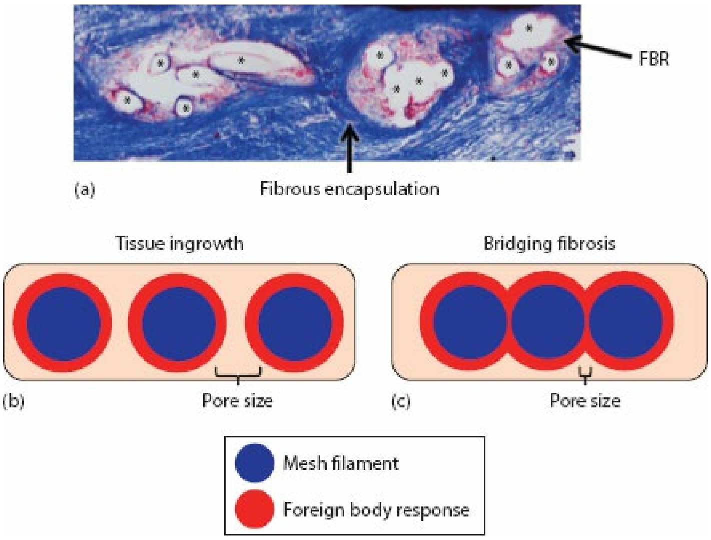


Figure 90.6 (a) Masson trichrome staining of vaginal tissue with mesh embedded demonstrates the fibrous encapsulation associated with individual mesh filaments. * represents polypropylene mesh filaments and FBR represents foreign body reaction to mesh fibers. (b) While each filament is encased in fibrotic tissue, large pore sizes allow for tissue to grow in between separate foreign body responses. (c) However, if filaments become too close to one another, the foreign from individual filaments joins creating bridging fibrosis.

Mesh Burden

Finally, it should be mentioned that the area density of the mesh, referred to as mesh weight, is not a significant factor in dictating the host response. Often, heavyweight meshes (>1 g/cm^2) are constructed to have small pore sizes, thereby increasing their mesh weight, while lower-weight meshes (<1 g/cm^2) are often constructed with a large range of pore sizes. Thus, the negative effects of heavyweight meshes are likely due to small pore dimensions rather than the specific gravity of the device. Weyhe et al. demonstrated the concept that pore size, rather than mesh weight, is more predictive of the host response as a lightweight, microporous mesh was found to provoke a more intense foreign body response with poor tissue integration compared to heavyweight meshes with larger pore sizes [47]. Given these results, it appears that the relative density or spatial distribution of material has a greater impact on the host response than the total amount of material implanted. The spatial distribution, or mesh per unit volume, of a device is defined by the term “mesh burden.” Mesh burden is directly derived from the concept that mesh fibers are encapsulated in fibrous granulations, which may form bridging fibrosis if mesh fibers are sufficiently close. Increases in mesh burden imply that mesh filaments have been brought closer together in three-dimensional space, increasing the likelihood of encapsulation and scar plate formation. Data regarding this characteristic is limited, though understanding the distribution of mesh material in 3 dimensions may prove useful in guiding future mesh designs.

CONSIDERATIONS FOR VAGINAL MESH IMPLANTS

Much of the advancement in prolapse mesh can be attributed to knowledge gained from hernia mesh studies. Yet this criterion is merely a starting point, as optimization of grafts for the vagina requires a greater understanding of the environment in which these devices are placed and the function they are being asked to perform. Relative to the abdominal wall, the environment of the vagina is much more complicated from a biological and mechanical perspective, requiring consideration of the role of the implant in this anatomic location. As such, the requirements for mesh repair are not translatable from the abdominal wall to the vagina.

Biological Environment

Importantly, synthetic meshes are directly fixed to the vagina, an organ that is heavily colonized with bacteria, creating a clean-contaminated surgical field for transvaginal procedures. Generally, the vagina and its supportive tissues are metabolically active as their tissue compositions dramatically change with normal aging and during hormone driven events such as pregnancy, menstrual cycle, and menopause [49,50]. The activity of these tissues is an important consideration for implantable devices.

Several studies have found mesh implantation to elicit a markedly different host response in the vagina compared to the abdominal wall. Using a rabbit model, Pierce et al. found that implanted polypropylene mesh elicited no mesh exposures abdominally, yet exposure rates for the same mesh were 27% at the vaginal site [51]. In addition, the authors stated that the graft length was often decreased upon explanation from the vagina—a phenomenon commonly referred to as “shrinkage.” Additionally, histological analysis revealed increased inflammation and fibroblast proliferation scores for vaginal implants relative to those in the abdominal site, further emphasizing the disparate biologic environments. Pierce et al. also examined the outcomes of cross-linked collagen grafts in the abdominal wall versus the vagina of rabbits. Cross-linked grafts were noticeably degraded in 37% of abdominal implants, while 70% of grafts implanted on the vagina were degraded. Degradation at the vaginal site was so dramatic that nearly half of all grafts were found to be missing upon sample harvesting [51]. Similarly, using a sheep model, Manodoro et al. found no exposures in the abdominal wall, while 30% of vaginal implants resulted in exposures [52]. Interestingly, Manodoro et al. reported increased folding and nearly twice the amount of mesh “contraction” or “shrinkage” in vaginally placed mesh samples. It is important to note that in each of the mentioned studies, mesh was simply sutured to the vagina and not tensioned as is done for prolapse and incontinence surgeries utilizing mesh. As such, these studies ignore the impact of mechanics on mesh outcomes and highlight that the biological response to a material is vastly different in the vagina relative to the abdominal wall.

Overall, the vagina is a harsher biologic environment for mesh implantation compared to the abdomen. Still, questions regarding vaginal graft implantation remain. For example, no studies have considered the impact of route of delivery in TVM placement. Surgical entry for transvaginal procedures may potentially contaminate the mesh via vaginal microflora, resulting in subclinical infection, and intensifying the host response. The failure to acknowledge the biologic environment in the development of urogynecologic meshes has likely resulted in high complication rates of polypropylene mesh; however, the mechanical demands place on synthetic meshes used for prolapse repair is another significant factor that must be considered.

Mechanical Environment

Mechanical Demands of Mesh

Pelvic organ support is a complex mechanical system in which support to the vagina is provided by the levator ani muscles and connective tissue attachments to the pelvic sidewall. The vagina, in turn, orchestrates support to the pelvic organs by maintaining static equilibrium and resisting transient changes in abdominal pressure. Given the interactions between these components, imbalance or degradation of any tissue may lead to dysfunction or conditions such as prolapse. Current synthetic graft repair attempts to restore support, mimicking the mechanical role of connective tissue, as current meshes have no active properties. While it may seem inconceivable to truly recreate native pelvic organ support, understanding nonpathological support and the mechanical behavior of both grafts and healthy native tissues would greatly improve outcomes of reconstructive surgery in the soft tissues of the pelvis.

During prolapse repair, synthetic meshes are typically attached to the vagina and then secured to the sacrum (sacrocolpopexy) or to structures along the pelvic sidewall (transvaginal procedure). Under these conditions, mesh devices assume the role of suspension cables, maintaining the position of the vagina while resisting the downward forces of abdominal pressure and the weight of other pelvic floor viscera. This function results in a predominately uniaxial tensile loading condition, which is quite dissimilar from in vivo loading for hernia repair. During a hernia repair, the mesh is often fixed along its perimeter in the abdominal wall, over the defect. This scenario, analogous to the wall of a pressure vessel, places hernia mesh in tension along all axes simultaneously, much like the surface of a balloon upon inflation. The omniaxial loading in the abdomen helps maintain geometric features of mesh, such as geometry and pore size. While stable graft geometries are expected in the abdominal wall, tensile loading conditions of the vagina provides an increased likelihood of mesh deformation highlighted by reports of significant mesh contraction (Figure 90.7) [10,52]. Thus, for urogynecological meshes to function as intended, it is necessary to understand how mesh products deform under loading conditions similar to those in the pelvic floor.

Many studies have evaluated the mechanical behavior of mesh in response to uniaxial loading, often reporting structural properties such as ultimate elongation, ultimate load, and stiffness [32–34]. While these studies are useful for comparing mesh behavior, often the focus is placed on the failure criteria for grafts, with loads typically exceeding 30 N. Yet, structural failure of synthetic mesh is extremely rare clinically. Rather, focus should be placed on mesh behavior at loads that are experienced in vivo [53,54]. Perhaps the greatest impact of mechanical loads on mesh behavior is on the mesh porosity and pore size, properties that dictate the host response. Indeed, uniaxial loads dramatically decrease the maximum pore size and porosity of nearly all current synthetic meshes [32,34,42].

Uniaxial loading of composite, porous materials results in elongation of the graft in the direction of applied force and causes individual filaments to rotate and reorganize to resist the applied force. The degree of reorganization is largely governed by the geometry of a mesh and contributes to the nonlinear behavior observed for mesh products. Meshes whose filaments are highly aligned with the loading axis exhibit little nonlinear load–elongation behavior, while the same mesh tested with filaments offset 45° from the loading axis have elongated toe regions and significant pore deformation before resisting applied forces. For most materials, elongation along one axis results in narrowing of the axis perpendicular to the applied force. This phenomenon is known as Poisson’s effect for continuous materials, though a similar occurrence is observed for porous materials. Typically for porous structures, this narrowing results from a reduction in pore size as pores collapse during filament reorganization. Uniaxial tension dramatically reduces pore size for most mesh products, as pores in a tensioned mesh are often less than 1 mm in diameter even at low levels of force (Figure 90.8) [55]. Given the importance of pore size on the host response, one would anticipate a diminished potential for tissue ingrowth and a high likelihood of bridging fibrosis for meshes implanted under tension. This mechanical deformation provides a potential mechanism for the clinical observation of mesh “shrinkage” or “contraction” after implantation, specifically for TVM products [10,52]. Though mesh shrinkage may also involve contraction of fibrotic tissue or other biological mechanisms, tensile forces have the potential to cause large alterations in mesh dimensions and induce fibrosis. Factors including tissue ingrowth and the boundaries imposed by the vagina may help to limit pore size reduction in vivo to some extent. Nonetheless, mesh deformation must be considered when “tensioning” or placing a mesh surgically, as well as during in vivo loading conditions both before and after host tissue integration occurs, as this dictates the initial host response following implantation.

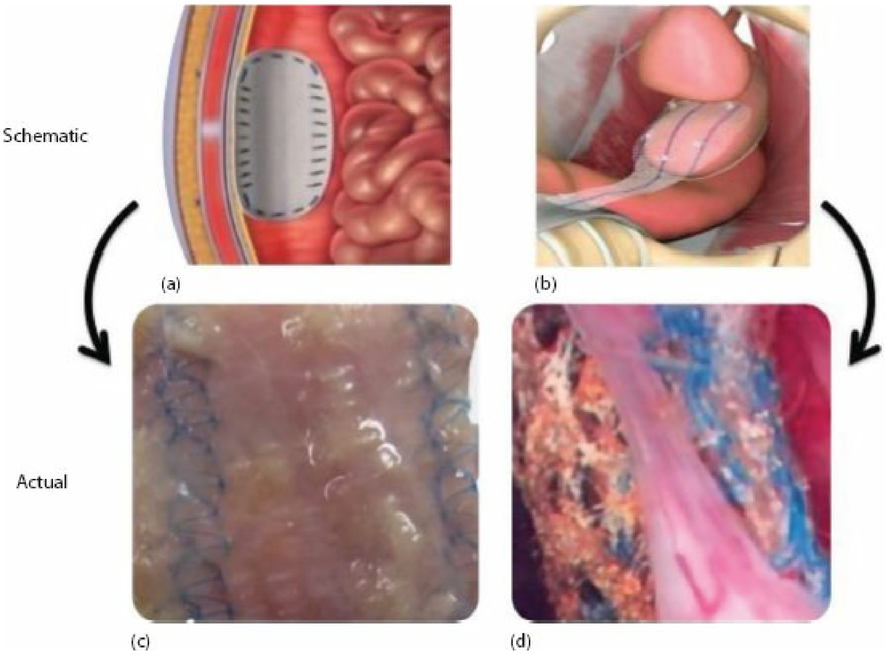


Figure 90.7 The mechanical function of synthetic mesh is quite distinct between (a) hernia mesh repair and (b) prolapse repair. For hernia repair, mesh is placed in the abdominal wall and loaded along all axes simultaneously to resist expansion of the abdominal cavity resulting from internal pressure. Vaginally, mesh arms are placed in tension, acting as support cables to hold the vagina in place. This disparity in mechanical loading leads to notably different deformation of mesh products in vivo. Explanted hernia mesh is typically flat and pore geometries appear similar to the preimplanted state (c), while prolapse mesh is often bunched with dramatic alterations in pore geometry and decreased pore size (d).

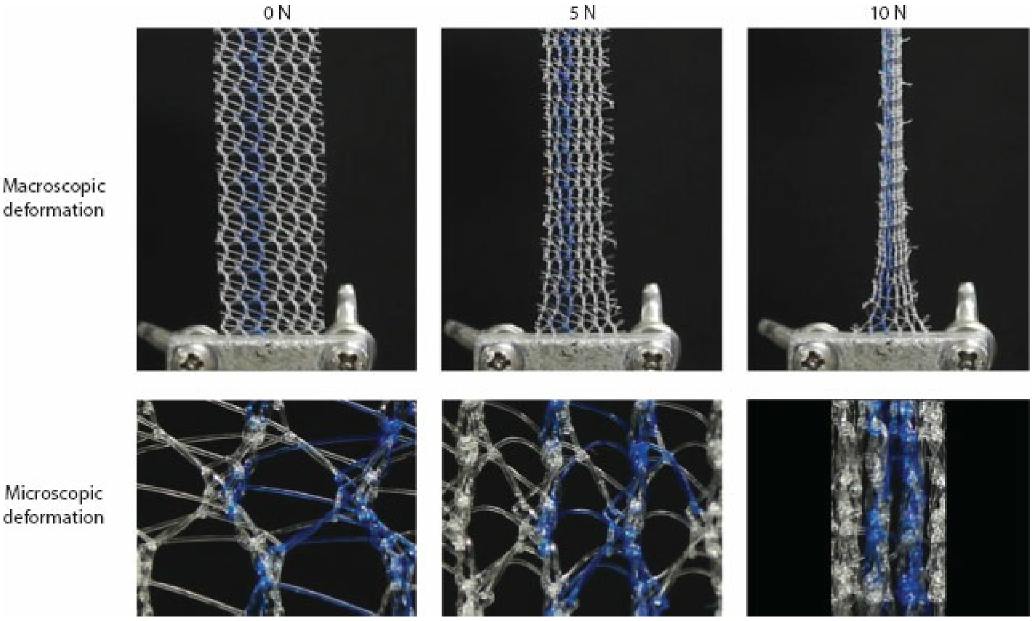


Figure 90.8 Uniaxial tensile loading dramatically alters the pore size and pore geometries of nearly all mesh products. As shown here, Gynemesh, representative of current wide-pore, low-weight polypropylene synthetic meshes, experiences significant deformation at forces well below its ultimate load. Macroscopically (top), the mesh undergoes lateral contraction, similar to that shown in Figure 90.7. Microscopically (bottom), pore dimensions are drastically reduced bringing filaments closer together. (From Shepherd JP, Feola AJ, Abramowitch SD, Moalli PA. Uniaxial biomechanical properties of seven different vaginally implanted meshes for pelvic organ prolapse. *Int Urogynecol J Pelvic Floor Dysfunct* 2012;23(5):613–620.)

Boundary Conditions

Additional boundary conditions, such as the tissue substrate or the method of mesh anchoring, also have significant effects on the mesh deformation under application of force. To date, nearly all ex vivo structural testing of prolapse mesh have utilized clamps to applied forces to mesh, forcing mesh deformations to occur in plane only. Though the assumption of planar deformation is necessary for measurement of structural properties such as stiffness, clamped restraints at the boundary are not representative of mesh fixation in vivo. Recently, discrete suture fixation of mesh products was found to significantly increase the amount of folding and wrinkling that occurs upon application of tensile forces. Inclusion of suture attachments resulted in a 15-fold increase in surface curvature for tested mesh devices at just 10 N of force, relative to traditional mechanical testing boundary conditions (Figure 90.9) [56]. Increased folding of the mesh provides an additional mechanism by which filaments can be brought closer (increasing mesh burden), increasing the likelihood of bridging fibrosis. Given these results, it is clear that the number and placement of sutures used to fix mesh in vivo greatly impacts the manner in which forces are transferred throughout a graft, creating regions that are at increased risk of complication.

When considering the interface between two materials, such as the vagina and implanted mesh, the properties of the each material must be considered. Mechanically, material interfaces are subject to stress concentrations, with the magnitude of stress proportional to the difference in stiffness between the materials [57,58]. This principle is quite noticeable in many biological structures. Examination of tendons, tissues that transfer force from the compliant muscle to the stiff bone, reveals a variable stiffness along their length. Tendons have increased stiffness at the boney insertions, relative to the muscular attachments, which are quite compliant (low stiffness). Such a distribution of stiffness is created by variable tissue composition and functions to minimize stress concentrations at the respective boundaries [58,59]. The importance of this interface has also been demonstrated in other medical implants, as increased implant stiffness was found to induce a maladaptive remodeling response through a phenomenon known as “stress shielding” [60–62]. This common mechanical phenomenon occurs in composite materials (i.e., device–tissue complex) when a stiffer material is the primary load-bearing structure, “shielding” surrounding tissues from in vivo forces. When prothesis bear are the primary load bearing structure, biological tissues, which respond to mechanical stimuli, may atrophy. Stress shielding was detrimental to soft tissues following hip arthroplasty, resulting in increased periprosthetic breakdown of both collagen and elastin upon implantation of implants of increasing stiffness [63–66].

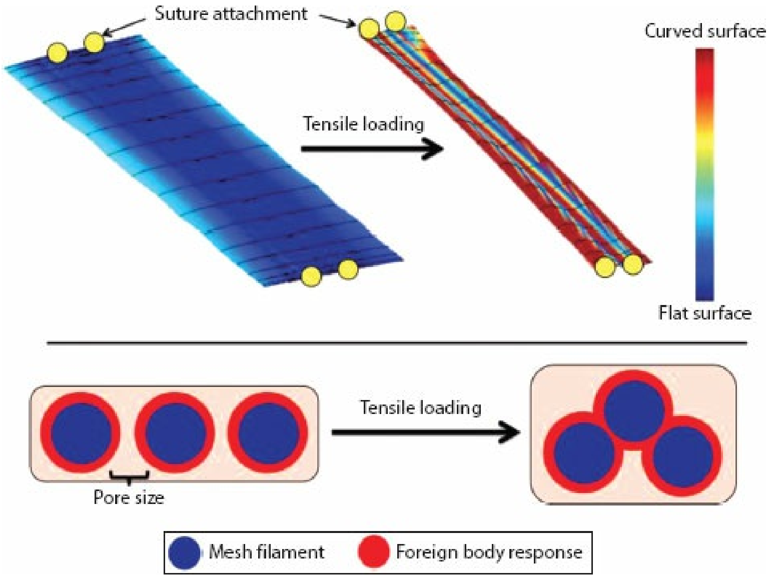


Figure 90.9 The boundary conditions applied during mechanical loading greatly influence the deformation of mesh products. When examining the surface curvature of synthetic mesh (top), discrete placement of sutures (yellow circles) results in significant curvature or bunching of mesh upon application of tensile loads. Bunching of mesh brings mesh fibers closer together, including fibers that have deformed out of plane (bottom). Similar to the planar deformations shown in Figure 90.6, bunching of mesh allows for individual

foreign body responses to join, creating bridging fibrosis. (From Barone WR et al., *J Biomech*, 2015;48(9):1566–1574.)

Vaginal tissue, like most biological tissues, has been shown to respond to mechanical stimuli. When a prothesis, such as mesh, alters mechanical stimuli, homeostatic processes may be impacted. Previously it has been found that matrix metalloproteinase (MMP) activity of fibroblasts from full-thickness vaginal biopsies is significantly altered by application of mechanical forces. Specifically, MMP activity increases of 76% and 188% were observed in fibroblasts after undergoing repetitive mechanical stretching to 8% and 16%, respectively [62]. Interestingly, fibroblasts cultured with 17β-estradiol and progesterone returned collagenase activity to control levels despite the presence of mechanical stimulation. Clearly, mechanical stimulation is important for vaginal tissues, though the effects of such forces may have increased importance in postmenopausal women, the primary demographic for prolapse mesh implantation.

SUMMARY

Support to the vagina and, hence, the pelvic organs is a complex, poorly understood system, with numerous components vital for maintaining the anatomy and its proper function. It is understandably difficult to mimic the natural support system of the vagina and urethra as connective tissues and muscles provide a wide base of support with broad attachments. However, as a community, it is important to recognize deficiencies in our understanding of this complex highly orchestrated system. Advancements in hernia mesh technology has provided significant advances in the design of synthetic grafts for prolapse repair, yet the complications arising from such materials provide a strong reminder that synthetic meshes were not designed with the vaginal support system in mind. The success of future generations of synthetic grafts is dependent on creating devices specifically designed for the unique biological and mechanical environment of the vagina. These considerations, alongside advanced knowledge of native support, are key to designing more effective grafts for prolapse repair.

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91 Complications of Synthetic Mesh Used to Repair Pelvic Organ Prolapse

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INTRODUCTION

Pelvic reconstructive surgery for genital prolapse usually results in improved quality of life. However, numerous complications from mesh-augmented prolapse repairs have been reported in the literature. This chapter is aimed at discussing these various complications and how best to manage them.

Pelvic organ prolapse (POP) and stress urinary incontinence are common and often comorbid disorders in women that can greatly impact quality of life. Population-based studies report an 11%–19% lifetime risk of women undergoing surgery for one of these conditions with a recurrence of symptoms common in both groups. Six to twenty-nine percent of women who undergo a pelvic floor repair have additional surgery for recurrent prolapse, stress incontinence, or related complications [1,2].

The success initially observed with the use of surgical mesh in general surgery combined with the perceived high failure rates for traditional native tissue suture repairs for prolapse initially led gynecologic surgeons to implement surgical approaches that utilize prosthetic materials. Medical device manufacturers have estimated that in 2006 and 2007, approximately 30% of POP repair procedures utilized adjuvant materials. However, recently, there have been concerns raised around the safety of transvaginal mesh due to a variety of outcomes related to mesh erosion, pain, vaginal constriction, and other complications. While similar types of complications have occurred with native tissue suture repairs, the perception is that graft-related complications have been more severe and difficult to manage.

Historically, loss of pelvic floor support resulting in POP has been compared to a hernia. In 1973, Dr. Stanley Birnbaum [3] described a novel technique for treatment of vaginal prolapse in which fixation of the vaginal vault with a Teflon mesh bridge anchored the vagina to the hollow of the sacrum. This was the initial description of a sacrocolpopexy using a synthetic material. A follow-up article 6 years later noted 20 of 21 patients treated with this technique maintained good support and vaginal function.

Over the last 15 years, there has been a significant refinement and improvement in surgical mesh materials. Early on, there were problems with some surgical meshes, which increased erosion and infection rates. In most cases, these meshes were microporous multifilament materials, which require complete explantation for symptom improvement [4]. Fortunately, the majority of these products have been taken off the market. Currently utilized meshes are type 1 mesh, meaning they are macroporous monofilament polypropylene with a pore size greater than 75 μm. They can further be divided by weight (heavy-, mid-, or lightweight) [5,6].

Synthetic mesh utilized for prolapse repairs can be placed abdominally (abdominal sacral colpopexy) or transvaginally. Transvaginal mesh can be self-fashioned, cut to order, or packaged in a kit. The first synthetic mesh kit for prolapse was FDA approved in 2001 and the first trocar-based kit was approved in 2004 [7].

FDA WARNINGS

On October 20, 2008, the FDA issued a public health notification regarding the use of mesh in gynecologic surgery titled “Serious Complications Associated with Transvaginal Placement of Surgical Mesh in Repair of Pelvic Organ Prolapse and SUI.” This was done in response to over 1000 reports of these complications involving nine different surgical mesh companies. These reports were reported through the manufacturer and user facility device experience (MAUDE) database. The most common complications reported were mesh erosion, infection, pain, and urinary symptoms. Serious injury to the bowel, bladder, and blood vessels did also occur albeit rare. Several general recommendations were made by the FDA at that time based on these reports. These included the following:

1. Physicians seek specialized training for procedures involving the use of mesh and should be alert and recognize complications early.
2. Physicians should inform patients of the permanent nature of surgical mesh and that some complications associated with implanted vaginal mesh may require subsequent surgery that may or may not correct the complication.
3. The physicians were advised to inform patients about the potential for serious complications and the effect on quality of life including pain during intercourse and scarring and narrowing of the vagina after prolapse repairs.

The FDA continued to investigate mesh complications and, based on an updated analysis of reported adverse events and complications described in the scientific literature, released a scientific communication on July 13, 2011: “Update on Serious Complications Associated with Transvaginal Placement of Synthetic Mesh for Pelvic Organ Prolapse and SUI.” They noted that the use of surgical mesh for transvaginal repair of prolapse is an area of continuing serious concern and concluded that “serious complications associated with surgical mesh for transvaginal repair of prolapse are not rare.” They did not find clear evidence to support increased efficacy of mesh repairs when compared to traditional native tissue repairs, and patients undergoing mesh placement may be exposed to greater risk. It was also noted that mesh placed abdominally for the treatment of POP via sacrocolpopexy had a lower rate of mesh complications when compared to vaginally placed mesh.

In the light of these FDA findings, it is important to understand the current FDA approval process for new materials, as there is a proposed reclassification of surgical mesh used for transvaginal repair of POP. Currently, mesh products on the market were allowed to bypass a rigorous FDA approval process that mandates premarket testing called a “premarket analysis.” In lieu of this process, they were allowed to proceed with a much more simplified regulatory process called a “510K.” This process allowed new medical devices that were similar to a currently approved FDA device to be approved based on what is been termed as a “predicate” device eliminating the need for the companies to provide specific efficacy and safety data on a new product prior to obtaining FDA approval. Historically, transvaginal mesh kits were considered class II devices and able to use a 510K process with synthetic midurethral sling as the predicate device, even though the mesh utilized for prolapse repairs involved significantly increased volumes of mesh and utilized a different space in which the mesh was placed. Currently approved synthetic midurethral slings were approved by the same process based upon a prior product, “the Protegen sling,” which is no longer on the market due to a poor safety profile.

The FDA is considering a reclassification of vaginal meshes from a class II to a class III medical device, which would require premarket approval through a scientific review to ensure safety and efficacy prior to going to market. If this truly occurred, then it would require a significant investment to bring new mesh kits to the market. On January 4, 2012, the FDA did issue what have been termed 522 orders requiring postmarket surveillance studies for transvaginal mesh devices currently being sold for POP. These required studies are ongoing and will most likely ultimately decide the long-term fate of permanent transvaginal mesh.

PROFESSIONAL SOCIETY GUIDELINES

The American College of Obstetricians and Gynecologists and the American Urogynecologic Society (AUGS) issued a statement in December 2011 regarding vaginal placement of surgical mesh for POP repair. They advised that

- Surgeons placing vaginal mesh should undergo training specific to each device and have experience with reconstructive surgical procedures and a thorough understanding of pelvic anatomy
- Use of reconstructive materials by surgeons experienced with the specific procedure is a reasonable option for women with factors that increase the risk of prolapse recurrence (e.g., recurrent prolapse, medical comorbidities that preclude more invasive and lengthier open and endoscopic procedures) (Such use should be individualized and surgeons should counsel patients about the lack of efficacy and safety data and about alternative treatments.)
- Patients should provide their informed consent after reviewing the risks and benefits of the procedure, as well as discussing alternative repairs

In addition, the Society of Gynecologic Surgeons (SGS) issued a statement in July 2011, advising the following:

- SGS is in agreement with the interpretations and recommendations made in the FDA Safety Communication. The general consensus is that this reservation should not apply to synthetic midurethral sling procedures or sacral colpopexies utilizing the same mesh materials, but further longer-term evaluations of all of these procedures is important.
- For now, thoughtful, discriminant use of transvaginal mesh to augment vaginal defects should be performed by trained surgeons with experience in complex reconstructive surgery, and only on patients who are perceived to have an unacceptable risk of clinical failure when other procedures are performed.
- We should all follow outcomes when we employ new procedures, and should feel comfortable about the benefits versus the risks before employing them. It is important that patients are informed of the risks and benefits of any surgical procedure, as well as the specific potential adverse events associated with transvaginal mesh use, including outcomes that may still be unclear and require further investigation. Alternative treatments should be explained.

The International Urogynecological Association (IUGA) convened a Grafts Roundtable regarding transvaginal graft use in 2010 [8] and advised the following:

- Individual patient characteristics have to be included in the risk/benefit ratio when counseling patients regarding transvaginal mesh repair.
- Informed consent for vaginal reconstructive surgery with mesh should include verbal and written review with the patient of expected benefits, therapeutic alternatives, and potential risks.
- Manufacturers should provide detailed product description, data on biologic properties, cadaveric studies, and well-designed prospective clinical trials to support the claimed benefits of the new product.
- A process of added surgeon qualification for transvaginal mesh placement is desirable.

The AUGS issued guidelines for providing privileges and credentials to physicians for transvaginal placement of mesh for POP.

In the past, there were minimal guidelines for this process and physicians usually attended an industry sponsored 1- or 2-day course to learn these procedures using cadaveric trainers. The new AUGS recommendations call for documentation of each of the following: (1) knowledge of pelvic anatomy, (2) surgical skill, (3) surgical experience, and (4) internal audits for quality assurance. Informed consent should highlight potential benefits and complications of transvaginal mesh, alternatives including nonsurgical options and other surgical treatments, and potential complications of transvaginal mesh, which may require additional interventions, as well as the fact that symptoms may not be completely resolved with mesh removal. The article addresses surgeons who are not performing transvaginal mesh repairs but would like to begin, as well as those currently performing these procedures. The surgeon who approaches management of mesh complications after pelvic surgery should possess a comprehensive understanding of materials utilized in POP repair, pelvic floor anatomy, and advanced surgical skills in order to individualize the management of such complications specific to each patient. Patients should also understand that removal of mesh may not completely resolve all symptoms.

TERMINOLOGY

In response to increasing complications associated with mesh use in gynecologic surgery, the IUGA and the International Continence Society recently agreed on standardized terminology and a classification method for complications associated with insertion of mesh [9]. Terminology is specifically defined in the article and the classification system is based on three items: category, time, and site (CTS) (Appendix D).

Category includes seven complication types (vaginal without epithelial separation, vaginal with <1 cm epithelial separation, vaginal with >1 cm separation, urinary tract, rectal/bowel, skin/musculoskeletal, and patient compromise). Each has lettered modifiers for patient symptoms and infection (A, asymptomatic; B, symptomatic; C, infection; D, abscess).

Time includes four time periods (T1, intraoperative to 48 hours; T2, 48 hours to 2 months; T3, 2 months to 12 months; T4, over 12 months).

Site has five categories (S1, vaginal area of suture line; S2, vaginal area away from suture line; S3, adjoining viscus [bladder or bowel]; S4, other skin or musculoskeletal site; S5, intra-abdominal). As an example, a patient with mesh fiber exposure in the lateral vagina on her 6-week post-op check whose partner describes discomfort with intercourse would be classified as B1/T2/S2. Although somewhat complex, when broken down, it is a simple way to classify mesh complications with the CTS system intended to be an improved method for standardizing reporting of complications associated with graft placement. This classification system will also allow for identification and classification of all complications from minor, asymptomatic problems to complex pathology.

AVOIDING SYNTHETIC MESH COMPLICATIONS

Patient Selection

To date, there has been no systematic evaluation of which patients with POP should undergo transvaginal mesh repairs to correct POP. Some have argued that use of transvaginal mesh be restricted to patients who fail native tissue suture repairs. The stage or grade of POP is also a commonly cited reason to proceed with a transvaginal mesh repair. While intuitively these indications may make sense, there are no published data to support either rationale. Other commonly cited indications for mesh augmentation include patients who are not sexually active or patients who are felt to be at high risk for failure of a native tissue repair secondary to lifestyle, body habitus, etc. Unfortunately, there are also no data to support any of these rationales. Regardless, it seems prudent to avoid transvaginal mesh procedures in patients with underlying pelvic pain disorders, for example, pelvic floor tension myalgia, interstitial cystitis, or vestibulitis. Pelvic surgeons should be aware of the high prevalence of female sexual dysfunction in the community and should preoperatively screen patients for a history of dyspareunia, pelvic pain, and sexual abuse. Abnormalities of the pelvic tone or sensation should be elicited during the preoperative physical exam by palpating the levators, obturator internus, and vaginal sulci and evaluating for signs of vulvodynia. Patients who have these findings should be referred to physical therapy in the hope of treating the underlying condition prior to any surgical intervention. In addition, they should be explicitly informed that surgery, if undertaken, is not meant to improve these symptoms and may make them worse. Patients that are chronically immunosuppressed (e.g., due to medication for other systemic diseases or due to underlying disease) or who are current smokers should be similarly approached with caution. Finally, patients with severe atrophy, vaginal ulcers due to severe prolapse, or chronic pessary use should receive preoperative estrogen therapy for at least 4 weeks or until the aforementioned symptoms or signs resolve. Ideally, they should continue local estrogen therapy for the foreseeable future following surgery. The optimal time to start postoperative local estrogen therapy has not been studied; however, we recommend starting about 3 weeks following surgery to avoid inadvertent disruption of any suture line during insertion of the applicator.

Surgical Technique and Mesh Selection

Expert opinion states that the key distinction between mesh- and suture-based repairs is the tissue plane and thickness of the dissection. In traditional plication repairs, which most gynecologists are familiar with, the vaginal epithelium is dissected from the underlying pubocervical connective tissue, which is subsequently plicated in the midline with a delayed absorbable suture. Conversely, mesh repairs require a “full-thickness” dissection. Successful “full-thickness” dissection requires adequate hydrodissection (not typically used with traditional repairs) and dissection in a deeper surgical plane that leaves the pubocervical connective tissue attached to the epithelium. This allows, in theory, for decreased risk of vaginal mesh exposure, maintenance of better vascular supply to the epithelium and improved healing, with the goal of diminishing graft exposure. It is also felt that although the mesh is “suspended” tension-free via the arms, the mesh body needs to be trimmed and even possibly secured to the underlying tissue to prevent rolling or bunching, as this phenomenon has been observed in patients who experience mesh exposure and/or pain (Hurtado et al., 2009) [10]. Finally, it is felt that the mesh needs to be deployed in a tension-free fashion. Excessive tension on the arms has been associated with tight vaginal bands, pain, and exposures [11]. It is unclear if overtensioning results from mesh shrinkage (less likely as this phenomenon has not been documented with sacrocolpopexy) or inadvertent tensioning at the time of implantation (more likely) or a combination of factors. A thorough understanding by the treating surgeon of the nuances of mesh-based repairs is of the utmost importance to reduce these complications. In fact, there is evidence that complications are higher among providers with less experience. As a result, new providers should seek proctoring by experienced, unbiased providers until achieving a level of expertise needed to safely perform these types of procedures. Additionally, documentation and tracking of complications should be mandatory for all new implanters to ensure patient safety.

Modifiable Risk Factors for Mesh-Related Complications

There are several modifiable risk factors that may diminish mesh-related complications (Table 91.1). A major determinant is material selection. As previously discussed, Amid type II (e.g., microporous materials) and type III (e.g., grafts with microporous components or with multifilament weave) synthetic meshes should be avoided because of increased risk of mesh-related complications [12]. These materials undergo an encapsulation response and are more prone to erosion, sinus tract formation, and infection.

A recent secondary analysis of the colpopexy and urinary reduction efforts (CARE) trials showed that Gore-Tex mesh use was associated with a 4.5-fold increased risk of exposure compared to macroporous polypropylene [13]. Previous devices (ObTape and IVS Tunneler), which utilized materials that are encapsulated, have been removed from the market due to the increased risk of mesh-related complications. Mesh-related complications associated with these materials require complete excision of the mesh and are not the focus of this chapter.

Smoking increases the risk of mesh erosion by nearly fivefold presumably by inhibiting wound healing. Current tobacco users had a 5.2- and 3.2-fold increased risk of mesh exposure following sacrocolpopexy and vaginal mesh, respectively [13,14]. It would seem prudent for surgeons to recommend that patients should stop smoking for at least 1 month before and after elective procedures with mesh. Similarly, increased blood loss during the index surgery greatly increased the risk of mesh exposure. In a case-controlled study, patients who experienced excessive blood loss had a 7.3-fold increase in mesh exposure compared to patients who did not experience excessive blood loss [14]. When excessive blood loss is encountered during these procedures, surgeons should consider suture-based repairs or simply aborting the case. Tissue ischemia due to tobacco use or hematoma formation may lead to impaired wound healing.

MESH-RELATED COMPLICATIONS AFTER SACROCOLPOPEXY

Sacrocolpopexy is an abdominal, laparoscopic, or robotic procedure that involves attaching a Y-shaped graft (usually synthetic mesh) to the anterior and posterior vaginal wall and securing it to the anterior longitudinal ligament of the sacrum. Mesh complications after abdominal sacrocolpopexy are fairly rare and primarily center on mesh or suture erosion (Figure 91.1). A comprehensive review of abdominal sacrocolpopexy revealed an overall mesh erosion rate of 3.4%. Polypropylene had the lowest erosion rate at 0.5%, while Teflon had the highest rate of erosion at 5.5% [15]. A more recent follow-up of the CARE trial noted the probability of mesh erosion at 7 years increased to 10.5% [16]. There are mixed data regarding the risk of mesh erosion when sacrocolpopexy is performed with concomitant hysterectomy. Culligan et al. [17] reported an increased erosion rate with concomitant hysterectomy; however, this study had a small sample size ($n = 11$). While Brizzolara and Pillai-Allen [18] reported no increased erosion rate in 60 women undergoing sacrocolpopexy with concomitant hysterectomy when compared to 61 women undergoing sacrocolpopexy alone, another study compared mesh erosion rates after sacrocolpopexy with concomitant supracervical hysterectomy as compared to sacrocolpopexy alone. A total of 277 patients were included in this study, 195 with concomitant supracervical hysterectomy with sacrocolpopexy and 82 with sacrocolpopexy alone. There were three patients with mesh erosion diagnosed at a mean follow-up of 8 months, 1 (0.5%) in the supracervical hysterectomy with sacrocolpopexy group and 2 (2.4%) in the sacrocolpopexy alone group. There was no statistical difference in mesh erosion rates among the two groups [19].

Table 91.1 Suggestions to Decrease the Risk of Erosion or Exposure after Reconstructive Pelvic

Surgeries Using Synthetic Grafts

Patient centered

- Stop smoking before and after surgery.
- Appropriately use vaginal estrogen in postmenopausal women before and after surgery (authors' opinion).
- Have regular postoperative follow-up visits with your surgeon.

Physician centered

Preoperative

- Understand technical aspects and surgical anatomy of the planned procedure that involves mesh placement; gain as much experience as possible with the procedure.
- In a patient with uterovaginal prolapse, consider a uterine-preserving procedure or a supracervical hysterectomy.
- Educate patients preoperatively on the importance of avoiding the future development of urogenital atrophy.

Intraoperative

- Utilize lightweight large-pore polypropylene.
- Use hydrodissection to facilitate the appropriate plane of dissection.
- Avoid mesh bunching, taking care to make sure that the mesh lies flat.
- Trim mesh appropriately to the specific prolapse repair to limit mesh load.
- Consider abandoning mesh placement if excessive blood loss is encountered.
- Consider abandoning mesh placement if inadvertent injury to the urethra (sling placement), bladder, or bowel (mesh-augmented prolapse repairs) occurs.
- Avoid overzealous trimming of vaginal mucosa.

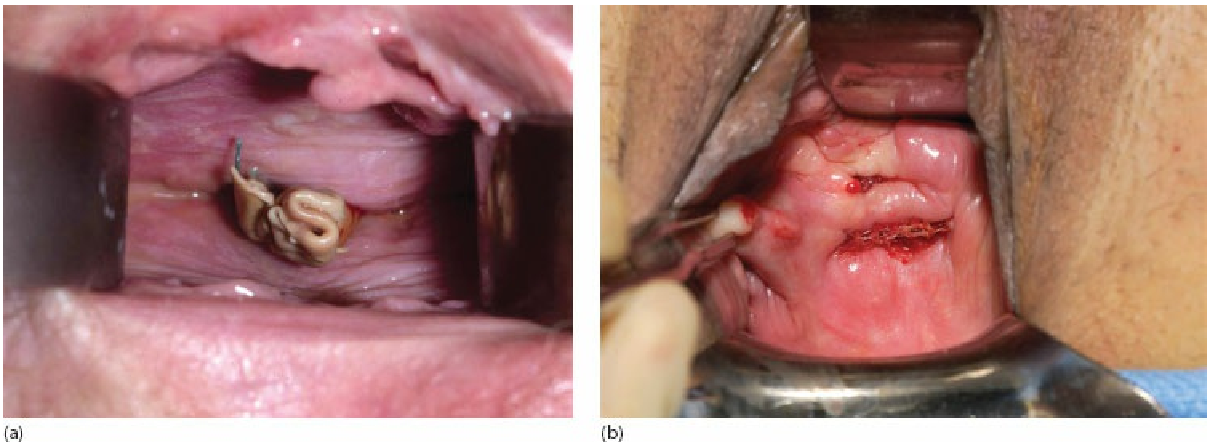

Figure 91.1 Vaginal mesh erosion after abdominal sacrocolpopexy. (a) Gore-Tex mesh erosion seen transvaginally after abdominal sacrocolpopexy. (b) Polypropylene mesh erosion seen transvaginally after abdominal sacrocolpopexy.

A variety of risk factors have been identified for mesh and suture erosion after sacrocolpopexy. A secondary analysis from the CARE trial evaluated mesh and suture erosion rates among the 322 women who underwent sacrocolpopexy [20]. They identified 20 women with mesh/suture erosion within 2 years of surgery, 3 were suture only, and 17 had exposed mesh. Three identifiable risk factors were found, which included concurrent hysterectomy, which increased erosion rate from 4% to 14% in this study population; also, the use of expanded polytetrafluroethylene (ePFTE; Gore-Tex, GORE Medical, Newark, NJ) had a fourfold higher risk (19% vs. 5%) of mesh erosion when compared to those with non-ePTFE mesh, and finally, smoking was associated with a fivefold increased risk of mesh erosion. No other significant factors were identified as risk factors for mesh erosion including estrogen status, diabetes, and prior surgery. The management of the three women with suture erosion included simple suture removal and two of the three had confirmed complete healing. Four of the 17 mesh erosions were managed without surgery and no resolution was noted in any of these 4. While 1 had 2 surgeries and 1 had 3 surgeries, 13 underwent at least one surgery. Of these 13, 2 had symptom resolution, 6 had persistent mesh erosion, and 5 were lost to follow-up.

Managing mesh erosion after sacrocolpopexy may only require observation and topical estrogen; however, in the authors' experience, it almost always requires surgical excision. Surgical management of mesh erosion after sacrocolpopexy can be technically challenging, partially due to the usually high location within the vaginal canal, the amount of mesh used in the procedure, and the ingrowth of the tissue into the mesh making surgical dissection difficult. Vaginal and abdominal routes for mesh excision have been described. In the authors’ experience, most mesh exposures can be successfully managed vaginally utilizing a technique of sharp dissection of the exposed mesh away from the surrounding tissue, with aggressive downward traction on the mesh. The mesh is cut away as high as possible and the vaginal defect closed (Figure 91.2). Vaginal entrance into the peritoneum significantly facilitates successful removal of the mesh.

South et al. [21] published their experience with excision of mesh in 31 patients after sacrocolpopexy, including a novel method for endoscopic-assisted transvaginal excision of mesh. Vaginal excision is described as sharp dissection of the vagina around the area of erosion and excision of the mesh with closure of mucosal edges with suture. Endoscopic-assisted transvaginal excision was used for patients with a sinus tract at the vaginal apex. The sinus tract opening was extended using a scalpel, if needed, to accommodate a 17-French cystoscope. The endoscope was placed into the sinus tract and advanced toward the sacrum to view the extent of the mesh. The scope was used for direct visualization during dissection of mesh from retroperitoneal tissues and during mesh excision. Abdominal excision of mesh was done by laparotomy and the presacral space was entered and mesh was detached from the sacrum and removed from the vaginal apex. Fourteen women underwent transvaginal mesh excision and this was successful in 9, while 17 women underwent endoscopic-assisted transvaginal mesh excision and this was successful in 7. The overall success rate for vaginal excision was 53%. However, multiple attempts at vaginal excision were required on several patients for symptom resolution. Seven patients underwent abdominal excision, each having failed one of the two transvaginal excision methods. All had symptom resolution and no severe complications were noted. The abdominal group had two intraoperative bowel injuries during lysis of adhesions: one wound infection and one readmission for fever requiring antibiotics. They concluded that complete removal of mesh may improve outcomes and decrease persistent symptoms, although significant morbidity can occur.

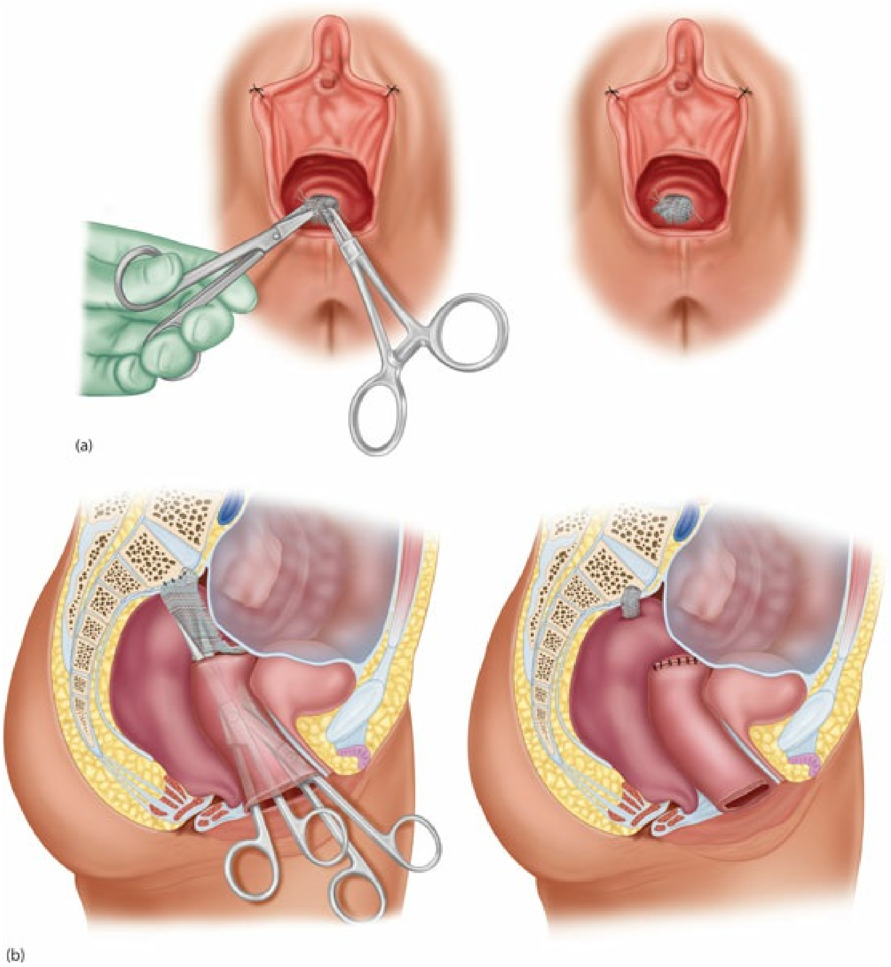

Figure 91.2 The technique of vaginal removal of an eroded synthetic mesh after abdominal sacral colpopexy. (a) Note that the mesh is undermined and grasped (usually with Kocher-type clamps), with aggressive downward traction applied on the mesh. (b) The mesh is sharply dissected away from the vaginal tissue and any other tissue that it is adherent to, and, with aggressive downward traction, it is excised as high as possible. The goal is to create as much distance as possible between the closed vaginal cuff and the cut edge of the mesh (see insert). (From Walters MD and Karram MM, *Urogynecology and Reconstructive Pelvic Surgery,* 4th ed., Elsevier, 2015. With permission.)

COMPLICATIONS AFTER TRANSVAGINAL MESH PLACEMENT FOR PELVIC ORGAN PROLAPSE

There are potential benefits and risks with the use of transvaginal mesh for the treatment of POP. Proposed benefits include improved anatomic outcomes. These benefits must be weighed against potential complications, which include vaginal mesh erosion or extrusion, pelvic pain, and dyspareunia [22]. Also reported, albeit very rarely, are bladder and bowel perforation and/or injury.

A complete history and examination of all patients with suspected mesh-related complications should be completed. On pelvic examination, one should attempt to identify urogenital atrophy, palpation/visualization of any exposed mesh, mesh under tension, location of mesh arms, pain with palpation of the mesh (note location), bunching of mesh or palpable abnormalities beneath the epithelium, pain with palpation of pelvic floor musculature, or evidence of fistula. Rectal exam should be performed and cystoscopy and proctoscopy may be indicated in select cases. In patients with urogenital atrophy, the authors prefer to aggressively treat patients with local estrogen cream prior to any surgical intervention.

Mesh Erosion/Extrusion

This is the most common mesh-related complication after transvaginal placement of mesh for the management of POP (Figure 91.3). Common presenting symptoms of women with vaginal extrusion include vaginal drainage/bleeding, pelvic pain, and dyspareunia. On examination, pain with palpation of the mesh, visible mesh exposure, and vaginal shortening/tightening may also be seen. Published rates for mesh extrusion range from 3% to over 30% with large review articles suggesting overall rates between 10% and 15% [23,24]. Risk factors include concomitant hysterectomy, smoking, total mesh volume, young patient age, early resumption of sexual activity, diabetes mellitus, and surgeon experience. Local injection with lidocaine plus epinephrine at the time of mesh placement has not been shown to increase the risk of mesh extrusion [25]. Conservative management with topical estrogen and/or topical antibiotics can be attempted; however, little evidence of success exists with this treatment. Often, partial or complete excision is necessary for symptom improvement [26]. Both office-based and operating room excisions are options for management. Office-based excision should be reserved for those with small exposures (usually <1 cm), adequate access to the exposed mesh, and healthy vaginal tissues. Similar to the description of office-based management of synthetic midurethral sling exposure, local anesthetic is injected around the extrusion and the adjacent vaginal epithelium is mobilized. The mesh can be excised and the vaginal epithelium brought together in a tension-free fashion with interrupted sutures.

The operating room affords the surgeon improved visibility, better patient anesthesia, and a wider array of instrumentation for managing meshes' extrusions. The question that continues to be unanswered is how much mesh should be excised? There seems to be a balance, with an increased risk of repeat surgery for mesh excision when partial excision is undertaken and an increased risk of recurrent prolapse as well as more intraoperative morbidity with complete excision [27]. For extrusions that are small and straightforward, mobilization of the surrounding epithelium to cover the mesh or simple excision of a small amount of mesh and closing the epithelium is usually all that is needed. If pain and a large-scale extrusion are noted, then more aggressive resection is usually performed. Techniques for surgical excision revolve around dissection of the overlying vaginal epithelium away from the mesh, followed by the dissection of the mesh away from the adjacent organ (bladder or rectum) (Figure 91.4). Margulies (2008), Ridgeway et al. [28], and Muffly and Barber [29] each describe in detail surgical techniques for transvaginal mesh removal. Many mesh kits consist of a body of mesh and with arms used for anchoring the mesh. After implantation and incorporation of the mesh, these arms may become vascularized. When a more complete excision is desired and the mesh body has been mobilized satisfactorily, the authors advocate for clamping and tying of the mesh arms prior to transection to decrease the risk of bleeding. After mesh removal, when possible, midline plication of underlying connective tissue is performed to help resupport the prolapsed tissue and possibly decrease the risk of recurrent prolapse. Also, if appropriate, a native tissue suture suspension of the vaginal apex to the uterosacral ligaments or sacrospinous ligaments can be performed. If mobilization of the vaginal tissue does not allow for a tension-free closure of the vaginal epithelium, a porcine small intestine submucosa graft (Surgisis Biodesign®, Cook Surgical, Bloomington, IN) can be secured in place over the vaginal defect [30]. It acts as a scaffold and encourages host response to mediate the healing process. It can be used as a patch to close a vaginal defect. Biodesign will ultimately convert to normal skin in the majority of cases assuming a good blood supply is maintained (Figure 91.5). Vulvar skin flaps may also be used in instances where large defects are present after mesh removal.

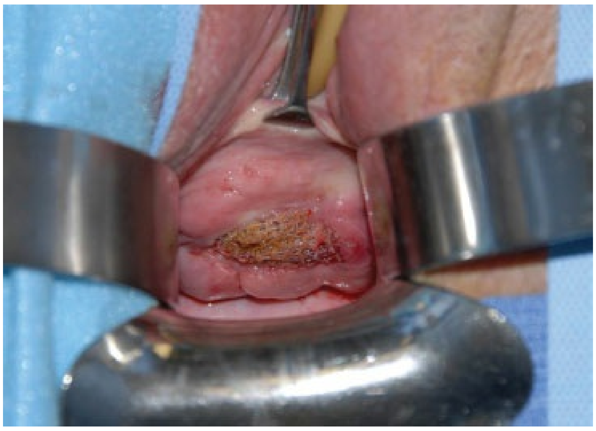

Figure 91.3 Vaginal extrusion of synthetic mesh after transvaginal mesh placement.

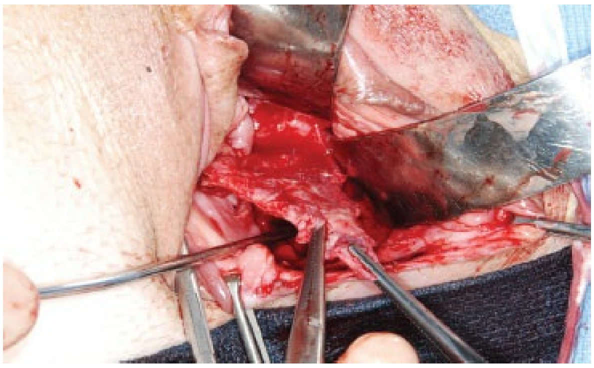

Figure 91.4 Technique for transvaginal removal of mesh; note the synthetic mesh is sharply dissected off the underlying viscera and overlying vaginal epithelium.

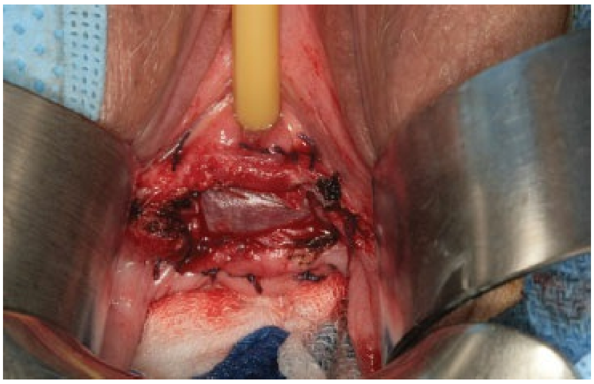

Figure 91.5 Surgisis Biodesign (Cook Medical, Bloomington, IN) used to replace vaginal epithelium after removal of eroded mesh.

Dyspareunia and Pelvic/Vaginal Pain

Dyspareunia and/or pain may develop after transvaginal mesh placement for POP. In a systematic review, the overall incidence of new-onset dyspareunia after vaginal mesh placement was 9.1% (with a range of 0%–67%) [23]. Pelvic muscle spasm/pelvic floor tension myalgia can present as chronic pelvic pain and may be confused with mesh-related pain. Though they may be difficult to distinguish from each other, both may improve with nonsurgical treatments such as pelvic floor physical therapy [31]. The authors recommend exhausting nonsurgical measures for the treatment of pelvic pain possibly related to mesh placement since patients undergoing surgical excision often have persistent pain [32]. Of all mesh-related complications, pain remains the symptom most resistant to medical and surgical treatment. It is often improved after mesh excision but may never disappear completely [33]. Thus, counseling patients prior to surgery about risks associated with mesh removal is paramount. These include bleeding, infection, injury to adjacent organs, new/persistent pain, and recurrent prolapse.

El-Nashar and Trabuco [32] performed an early excision of vaginal mesh, 11 days after implantation. This was performed for severe vaginal pain and urinary urgency/frequency, which began immediately after vaginal mesh placement. Complete excision, including mesh arms, was performed and the patient had resolution of all symptoms. The implanting surgeon was not the referring provider in the case earlier, and this is consistent with findings by Blandon and colleagues. In their study, only 14% of patients with mesh-related complications were referred by the surgeon who placed the mesh; about half were referred by a different physician/health-care provider and the remainder were self-referred.

Visceral Injury

Albeit rare, injury to the bladder and bowel can occur during placement of vaginal mesh. Significant emphasis has been placed on the concept that mesh placement requires a deeper dissection plane, i.e., through the full thickness of the vaginal epithelium to avoid vaginal erosion. However, the surgeon must also go to great lengths to avoid an inadvertent proctotomy or cystotomy and to avoid placing the mesh too deep (i.e., in the wall of the bladder or rectum).

If a bladder or bowel injury were to occur during dissection of the vaginal epithelium, the authors would recommend aborting mesh placement and proceeding with a native tissue suture repair. When performing a trocar-based mesh procedure, rectal exam and cystoscopy should routinely be performed with the trocars in place (prior to passage of arms) to assure no visceral penetration had occurred. In the rare situation where mesh is found postoperatively in the bladder or rectum, usually a major surgical procedure will be required to remove the mesh. If mesh is found in the rectum, a diverting colostomy may be necessary prior to attempting mesh removal.

CONCLUSION

Complications and untoward sequelae from reconstructive pelvic surgery occur with both native tissue and graft-augmented surgeries. Gauging the true incidence of these complications is difficult, because there is no good source for how many total procedures are being done and the frequency with which mesh augmentation is being used. As new procedures to correct pelvic floor disorders continue to evolve, open discussions among surgeons on how best to manage new and/or unforeseen complications are important.

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92 Episiotomy and Perineal Repair

Ranee Thakar and Christine Kettle

INTRODUCTION

Perineal injury is inherent in childbirth, and various methods and materials have been used by accoucheurs in an attempt to restore perineal integrity. Surgical treatment in the form of a crossed or bootlace suture was first mentioned in Avicenna's famous Arabic book. However, the first recorded perineal suture was by Guillemeau in 1610 [1].

Perineal trauma resulting from childbirth remains a common problem [2] that causes a significant increase in maternal morbidity and may also have devastating effects on family life and sexual relationships. More than 85% of women sustain perineal trauma after childbirth [3], and up to two-thirds need suturing [2]. Perineal pain and discomfort affect up to 42% of women at 10 days postpartum, and in 10% of women, these problems persist at 18 months following childbirth [4]. Moreover, up to 58% of women experience superficial dyspareunia at 3 months postpartum [5].

This chapter covers the management and repair of episiotomy and first- and second-degree tears. Preventive measures are also discussed.

APPLIED ANATOMY

Anatomy of the Perineum

The perineum corresponds to the outlet of the pelvis and is somewhat lozenge-shaped. The perineum can be divided into two triangular parts by drawing a line transversely between the ischial tuberosities. The anterior triangle, which contains the urogenital organs, is known as the *urogenital triangle*, and the posterior triangle, which contains the termination of the anal canal, is known as the *anal triangle*.

Urogenital Triangle

The muscles are classified into a superficial and a deep group relative to the perineal membrane. The bulbospongiosus, superficial transverse perineal, and the ischiocavernosus muscles lie in the superficial compartment (Figure 92.1). The bulbospongiosus muscle encircles the vagina and inserts anteriorly into the corpora cavernosa clitoridis. Posteriorly, some of its fibers may merge with those of the superficial transverse perineal muscle and also with the external anal sphincter. Beneath the bulbospongiosus muscles lie the vestibular bulbs anteriorly and the Bartholin's glands posteriorly. The Bartholin's gland is a pea-shaped structure and its duct opens at the introitus just distal to the hymen at the junction of the upper two-thirds and the lower one-third of the labia minora. The deep transverse perineal muscle lies below the perineal membrane. It is thin and difficult to delineate and hence some authors deny the existence of this muscle [6].

Anal Triangle

This area includes the anal sphincters and ischioanal fossae. The external anal sphincter is subdivided into three parts—subcutaneous, superficial, and deep—and is inseparable from the puborectalis muscle posteriorly (Figure 92.2). The internal anal sphincter is a thickened continuation of the circular smooth muscle of the bowel. It is separated from the external anal sphincter (striated muscle) by the conjoint longitudinal muscle, which is a continuation of the longitudinal smooth muscle of the bowel but may receive contributions from the puborectalis muscle and the deep external sphincter [7] (see Chapter 92).

Perineal Body

The perineal body is the central point between the urogenital and the anal triangles of the perineum. Its 3D form has been likened to that of the cone of the red pine, with each "petal" representing an interlocking structure such as an insertion site of fascia or a muscle of the perineum [8]. Within the perineal body, there is interlacing of muscle fibers from the bulbospongiosus, superficial transverse perineal, and external anal sphincter muscles. Above this level, there is a contribution from the longitudinal rectal muscle and the medial fibers of the puborectalis muscle.

DEFINITION OF PERINEAL TRAUMA

Perineal trauma may occur spontaneously during vaginal birth or when a surgical incision (episiotomy) is intentionally made to facilitate delivery. It is possible to have an episiotomy and a spontaneous tear (e.g., extension of an episiotomy). Anterior perineal trauma is defined as injury to the labia, anterior vaginal wall, urethra, or clitoris; posterior perineal trauma is defined as any injury to the posterior vaginal wall or perineal muscles and may include disruption of the anal sphincters.

Structures Involved

First-degree perineal trauma is very superficial and may involve the skin and subcutaneous tissue of the anterior and posterior perineum, the vaginal mucosa, or a combination of these. Second-degree tears or mediolateral episiotomy involves the superficial perineal muscles (bulbocavernosus, transverse perineal) or the perineal body if a midline episiotomy incision is made. Rarely, more complex trauma can occur, whereby the tear extends in a circular direction, behind the hymeneal remnants, bilaterally upward toward the clitoris, causing the lower third of the vagina to detach from the underlying structures [6].

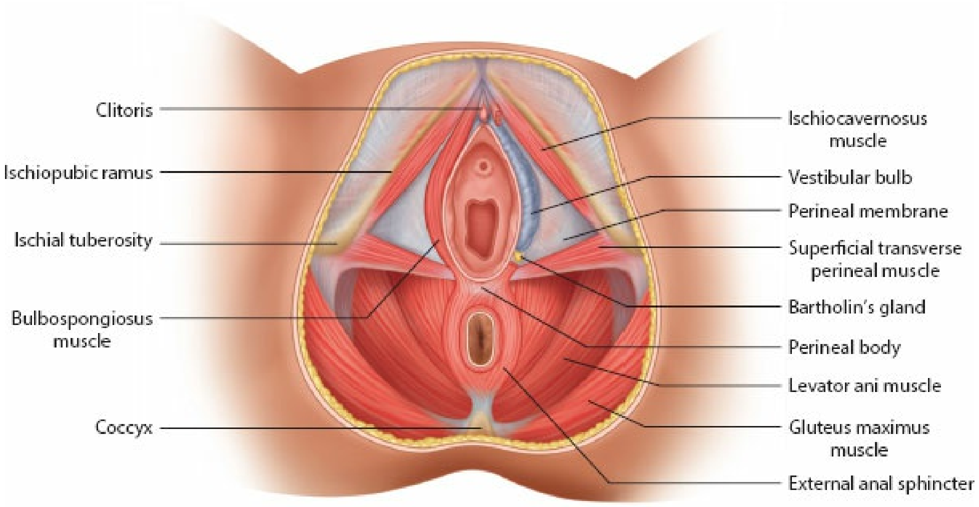

Figure 92.1 The superficial muscles of the perineum.

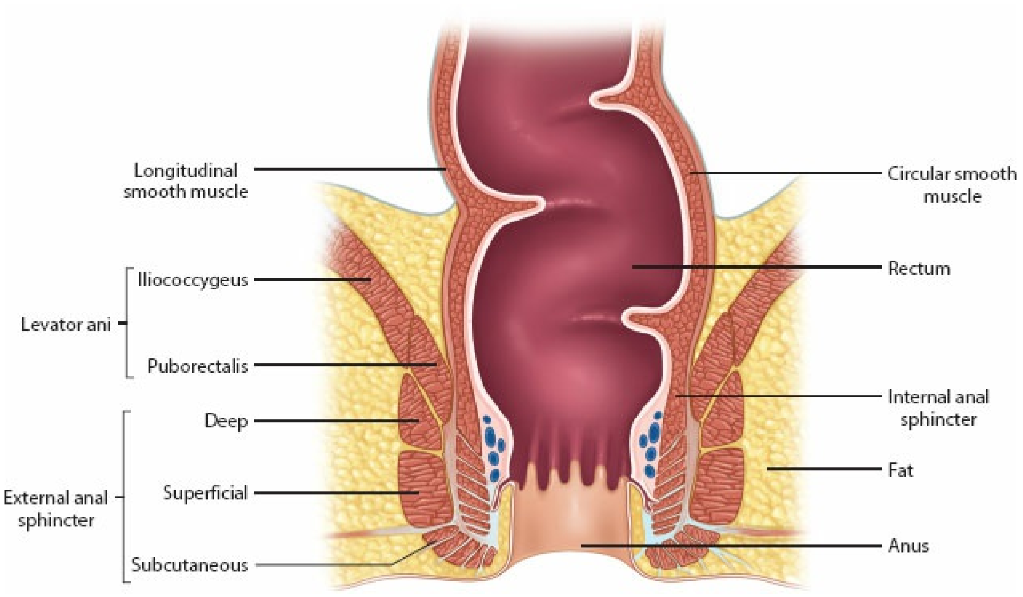

Figure 92.2 The anal sphincter.

EPISIOTOMY

Episiotomy is a surgical incision made with scissors or a scalpel into the perineum in order to increase the diameter of the vulval outlet and facilitate delivery [9]. The two main types of episiotomy incision are midline and mediolateral [10] although other types have been described [11]. When a midline episiotomy is undertaken, the incision is made from the central point of the posterior introitus and is directed vertically toward the anus; with a mediolateral episiotomy, the incision begins in the midline but is directed directly away from the anal sphincter and rectum. It is claimed that the midline incision is easier to repair and that it is associated with less blood loss, better healing, less pain, and earlier resumption of sexual intercourse. However, there is no reliable evidence to support these claims [4]. Limited evidence from one quasi-randomized trial suggested that the midline incision may increase the risk of third- and fourth-degree tears compared with the mediolateral incision [12]. However, these data should be interpreted with caution as there may be an increased risk of selection bias due to quasi-random treatment allocation and the analysis was not by intention to treat.

There is evidence accumulating that episiotomies angled too close to the midline are at a higher risk of causing obstetrical anal sphincter injuries (OASIS) [13–15]. This risk reduces by 50% for every 6° the episiotomy is angled away from the midline [14]. However, if the episiotomy angle becomes nearly horizontal (90°), the pressure on the perineum is not relieved and OASIS incidence increases ninefold [15]. The current recommendation is to cut an episiotomy at 45°–60° from the midline [16]. It is important to note that the angle of a mediolateral episiotomy will reduce significantly after the baby is born, i.e., a 40° episiotomy incision results in a suture angle of 22° from the midline [17]. If an episiotomy is performed at a 60° angle, when the perineum is distended, this will result in a suture angle of 45°, which is associated with a lower incidence of anal sphincter tears, anal incontinence, and perineal pain [18].

Incidence

There is a wide variation in the incidence of episiotomies performed in different countries. Clinicians' experiences, practices, and preferences of intrapartum interventions may influence the rate and severity of perineal trauma. Moreover, episiotomy rates may vary considerably according to individual practices and policies of staff and institutions. In the United Kingdom, it is estimated that over 85% of women who give birth will sustain some degree of perineal trauma and, of these, 60%–70% will require suturing [19]. However, episiotomy rates have decreased in English-speaking countries and Europe over the last 20 years, probably due to the accumulation of evidence supporting restrictive use of the procedure.

Episiotomy is a common obstetrical procedure, yet statistics relating to prevalence are not always easily located. Figure 92.3 presents data graphically to illustrate the considerable variation in the use of episiotomy [20]. Episiotomy rates that include both primiparous and multiparous women range from as low as 9.7% (Sweden) to 100% (Taiwan); rates for primiparous women range from 63.3% (South Africa) to 100% (Guatemala) [20].

Indications for Episiotomy

Episiotomy is still performed routinely in many parts of the world in the belief that it protects the pelvic floor. However, evidence from randomized controlled trials suggests that routine episiotomy does not prevent severe posterior perineal tears. A systematic review of randomized clinical trials using the Cochrane Collaboration methodology to determine the possible benefits and risks of restrictive episiotomy versus routine episiotomy included eight studies [4]. This revealed that, compared with routine use, restrictive use of episiotomy resulted in less severe perineal trauma, less suturing, and fewer healing complications. There were no significant differences in severe vaginal/perineal trauma, dyspareunia, urinary incontinence, or severe pain measures. The only disadvantage shown in restrictive use of episiotomy was an increased risk of anterior perineal trauma. The systematic review concluded that there is evidence to support the restrictive use of episiotomy compared to routine episiotomy (irrespective of the type of episiotomy performed) [4].

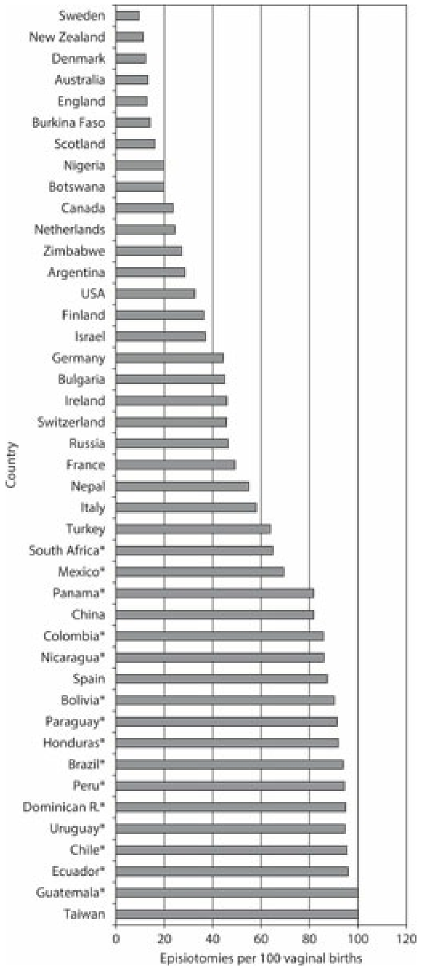

Figure 92.3 Graphical presentation of the considerable variation in the use of episiotomy: rates by country, 1995–2003. * indicates primiparous data only. (Reproduced from Graham ID and Davies C, Episiotomy: The unkindest cut that persists, in: Henderson C and Bick D, eds., *Perineal Care: An International Issue*, Quay Books, Salisbury, U.K., 2004, pp. 58–86. With permission.)

There is currently the absence of clear, evidence-based clinical indications for the use of episiotomy. However, it is reasonable to suggest that an episiotomy should be performed to accelerate vaginal delivery in cases of fetal distress, to facilitate safe delivery if shoulder dystocia occurs, to prevent severe perineal trauma during an instrumental delivery (forceps), and to aid vaginal delivery in cases where the perineal tissue is thick or rigid causing serious delay and in cases in which prolonged "bearing down" may be harmful for the mother (e.g., severe hypertensive or cardiac disease). However, these indications are not absolute and clinical discretion should always be used.

Episiotomy Rate

Although there is clear evidence to recommend restrictive use of episiotomy, there appears to be no consensus regarding the ideal episiotomy rate. Henriksen et al. [21] performed an observational study involving 2188 pregnant women and found that those allocated to the group of midwives with the lowest rate of episiotomies were more likely to have an intact perineum and more spontaneous perineal tears, but no increased risk of having an anal sphincter tear. In a further publication [22], the authors reported a relative decrease of 18% in episiotomy rates after distributing awareness profiles to the midwives, but the rate of anal sphincter tears did not change. There was a tendency toward an increased risk of tears if the midwives tried to reduce episiotomy rates below 20%. This supports the view that the overall ideal episiotomy rate should be between 20% and 30% but fails to indicate the ideal rate for nulliparae versus multiparae. The World Health Organization recommends that an episiotomy rate of 10% for spontaneous vaginal deliveries would be "a good goal to pursue" [23]; however, there is no robust evidence to support this recommendation.

MANAGEMENT OF PERINEAL TRAUMA

For many centuries, there has been a long-standing debate relating to suturing of perineal trauma following childbirth. Some accoucheurs believe that it is much better to leave perineal trauma unsutured to facilitate "ensuing" deliveries, while others argue that the outcome for women and their partners is considerably improved if the trauma is sutured.

Nonsuturing of Perineal Skin

Two trials included in a recent updated Cochrane review compared a two-stage repair technique where the skin was left unsutured but apposed (the vagina and perineal muscles were sutured) to the traditional three-stage approach where all three layers (vagina, perineal muscles, and skin) were sutured. The two large randomized controlled trials were carried out in Ipswich, United Kingdom (single center—n = 1780 women), and the other in Nigeria (multicenter—n = 1077 women) [24,25]. The pooled results suggested that the two-stage repair technique was associated with fewer women experiencing perineal pain up to 14 days; however, the difference between groups did not reach statistical significance at 2 days postnatal. There was a significant increase in wound gaping (more that 0.5 cm) in the two-stage repair group up to 10 days postpartum, but there was no clear evidence of any difference in long-term pain. Women undergoing two-stage repairs were less likely to report dyspareunia up to 3 months after delivery [26].

Nonsuturing of Perineal Trauma

It is unclear whether first- and second-degree tears need suturing. A recent Cochrane review included two RCT's comparing suturing versus nonsuturing (natural healing) of first- and second-degree tears (n = 154 women) [27,28]. These two studies found no difference in pain and discomfort up to 8 weeks postpartum, but one of the studies suggests that wound healing may be faster after suturing. However, the rate of breast feeding in this group was lower. In the other study, the use of analgesics was still high at 8 weeks in the sutured group, while no analgesics were used in the nonsutured group. Long-term effects of the two techniques have not been described, and there is a need for further research in this area. Until such evidence is available, women should be offered informed choice, and information provided should include the lack of available data on the long-term outcomes [29].

Suture Material

A Cochrane systematic review of 18 randomized controlled trials [30] involving 10,171 women carried out to assess the effects of different suture materials on short- and long-term morbidity following perineal repair. The pooled results from nine of the included studies showed that absorbable synthetic material (polyglycolic acid and polyglactin 910), when compared with catgut suture material, was associated with less pain up to 3 days after delivery and less analgesia up to 10 days postpartum. More women with catgut sutures required resuturing compared with synthetic sutures, while more women with standard synthetic sutures required the removal of unabsorbed suture material. Currently, the use of catgut has been largely superseded in developed countries by absorbable suture material.

Standard polyglactin 910 is not totally absorbed from the wound until 60–90 days. However, a more rapidly absorbable form of material is now available. This material has the same chemical composition as polyglactin 910 but is sterilized by gamma irradiation, which causes loss in tensile strength at 10–14 days and is completely absorbed from the tissue by 42 days [31]. Five RCTs included in the Cochrane review compared standard synthetic with rapidly absorbing synthetic suture material. The pooled results showed that short- and long-term pain were similar in both standard and rapidly absorbing synthetic suture group [30]. However, more women in the standard synthetic suture group required suture removal.

Method of Repair

Perineal trauma has traditionally been repaired using a continuous "locking" stitch to close the vaginal trauma, three or four interrupted sutures to reapproximate the deep and superficial muscles and continuous or interrupted transcutaneous stitches to close the perineal skin. For many years, researchers have been suggesting that continuous nonlocking suture techniques for repair of the vagina, perineal muscles, and skin are far better than "traditional" interrupted methods in terms of reduced postpartum pain.

The reason for the reduction in pain is probably due to the fact that the skin sutures are placed in the subcutaneous tissue, thus avoiding the profusion of nerve endings in the superficial skin surface. The rationale behind using the continuous technique is that stitch tension due to reactionary edema is transferred throughout the whole length of the single knotless suture in comparison with interrupted sutures that are placed transversely across the wound. Another advantage of the continuous suturing technique is that only one piece of suture material is required to complete the perineal repair as compared to two to three pieces for the interrupted method, thus reducing the overall expenditure.

A recent Cochrane systematic review [26] of 16 studies involving 8184 women showed that continuous suture techniques compared with interrupted sutures for perineal closure (all layers or perineal skin only) was associated with less pain up to 10 days postpartum. Furthermore, there was a greater reduction in pain when the continuous suturing technique was used for all layers. There was an overall reduction in analgesia use associated with the continuous subcutaneous technique versus interrupted stitches for repair of perineal skin. Subgroup analysis showed some evidence of reduction in dyspareunia experienced by participants in the groups that had continuous suturing of all layers. There was also a reduction in suture removal in the continuous suturing groups versus those with interrupted sutures, but no significant differences were seen in the need for resuturing of wounds or long-term pain. The authors concluded that the continuous suturing techniques for perineal closure, compared to interrupted methods, are associated with less short-term pain. If the continuous technique is used for all layers (vagina, perineal muscles, and skin) compared to perineal skin only, the reduction in pain is even greater.

Based on the evidence earlier, it can be concluded that perineal trauma should be repaired using the continuous nonlocking suturing technique to reapproximate all layers (vagina, perineal muscles, and skin) with rapid-absorption polyglactin 910.

Procedure for Perineal Repair

Assessment of Perineal Trauma [32]

The person responsible for the woman's care must inspect the perineum thoroughly as soon as possible following the birth, using good lighting. Prior to commencing suturing, it is important that the health professional explains the procedure to the woman and her partner and obtains consent. The woman is placed in a comfortable position so that the trauma is easily visualized. It is not necessary to use lithotomy poles to support the woman's legs during the procedure unless she has a working epidural or spinal anesthetic. After confirming effective pain relief, a vaginal examination should be carried out to assess the extent of perineal trauma including identification of the apex of the vaginal wound and the structures involved. In addition, a rectal examination should be carried out to assess whether there is any damage to the anal sphincter muscles. If the external anal sphincter is torn, the separated ends of the torn muscles will be observed to retract backward toward either side of the ischioanal fossa. If the woman has an effective epidural, she will not be able to contract her external anal sphincter muscle. The woman should be referred to a more experienced health-care professional if any uncertainty exists as to the nature or extent of the trauma sustained. This systematic assessment and its results should be fully documented. It is useful to include a diagram to illustrate the extent of the trauma.

Suturing Technique [32] (Figure 92.4)

Repair of the perineum should be undertaken as soon as possible to minimize the risk of infection and blood loss. It should only be undertaken after ensuring effective analgesia. This can be established by infiltrating the trauma with up to 20 mL of local anesthetic (lignocaine 1%), topping up the epidural, or performing spinal anesthesia if necessary.

The following steps should be followed:

1. *Suturing the vagina*: The first stitch is inserted above the apex of the vaginal trauma to secure any bleeding points that might not be visible. Close the vaginal trauma with a loose, continuous, nonlocking technique, making sure that each stitch is inserted not too widely to avoid narrowing the vagina. Continue to suture down to the hymenal remnants and insert the needle through the skin at the posterior fourchette to emerge in the center of the perineal wound.
2. *Suturing the muscle layer*: Check the depth of the trauma and close the perineal muscle (deep and superficial) with continuous nonlocking stitches. If the trauma is deep, the perineal muscles can be closed using two layers of continuous stitches. Realign the muscle so that the skin edges can be reapproximated without tension, ensuring that the stitches are not inserted through the rectum or anal canal.
3. *Suturing the perineal skin*: At the inferior end of the wound, bring the needle out just under the skin surface reversing the stitching direction. The skin sutures are placed below the skin surface in the subcutaneous tissue thus avoiding the profusion of nerve endings. Continue to take bites of tissue from each side of the wound edges until the hymenal remnants are reached. Secure the finished repair with a loop or an Aberdeen knot placed, if possible, in the vagina behind the hymenal remnants.

The equipment should be checked and swabs and needles counted before and after the procedure. Good anatomical alignment of the wound should be achieved and consideration given to cosmetic results. A rectal examination should be carried out after completing the repair to ensure that the suture material has not been accidentally inserted through the rectal mucosa. A detailed account should be documented covering the extent of the trauma, the method of repair, and the materials used. Rectal or oral, nonsteroidal anti-inflammatory drugs should be offered routinely after repair, provided these drugs are not contraindicated. Information should be given to the mother regarding the extent of the trauma, pain relief, diet, hygiene, and the importance of pelvic floor exercises [16].

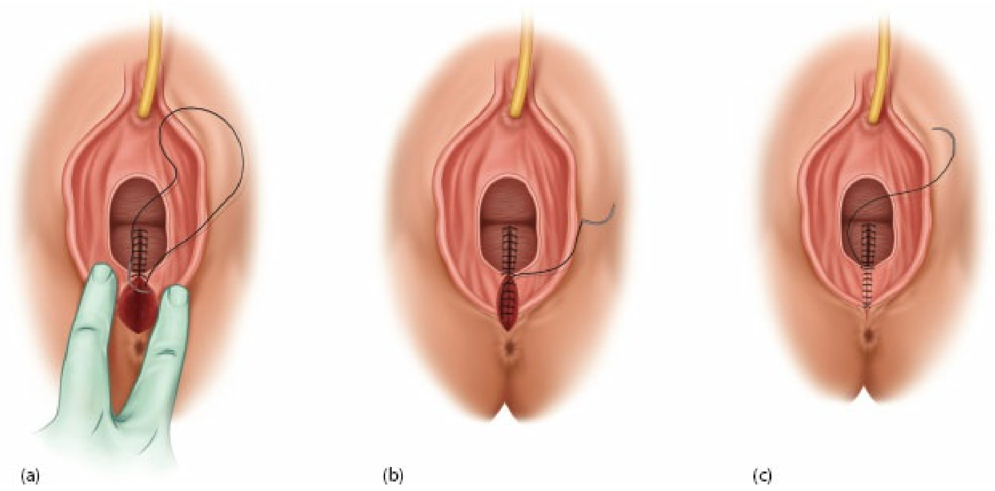

Figure 92.4 The continuous suturing technique. (a) Vaginal trauma is repaired using a loose, continuous nonlocking stitch to the vagina; (b) perineal muscle is repaired using a loose, continuous nonlocking stitch; and (c) skin is closed using a loose subcutaneous stitch. (Reproduced from Kettle C and Fenner D, Repair of episiotomy, first and second degree tears, in: Sultan AH et al., eds., *Perineal and Anal Sphincter Trauma*, Springer, London, U.K., 2007, pp. 20–32. With permission.)

Prevention of Perineal Trauma

Although the case for prevention of perineal trauma is compelling, how to accomplish this is less clear. Certain antenatal risk factors such as maternal nutritional status, body mass index, ethnicity, infant birth weight [33], race, and age [34] cannot be altered at the time of delivery but awareness of them might prompt modifications in the care pathway.

Episiotomy should only be performed when indicated and a mediolateral episiotomy preferable to a midline episiotomy [4]. Fewer women with vacuum delivery have anal sphincter trauma compared to forceps delivery [35]. Antenatal perineal massage reduces the likelihood of perineal trauma (mainly episiotomies) and the reporting of ongoing perineal pain, and it is generally well accepted by women. As such, women should be made aware of the likely benefit of perineal massage and provided with information on how to carry out perineal massage [36]. Other interventions such as water birth, position during labor and birth, delayed pushing with an epidural, second-stage pushing advice, perineal stretching, massage during the second stage, and perineal support at delivery have not been shown to reduce the risk of perineal trauma in randomized studies. Increased perineal trauma with epidural analgesia is due to the increased associated risk of an instrumental delivery [37].

TRAINING

Throughout the centuries, midwives have received very little formal training in the art of perineal suturing. In June 1967, midwives working in the United Kingdom were permitted by the Central Midwives Board (CMB) to perform episiotomies, but they were not allowed to suture perineal trauma [38,39]. In June 1970, the chairman of the CMB issued a statement that midwives who were working in “remote areas overseas” may be authorized by the doctor concerned to repair episiotomies, provided they have been taught the technique and were judged to be competent, but the final responsibility lay with the doctor. However, it was not until 1983 that perineal repair was included in the midwifery curriculum in the United Kingdom when the European Community Midwives Directives came into force and the CMB issued the following statement: “Midwives may undertake repair of the perineum provided they have received instruction and are competent in this procedure.”

However, there has not been enough emphasis on training. In 1995, Sultan et al. [40] carried out a survey in London to assess junior doctors’ and qualified midwives’ knowledge relating to perineal trauma and anatomy and to establish if they were satisfied with their training. Only 20% of junior doctors and 48% of midwives considered their training to be of a good standard when allowed to perform their first unsupervised perineal repair. Furthermore, many of the answers relating to anatomy and classification of tears were incorrect. To improve training, we have recently introduced a course using video presentations and specially designed models to demonstrate anatomy and techniques of repair (www.perineum.net) (Thakar, Kettle and Sultan, personal communication).

In a questionnaire survey of 208 health professionals attending this course, 64% were dissatisfied with their training prior to performing their first unsupervised perineal repair. Evaluation of the course carried out by administration of questionnaires 8 weeks following the course showed a significant increase in the participant’s ability to classify the degree of perineal trauma accurately. Participants changed their practice to evidence-based care after the course with significantly more performing the continuous suturing technique for repair of second-degree tears and episiotomy [41].

It has also been demonstrated that practitioners require more focused training relating to performing mediolateral episiotomies. Andrews et al. [13] carried out a prospective study over a 12-month period of women having their first vaginal delivery to assess positioning of mediolateral episiotomies. The depth, length, and distance from the midline, the shortest distance from the midpoint of the anal canal, and the angle subtended from the sagittal or parasagittal plane were measured following suturing of the episiotomy. Results of the study demonstrated that no midwives and only 13 (22%) doctors performed a truly mediolateral episiotomy and that the majority of the incisions were in fact directed closer to the midline [13].

A recent, pragmatic matched-pair cluster randomized controlled trial (PEARLS RCT) that enrolled women (n = 3681) sustaining a second-degree perineal tear in 1 of 22 UK maternity units (clusters) showed that implementation of the PEARLS-QI intervention was associated with a significant improvement in adherence to evidence-based repair practice and some of the women's reported outcomes. However, the study reported that regular training updates were essential to sustain the same level of improvement. An e-learning version of the PEARLS-QI intervention is now available for online access through StratOG (the Royal College of Obstetricians and Gynaecologists e-learning resource) and the Royal College of Midwives' e-learning suite [42].

The current recommendation is that all relevant health-care professionals should attend mandatory, multidisciplinary training in perineal/genital assessment and repair and ensure that they maintain these skills [43].

CONCLUSION

Obstetric perineal trauma can have a devastating effect on a woman's social life with associated psychological sequelae. Consequently, every attempt should be made to prevent such trauma, which may lead to short-term problems such as pain and dyspareunia or longer-term effects such as prolapse and incontinence. Practitioners must base their care on current research evidence and be aware of the potential maternal morbidity that may occur as a result of perineal injury following childbirth. Furthermore, there is a need for more structured training programs and national guidelines to ensure practitioners are appropriately skilled to identify, correctly classify, and repair perineal trauma in order to minimize morbidity and associated problems. Reducing the adverse sequelae of perineal trauma may make vaginal birth more desirable and could possibly decrease the escalating interest in cesarean section.

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93 Primary Repair of Obstetric Anal Sphincter Injuries

Abdul H. Sultan

INTRODUCTION

Obstetric anal sphincter injuries (OASIS) are the major cause of anal incontinence and can have a devastating effect on women's quality of life. Until the advent of anal endosonography, the cause was attributed largely to pelvic neuropathy. However, despite identification and immediate repair of OASIS, the outcome is suboptimal as more than a third of women suffer from impaired continence. This chapter deals with issues related to acute OASIS and a description of the various repair techniques is given.

DEFINITION

The terms "primary" and "secondary" anal sphincter repair can lead to confusion and need clarification. Following OASIS, a repair of the anal sphincter in the immediate postpartum period is usually performed by an obstetrician as a primary procedure. If the diagnosis is not made immediately after delivery, but for various reasons only identified within the next few days, a delayed primary repair can be performed. However, when a repair of the anal sphincter is performed to treat fecal incontinence (usually months or years after childbirth), it is regarded as a secondary sphincter repair even though a direct primary repair may or may not have been attempted following delivery. There is now evidence to indicate that sonographic "occult OASIS" [1,2] largely represents undiagnosed [3] OASIS during childbirth and is a major etiological factor in the development of fecal incontinence [4]. In the United Kingdom, primary anal sphincter repair is conducted by obstetricians while secondary sphincter repairs are predominantly performed by colorectal surgeons.

CLASSIFICATION OF PERINEAL TEARS

There has been considerable inconsistency in the literature regarding the classification of perineal tears especially relating to third- and fourth-degree tears [5]. In order to standardize the description of anal sphincter injury, Sultan [6] modified the existing classification of perineal tears, and the new classification has been accepted by the Royal College of Obstetricians and Gynaecologists [7], The British National Institute for Health and Clinical Excellence [8], and the International Consultation on Incontinence [9]. This classification is divided into four degrees outlined as follows:

> *First degree*: Laceration of the vaginal or perineal skin only.
> *Second degree*: Involvement of the vaginal/perineal skin, perineal muscles, and fascia but not the anal sphincter.
> *Third degree*: Disruption of the vaginal/perineal skin, perineal body, and anal sphincter muscles. This should be subdivided into (Figure 93.1)
> 3a: Less than 50% of external sphincter thickness torn
> 3b: More than 50% of external sphincter thickness torn
> 3c: Both external and internal sphincter torn
> *Fourth degree*: A third degree tear with disruption of the anal epithelium.

Isolated tears of the rectal mucosa without involvement of the anal sphincter (Figure 93.2) is a rare event and should not be included in the earlier classification but referred to as "button hole" tears.

INCIDENCE OF OASIS AND OUTCOME OF REPAIR

The reported incidence of OASIS varies from one unit to the next and is dependent on obstetric practice but is especially related to the type of episiotomy practiced. OASIS are reported to occur between 0.5% in earlier studies [10,11] to 7.5% [12] of deliveries in centers where mediolateral episiotomy is practiced. It has been reported in 16% of instrumental deliveries [13] and 11% [14] (19% in primiparae [15]) in centers where midline episiotomy is practiced. Midline episiotomies have been favored in North American practice while mediolateral episiotomies are favored in Europe. Over a 25-year period between 1980 and 2005, 35 studies have evaluated outcome following OASIS with follow-up ranging from 1 to 36 months [16] (Table 93.1). The prevalence of anal incontinence (including flatus as a sole symptom) and fecal incontinence (liquids and solids with or without flatus) following end-to-end repair ranges between 15% and 61% (*n* = 35; mean = 39%) and 2% and 29% (*n* = 25; mean = 14%), respectively (Table 93.1). In addition, fecal urgency can affect a further 6% [10,46] to 28% [48] of women. Despite repair, persistent sonographic anal sphincter defects were identified in 34% [23] to 91% [46] of women. Anal incontinence during coitus occurs in about 17% of women following OASIS [44].

Anal resting and squeeze pressures are consistently lower in women who have previously sustained anal sphincter rupture [10,11,30,32,38,41,44], and the anal canal is shorter after repair [10,22]. The development of incontinence does not appear to be directly related to a pelvic neuropathy as demonstrated by EMG [25,33] and pudendal nerve motor latency conduction studies [4,10,30]. Tetzschner et al. [33] reported that 3-month pudendal latency measurements are longer in women with a risk of incontinence. However, these measurements were still within the normal range and no relationship was demonstrated between abnormal latency and incontinence. Although anal sphincter disruption and repair is invariably associated with some degree of denervation and atrophy, current available neurophysiological tests are neither sensitive nor specific enough to quantify pudendal neuropathy. There is, however, evidence to show that poor outcome following primary [10,25,30] and secondary [4] repair may be related more to persistent mechanical disruption as demonstrated by anal endosonography rather than *pudendal neuropathy*.

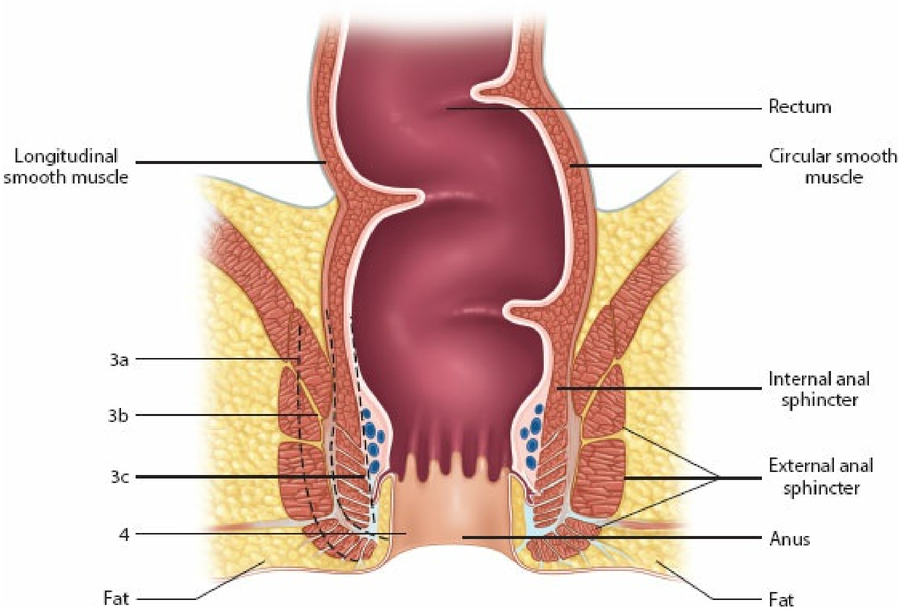


Figure 93.1 Schematic representation of the anal sphincter demonstrating the new classification of anal sphincter injury. (From Sultan AH, *Clin Risk*, 5(5), 193, 1999.)

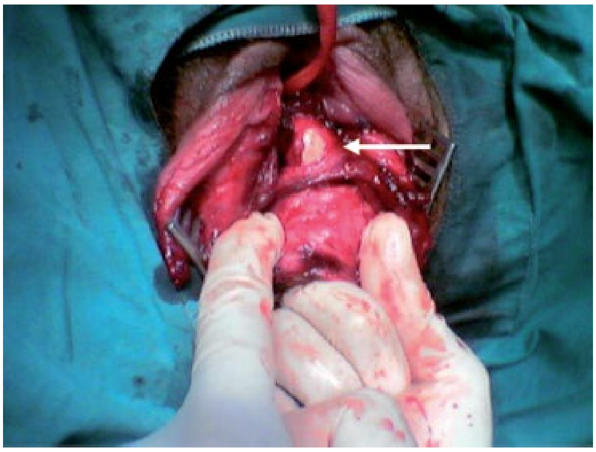


Figure 93.2 An isolated "button hole" tear of the rectal mucosa (arrow) inferior to which an intact anal sphincter can be seen.

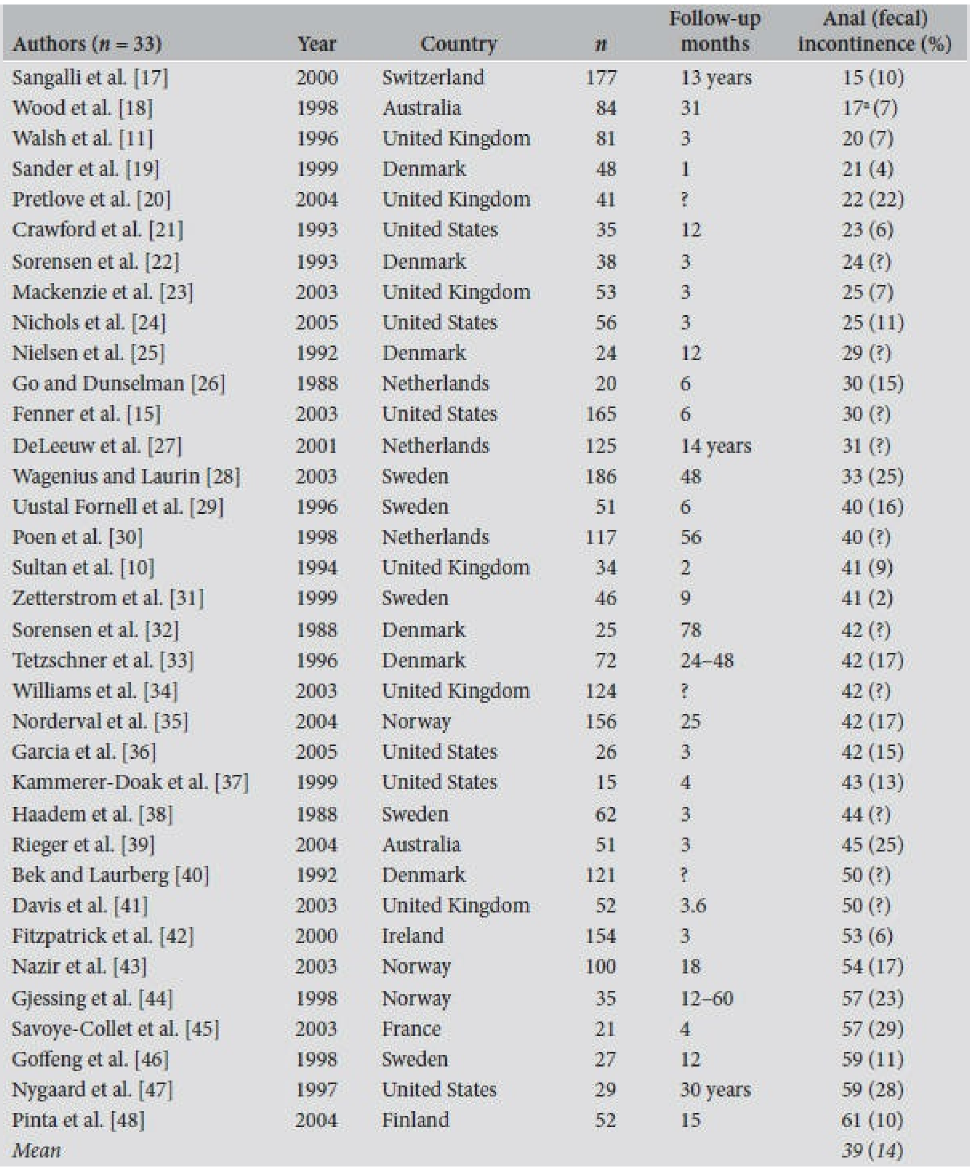
Unsatisfactory outcome following primary sphincter repair may be attributed either to operator inexperience or repair techniques and subsequent management. Training and experience of clinicians performing perineal repair have been questioned [49,50] and hands-on training workshops have been shown to influence a change in clinical practice [51].

TECHNIQUE OF PRIMARY REPAIR

In 1930, Royston [52] described a commonly practiced technique of repair following OASIS where the ends of the torn sphincter were approximated by inserting a deep catgut suture through the inner third of the sphincter muscle and a second set (mattress or interrupted) through the outer third of the sphincter. Subsequently, Ingraham et al. [53] described a modification of the Royston technique [52], where the sutures were only inserted in the fascial sheath or capsule of the sphincter ani. Fulsher and Fearl [54] also described this technique but emphasized that no sutures should pass through the sphincter muscle. More specifically, Cunningham and Pilkington [55] inserted four interrupted sutures in the capsule of the external sphincter at the inferior, posterior, and superior points. In 1948, Kaltreider and Dixon [56] described the end-to-end repair technique that was used since 1935 in which one mattress or figure-of-eight suture was inserted to approximate the sphincter ends.

Obstetricians have used the end-to-end repair technique for decades either by single-interrupted sutures, "figure-of-eight" sutures, or mattress sutures [10] (Figure 93.3). However, as shown in Table 93.1, despite repair, anal incontinence still occur in 39% of women (range 15% [17] to 61% [48]). In addition, fecal urgency can affect a further 6% [10,46] to 28% [48]. Frank fecal incontinence affected 14% (range 2% [31] to 29% [45]). Persistent anal sphincter defects following repair has been reported in 34% [23] to 91% [46] of women (Figure 93.4).

Table 93.1 Prevalence of Anal Incontinence (Including Flatus) Following Primary Repair of Obstetric Anal Sphincter Rupture (Mainly End-To-End External Sphincter Repair).



Authors (*n* = 33)	Year	Country	*n*	Follow-up months	Anal (fecal) incontinence (%)
Sangalli et al. [17]	2000	Switzerland	177	13 years	15 (10)
Wood et al. [18]	1998	Australia	84	31	17^a (7)
Walsh et al. [11]	1996	United Kingdom	81	3	20 (7)
Sander et al. [19]	1999	Denmark	48	1	21 (4)
Pretlove et al. [20]	2004	United Kingdom	41	?	22 (22)
Crawford et al. [21]	1993	United States	35	12	23 (6)
Sorensen et al. [22]	1993	Denmark	38	3	24 (?)
Mackenzie et al. [23]	2003	United Kingdom	53	3	25 (7)
Nichols et al. [24]	2005	United States	56	3	25 (11)
Nielsen et al. [25]	1992	Denmark	24	12	29 (?)
Go and Dunselman [26]	1988	Netherlands	20	6	30 (15)
Fenner et al. [15]	2003	United States	165	6	30 (?)
DeLeeuw et al. [27]	2001	Netherlands	125	14 years	31 (?)
Wagenius and Laurin [28]	2003	Sweden	186	48	33 (25)
Uustal Fornell et al. [29]	1996	Sweden	51	6	40 (16)
Poen et al. [30]	1998	Netherlands	117	56	40 (?)
Sultan et al. [10]	1994	United Kingdom	34	2	41 (9)
Zetterstrom et al. [31]	1999	Sweden	46	9	41 (2)
Sorensen et al. [32]	1988	Denmark	25	78	42 (?)
Tetzschner et al. [33]	1996	Denmark	72	24–48	42 (17)
Williams et al. [34]	2003	United Kingdom	124	?	42 (?)
Norderval et al. [35]	2004	Norway	156	25	42 (17)
Garcia et al. [36]	2005	United States	26	3	42 (15)
Kammerer-Doak et al. [37]	1999	United States	15	4	43 (13)
Haadem et al. [38]	1988	Sweden	62	3	44 (?)
Rieger et al. [39]	2004	Australia	51	3	45 (25)
Bek and Laurberg [40]	1992	Denmark	121	?	50 (?)
Davis et al. [41]	2003	United Kingdom	52	3.6	50 (?)
Fitzpatrick et al. [42]	2000	Ireland	154	3	53 (6)
Nazir et al. [43]	2003	Norway	100	18	54 (17)
Gjessing et al. [44]	1998	Norway	35	12–60	57 (23)
Savoye-Collet et al. [45]	2003	France	21	4	57 (29)
Goffeng et al. [46]	1998	Sweden	27	12	59 (11)
Nygaard et al. [47]	1997	United States	29	30 years	59 (28)
Pinta et al. [48]	2004	Finland	52	15	61 (10)
Mean					*39 (14)*

Source: Springer Science+Business Media: *Perineal and Anal Sphincter Trauma*, Third and fourth degree tears, 2007, 33, Sultan AH and Thakar R.

Note:Fecal incontinence rates are shown in parentheses. "?" indicates that the figure for fecal incontinence has not been stated by the authors.

[a] Includes 2 with secondary sphincter repair.

By contrast, when fecal incontinence is due to sphincter disruption, colorectal surgeons favor the "overlap technique" for secondary sphincter repair as described by Parks and McPartlin [57]. Jorge and Wexner [58] reviewed the literature and reported on 21 studies using the overlap repair with good results ranging from 74% to 100%. Engel et al. [4] prospectively studied 55 patients with fecal incontinence undergoing an overlapping anterior anal sphincter repair and reported a good clinical outcome in 80%. A poor result was found to be associated with an external anal sphincter (EAS) defect while demonstration of an overlap by anal endosonography (Figure 93.5) correlated with a favorable outcome. It is now known that similar to other incontinence procedures, outcome can deteriorate with time and the follow-up study at 5-year follow-up reported 50% continence [59]. However, a number of women in this study had more than one attempt at sphincter repair [59]. Another prospective study reported success in 80% at a 7-year follow-up [60]. Sultan et al. [61] first evaluated the EAS overlap technique for acute OASIS and more importantly, advocated separate identification and repair (Figure 93.6) of the internal anal sphincter (IAS). Sultan et al. [61] evaluated the feasibility of this technique in 27 women and demonstrated that EAS overlap repair as well as identification and end-to-end repair of the IAS was possible following acute OASIS. They observed that compared to matched historical controls [10,61] who had an end-to-end repair, anal incontinence could be reduced from 41% to 8% using the overlap technique and separate repair of the internal sphincter. Based on this, they recommended a randomized trial between end-to-end and overlap repair.

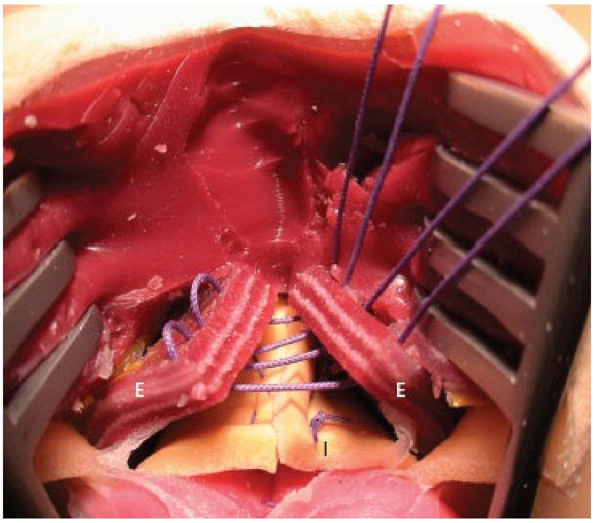


Figure 93.3 End-to-end approximation of the disrupted external sphincter (E) with two mattress sutures. The internal sphincter (I) has also been repaired by the end-to-end technique.

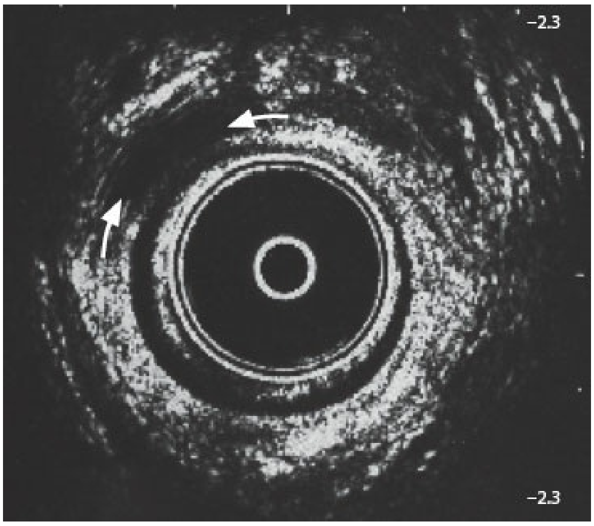


Figure 93.4 Anal endosonographic image demonstrating an external sphincter defect (between arrows) in a woman complaining of fecal incontinence following an end-to-end repair. The arrows overlie the two retracted ends of the muscle. (Reproduced from Sultan AH et al., *Br J Obstet Gynaecol*, 106, 318, 1999. With permission.)

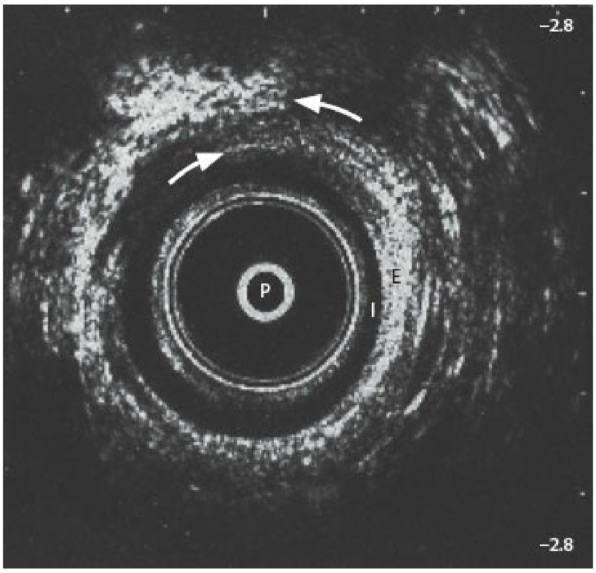


Figure 93.5 Anal endosonographic image demonstrating overlap of the two ends of the external sphincter. P = probe in anal canal with arrow showing its outer limit. Immediately adjacent to this is the anal epithelium. I, internal sphincter; E, external sphincter. The overlap can be seen between the open arrows. (Reproduced from Sultan AH et al., *Br J Obstet Gynaecol*, 106, 318, 1999. With permission.)

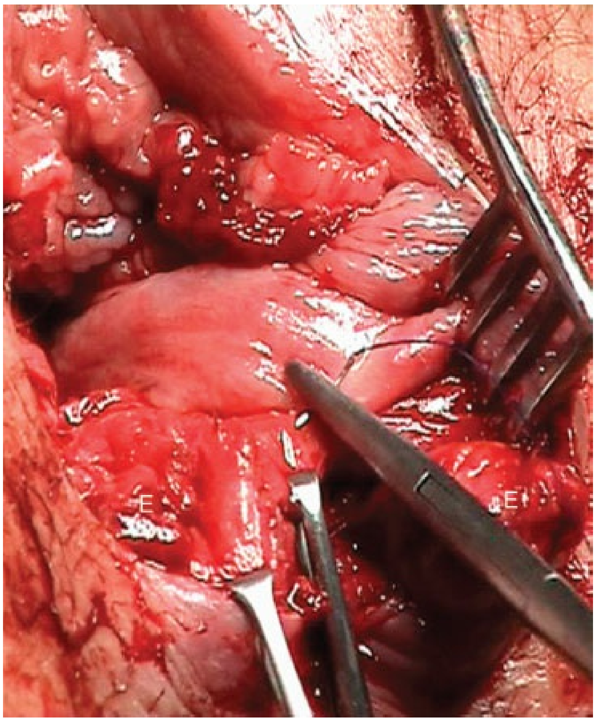


Figure 93.6 End-to-end approximation of the torn ends of the internal anal sphincter. The torn ends of the external sphincter (E) can also be seen.

The first published randomized trial by Fitzpatrick et al. [42] reported no significant difference between the two methods of repair at 3 months. In this study, they included partial EAS tears, and the torn IAS was not identified and repaired separately. They used a constipating agent for 3 days after the repair. However, a true overlap [10,57] is not possible if the sphincter ends are not completely torn, and attempts at overlapping would only place tension on the repair.

Garcia et al. [36] also performed a randomized trial of the two techniques, including only complete ruptures of the EAS (full-thickness 3b, 3c, and fourth-degree tears). Of the 23 women in the end-to-end group and 18 in the overlap group, only 15 and 11 women, respectively, returned for follow-up at 3 months. No significant difference was found between the groups in terms of symptoms of fecal incontinence or transperineal ultrasound findings. However, the authors acknowledged that the major limitations of their study were that randomization was inaccurate and that their study was underpowered.

Williams et al. [62] performed a factorial, randomized, controlled trial ($n = 112$) in which women were randomized into four groups: overlap with polyglactin (Vicryl; Ethicon, Edinburgh, United Kingdom), end-to-end repair with Vicryl, overlap repair with polydioxanone (PDS; Ethicon, Edinburgh, United Kingdom), and end-to-end repair with PDS. This trial was specifically designed to test the hypothesis regarding suture-related morbidity. At 6 weeks, there were no differences in terms of the need for suture removal due to pain, suture migration, or dyspareunia. The authors claim that there were no differences in outcome based on repair technique. Unfortunately, the majority of patients included in this trial were partial tears of the EAS (3a tears and as mentioned earlier), a true overlap cannot be performed if the EAS is only partially torn. Furthermore, their follow-up rate at 12 months was only 54%. These data need to be interpreted by caution.

Fernando et al. [63] performed an adequately powered randomized trial ($n = 64$) of end-to-end vs. overlap technique. At 12 months, they had an 81% follow-up rate and found that 24% in the end-to-end and none in the overlap group reported fecal incontinence ($p = 0.009$). Fecal urgency was reported by 32% in the end-to-end and 3.7% in the overlap group at 12 months ($p = 0.02$). There were no significant differences in dyspareunia and quality of life between the groups. After 12 months, 16% of women in the end-to-end group and no subjects in the overlap group reported deterioration of defecatory symptoms ($p = 0.01$).

Rygh and Korner [64] performed another randomized controlled trial ($n = 101$) with the primary outcome measure “of at least weekly solid stool incontinence.” They concluded that the overlap technique was not superior to the end-to-end repair. However, there were more women with symptoms of anal incontinence in the end-to-end repair group (34% vs. 20%).

Farrell et al. [65] performed a randomized controlled trial with a 6-month follow-up of an end-to-end ($n = 62$) vs. overlap ($n = 63$) EAS repair in primiparous women. They reported significantly higher rates of flatal but not fecal incontinence in the overlap group. However, there were more fourth-degree tears in the overlap group and therefore more IAS injury that could explain the increased flatal incontinence in this group [66]. At a 3-year follow-up however, there was no significant difference in anal incontinence between the groups, but the rate of fecal incontinence in the end-to-end group doubled while it remained static in the overlap group [67]. These support the findings of Fernando et al. [63], who demonstrated a significantly higher risk of deterioration in anal incontinence over time in the end-to-end group. This highlights the importance of longer term follow-up as one technique may prove to be more robust.

The Cochrane review [68] concluded that, compared with immediate primary end-to-end repair of OASIS, immediate primary overlap repair appears to be associated with a reduced risk for fecal urgency, anal incontinence score, and deterioration of anal incontinence symptoms at 12 months. At 36 months (based on only two small trials), there appeared to be no difference in flatus or fecal incontinence between the two techniques. They concluded that either an end-to-end or overlap repair of the EAS may be performed at the discretion of the clinician. It is important, however, to emphasize that the overlap technique has only been described for full-thickness EAS tears [61].

Kairaluoma et al. [69] presented results of 31 women who had sustained OASIS (3b and fourth degree) and had an EAS overlap repair immediately after delivery performed by two colorectal surgeons. In addition to an end-to-end repair of the IAS, they also performed a levatorplasty to approximate the levators in the midline with two sutures. At a median follow-up of 2 years, 23% complained of anal incontinence, 23% developed wound infection, 27% complained of dyspareunia, and one developed a rectovaginal fistula. Levatorplasty should be avoided during primary anal sphincter repair. By contrast, when primary repair with EAS overlap and separate repair of the IAS was performed by urogynecologists, none had fecal incontinence or any complications at 9 months [70].

PRINCIPLES AND TECHNIQUE OF REPAIR [16]

Ideally, primary repair should be conducted as soon as possible after delivery. However, a delay in repair may be justified in exceptional circumstances when an experienced obstetrician may not be available. In a recent randomized study, Nordenstam et al. [12] found no difference in anal incontinence 12 months after primary repair when women who had repair immediately after the tear were compared to others when repair was delayed for 8–12 hours. They concluded that there is no justification in delaying suturing except when a doctor competent in repair of OASIS is unavailable.

OASIS should only be repaired by a doctor who has been formally trained and is experienced in primary sphincter repair or by a trainee under supervision.

Ideally, the repair should be conducted in the operating theater where there is access to good lighting, appropriate equipment, and aseptic conditions. In our unit, we have a specially prepared instrument tray containing a Weitlander self-retaining retractor, four Allis tissue forceps, McIndoe/Metzenbaum scissors, tooth forceps, two artery/mosquito forceps, stitch scissors, and a needle holder (www.perineum.net).

General or regional (spinal, epidural, caudal) anesthesia is important as the inherent tone of the EAS can result in retraction of the torn muscle ends within its sheath. Muscle relaxation is necessary to retrieve the ends especially if the intention is to overlap the muscles without tension.

The full extent of the injury should be evaluated by a careful vaginal and rectal examination in lithotomy and graded according to the classification earlier (Figure 93.1). If there is any uncertainty about the grading of Grade 3a or 3b, it should always be given the higher grade.

On rare occasions, an isolated *button hole*–type tear (Figure 93.2) can occur in the rectum without disrupting the anal sphincter. This is best repaired transvaginally using interrupted Vicryl sutures. To minimize the risk of a persistent rectovaginal fistula, a second layer of tissue should be interposed between the rectum and vagina by approximating the rectovaginal fascia. A colostomy is rarely indicated for acute OASIS unless there is a large tear extending above the pelvic floor, or there is gross fecal contamination of the wound.

In the presence of a fourth-degree tear, the torn anorectal epithelium is repaired with a continuous nonlocking fine suture such as Vicryl 3-0. The technique of interrupted sutures with the knots tied in the anal lumen is recommended when catgut is used as catgut undergoes phagocytosis in tissues and increases the risk of infection. A subcuticular repair of the anal epithelium via the transvaginal approach has also been described [5] although there is some concern that the thin anorectal mucosa could tear with the passage of stool.

The sphincter muscles are repaired with 3-0 PDS dyed sutures (Figure 93.3). Compared to a braided suture, these monofilamentous sutures are believed to be less likely to precipitate infection. Nonabsorbable monofilament sutures such as nylon or Prolene (polypropylene) can cause stitch abscesses, and the sharp ends of the suture can cause discomfort, necessitating removal. Complete absorption of PDS takes longer than Vicryl, and therefore, to minimize the risk of suture migration, care should be taken to cut suture ends short and ensure that they are adequately buried by the overlying superficial perineal muscles. Alternatively, one randomized study has suggested that Vicryl 2-0 can also be used although the primary outcome was not the success of the repair but suture migration [62].

The IAS should be identified and, if torn, repaired separately from the EAS. The IAS lies between the EAS and the anal epithelium. It is thinner and paler than the striated EAS. The appearance of the IAS can be described as being analogous to the flesh of raw fish as opposed to the red meat appearance of the EAS. The ends of the torn muscle are grasped with Allis forceps and an end-to-end repair is performed with interrupted or mattress 3-0 PDS sutures. A torn IAS should be approximated with mattress sutures as overlapping can be technically difficult and will require unnecessary dissection. Mahony et al. [71] followed 500 women who sustained OASIS and found that a persistent IAS defect was independently associated with fecal incontinence. Nichols et al. [24] followed 56 women who sustained OASIS and found that, compared to an intact sphincter, combined defects of the IAS and EAS were associated with the highest risk of bowel symptoms. Roos et al. [72] performed a prospective study of 531 women who sustained OASIS and found that the outcome of primary repair of major (Grade 3c/fourth-degree) tears compared with that of minor (Grade 3a/3b) tears was less favorable. This suggests that tears involving the IAS are a poor prognostic factor. In women with major tears, defecatory symptoms were more prevalent and associated quality of life was worse. Furthermore, these women were more likely to have endosonographic isolated IAS or combined IAS and EAS defects and the maximum resting and squeeze pressures were lower. Women with endosonographic combined defects of the IAS and EAS were associated with a higher risk of loose fecal incontinence, lower maximum resting and squeeze pressures, lower incremental squeeze pressures, and a shorter anal canal length [72].

The torn ends of the EAS may retract and should be grasped and retrieved with Allis tissue forceps (Figure 93.7). In order to perform an overlapping repair, the muscle may need mobilization by dissection with a pair of McIndoe or Metzenbaum scissors, separating it from the ischioanal fat laterally. When performing an overlap repair, the EAS should be grasped with Allis forceps (Figure 93.8) and pulled across to overlap in a "double-breasted" fashion. The torn ends of the EAS can then be overlapped (Figure 93.9a and b) using PDS 3-0 (Ethicon) sutures. A proper overlap is only possible when the entire thickness is torn and the torn ends of the EAS in full length are free and mobile. Overlapping allows for a greater surface area of contact between muscles (Figure 93.9a and b). By contrast, an end-to-end repair can be performed without identifying the full length of the EAS giving rise to incomplete apposition [16]. Consequently, the woman may maintain continence in the short term but would be at risk of developing incontinence later in life. A shorter anal length has been reported following an end-to-end primary repair of the EAS [10,73]. It has also been shown that a shorter anal length is the best predictor of fecal incontinence following secondary sphincter repair [74]. Unlike end-to-end repair, if further retraction of the overlapped muscle ends were to occur, it is highly probable that muscle continuity would be maintained. However, if the operator is not familiar with the overlap technique or if the EAS is only partially torn (Grade 3a and some 3b), then an end-to-end repair should be performed. Two or three mattress sutures (Figure 93.3) should be inserted similar to that described for IAS repair. Hemostatic "figure-of-eight" sutures should not be used to repair the sphincters (or anorectal mucosa) as it could cause ischemia.

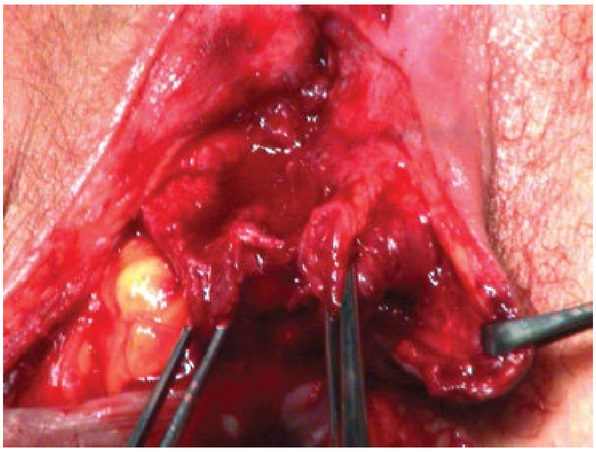


Figure 93.7 Torn ends of the external sphincter being elevated by two pairs of Allis forceps. Note the landmark yellow ischioanal fat lateral to the external sphincter.

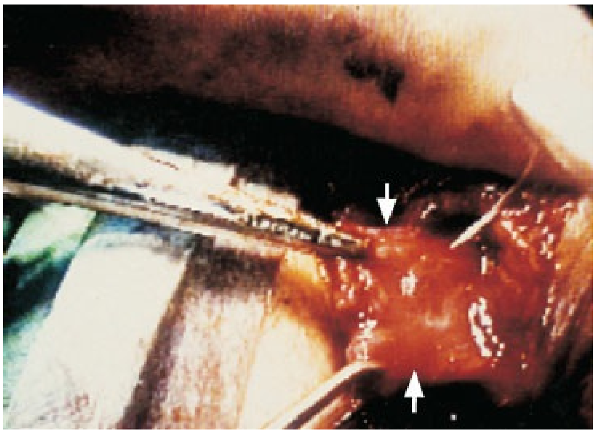


Figure 93.8 Full length of the external sphincter after mobilization. (Reproduced from Sultan AH et al., *Br J Obstet Gynaecol*, 106, 318, 1999. With permission.)

After repair of the sphincter, the perineal muscles should be sutured to reconstruct the perineal body. A short deficient perineum would make the anal sphincter more vulnerable to trauma during a subsequent vaginal delivery.

The vaginal skin is sutured and the perineal skin is approximated with a Vicryl 3-0 subcuticular suture.

A rectovaginal examination should be performed to confirm complete repair and ensure that all packs or swabs have been removed.

Intravenous broad-spectrum antibiotics such as cefuroxime 1.5 g and metronidazole 500 mg should be commenced intraoperatively, and we prefer to continue this orally for at least 3 days. In a prospective, randomized placebo-controlled study [75] of patients who had sustained OASIS (n = 147), it has been shown that patients who received a single dose of intravenous second-generation cephalosporin had a significantly lower risk of perineal complications (8% compared to 24%) compared to a placebo by 2 weeks after the repair.

Severe perineal discomfort, particularly following instrumental delivery, is a known cause of urinary retention, and following regional anesthesia, it can take up to 12 hours before bladder sensation returns. A Foley catheter should be inserted for 12–24 hours unless the midwifery staff can ensure that spontaneous voiding occurs at least every 3 hours.

Detailed notes should be made of the findings and repair. A pictorial representation of the tears proves very useful when notes are being reviewed following complications, audit, or litigation [16].

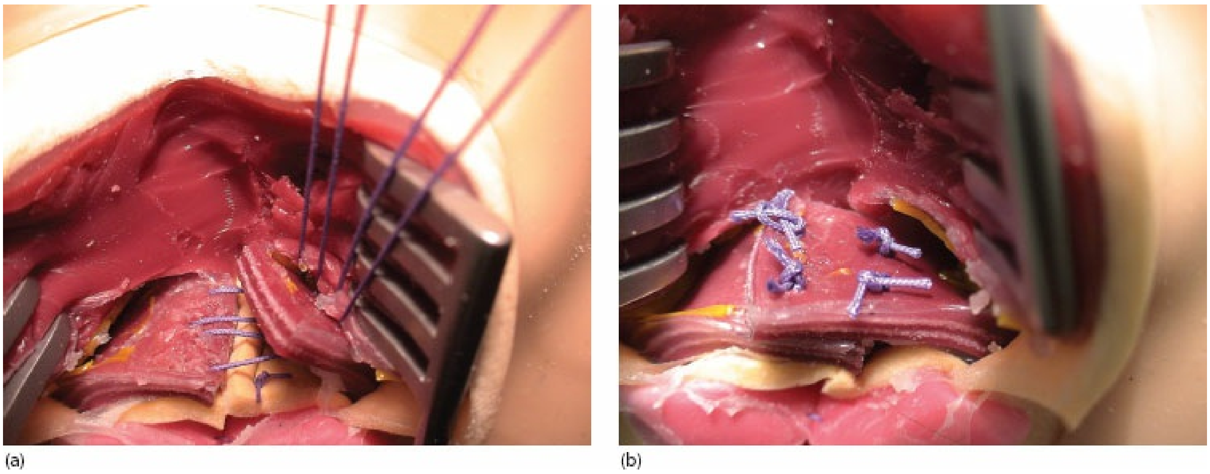


Figure 93.9 The technique of overlap repair of the external anal sphincter. (a) The first suture is inserted about 1.5 cm from the torn edge of the muscle and carried through to within 0.5 cm of the edge of the other arm of external sphincter. (b) A second row of sutures is inserted to attach the loose end of the overlapped muscle.

As passage of a large bolus of hard stool may disrupt the repair, a stool softener (lactulose 15 mL bd) is prescribed up to 10 days postoperatively. The dose can be titrated to ensure that stools are soft. A randomized trial (n = 105) of constipating versus laxative regimens found that the use of laxatives was associated with a significantly earlier and less painful first bowel motion as well as earlier discharge from hospital [76]. Compared to 5% in the laxative regimen group, 19% in the constipated regimen group experienced troublesome constipation (two required hospital admission for fecal impaction). There were no significant differences in continence scores, anal manometry, or endoanal scan findings. Bulking agents such as ispaghula husk (Fybogel) should be avoided as another randomized study [77] has indicated that incontinence occurred significantly more often (33% versus 18%) when lactulose and Fybogel were consumed compared to lactulose only.

It is important that the woman understands the implications of sustaining OASIS and should be informed how to seek help if symptoms of infection or incontinence develop.

Ideally, these women should be followed up in a dedicated perineal clinic by a team with a special interest in OASIS. All women should be given advice on pelvic floor exercises while others with weak or absent sphincter contractility may need electrical stimulation [78].

Management of Subsequent Pregnancy after OASIS

Women who sustain OASIS need careful counselling regarding their management in a subsequent pregnancy. It is known that the risk of recurrence of anal sphincter injury in centers that practice mediolateral episiotomy is 4.4% [79,80] to 7.1% [81,82].

All women who sustained OASIS should be assessed in a hospital by a senior obstetrician about 12 weeks after delivery. As there appears to be a rise in OASIS rates [13,83], there appears to be a need for dedicated multidisciplinary perineal or pelvic floor clinics. In a survey conducted in 2010 [83], 30% of hospitals in the United Kingdom had such a dedicated clinic. A structured bowel symptom questionnaire or scoring system should be used. A proper vaginal and rectal examination should be performed to check for complete healing, scar tenderness, and sphincter tone. Mild incontinence (fecal urgency, flatus incontinence, infrequent soiling) may be controlled with dietary advice, constipating agents such as loperamide, physiotherapy, and/or biofeedback. Women who have severe incontinence should, in addition, be assessed by a colorectal surgeon for a secondary sphincter repair or sacral nerve modulation.

There are no randomized studies to determine the most appropriate mode of subsequent delivery following OASIS. Women who have had a successful secondary sphincter repair for fecal incontinence should be delivered by cesarean section [84]. Some women with fecal incontinence may choose to complete their family prior to embarking on anal sphincter surgery. It would appear that these women may be allowed a vaginal delivery as the damage to the sphincter has already occurred and risk of further damage is minimal and probably insignificant in terms of outcome of surgery. The risk of worsening or de novo neuropathy has not been quantified and, in practice, does not appear to be clinically significant.

In order to counsel women with previous OASIS appropriately, Sultan and Thakar [16] advocate the use of a symptom questionnaire, anal ultrasound (Figures 93.4 and 93.5), and manometry results [9]. If vaginal delivery is contemplated then these tests should be performed during the current pregnancy unless performed previously and found to be normal. Therefore, asymptomatic women who have no evidence of compromised anal sphincter function (ideally, confirmed by anal ultrasound and manometry) should be counselled accordingly and encouraged to have a vaginal delivery [82]. Cesarean section is associated with increased morbidity and mortality [84]. Therefore, unless it is the explicit wish of the woman, it should be reserved for those who are symptomatic or women who had undergone a successful secondary anal sphincter repair for fecal incontinence. In a prospective study over a 5-year period, Scheer et al. [82] found that when women who had no evidence of significant anal sphincter compromise, based on anal endosonography and manometry, were allowed a vaginal delivery, there was no deterioration in symptoms, anorectal function, or quality of life.

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94 Surgery for Fecal Incontinence

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INTRODUCTION

Fecal incontinence (FI) is a common problem of varying severity, which may have a substantial negative impact on a person's life. Anal incontinence may range from mild leakage of gas causing social embarrassment to complete daily loss of control of feces and avoidance of all social activities. It is important to have an approach to quantifying the severity of FI when speaking with a patient, as this may impact their desire to undergo therapy and allow the physician to recommend the most appropriate treatment. There are many scoring systems and scales that have been developed to qualify the severity of FI; the Cleveland Clinic/Wexner Incontinence Score (CCIS) is the most commonly cited scoring system. The CCIS ranges from 0 to 20 and measures incontinence to gas, liquid, and solid stool, the need to wear a protective pad, and the impact of FI on daily activities [1]. Patients with a CCIS of greater than 10 have been shown to have significantly lower quality of life and are more likely to seek medical attention for their FI than individuals with scores less than 10 [2,3].

The exact prevalence of FI is unknown, though large population-based surveys estimate it to be up to 20%. A survey of 4000 American adults found the prevalence to be 8.3% [4]. However, in a more recent study of over 5800 women, called the Mature Women's Health Study, the prevalence of "accidental bowel leakage" was nearly 20% [5]. Interestingly, less than one-third of the women with accidental bowel leakage in the Mature Women's Health Study sought treatment, even though almost 40% of them had symptoms that were affecting their quality of life [3,6]. It is important to note that urinary incontinence and other pelvic floor dysfunction often occur in patients with FI, and so a thorough history must be obtained in every patient presenting with any of these symptoms [7]. Common factors associated with FI include obstetrical trauma causing internal sphincter injury or altered pelvic floor descent, age, obesity, diarrhea, frequent bowel movements, sedentary lifestyle, urinary incontinence, diabetes, neurological disorders, and a history of iatrogenic injury [4,5,8–13]. Once again, women with CCIS greater than 10 are more likely than women with scores less than 10 to seek medical attention [3].

The treatment of FI must be individualized to the patient, depending on the severity of symptoms and impact on quality of life. Options range from dietary modification to fecal diversion with a colostomy. In general, therapy may be categorized into nonsurgical treatment, sphincter repair, sphincter augmentation, sphincter replacement, nerve stimulation, and fecal diversion (Table 94.1). Each of these treatments has different risks, success rates, and degrees of invasiveness. A Cochrane review of the treatment of FI found that there is not enough comparative literature to adequately compare surgical options to each other, leaving much of the decision-making to the physician and patient [14]. A recent task force of the American Society of Colon and Rectal Surgeons reviewed newer treatment alternatives to offer guidance [15]. Not every treatment is appropriate for every patient; therefore, the physician must have a systematic approach to both FI and its potential treatment modalities.

NONSURGICAL THERAPY

Dietary Modification and Medical Treatment

In cases of mild FI, surgery may not be required to control symptoms and negate the impact on activities of daily living. Smoking cessation, weight loss, increased physical activity, and good diabetic control may all have a positive impact on FI [13]. A high-fat or low-fiber diet may cause loose stools leading to FI, either of which may be easily modified through nutritional counseling. Loose stools secondary to bile salt malabsorption after cholecystectomy may contribute to FI and can be improved with the use of bile acid sequestrants, again highlighting the importance of a full patient history during consultation [16]. The impact of dietary fiber must not be underestimated; in the treatment of incontinence, it provides stool bulk with little morbidity and has been shown to be very effective. A placebo-controlled randomized trial of patients in the community living with FI found that the addition of fiber supplements improved stool consistency and reduced FI [17]. These results can be extrapolated to the general population and should be considered in all patients with FI and specifically to individuals with loose stools. Other medications, such as loperamide (Imodium^{TM}), diphenoxylate with codeine (Lomotil^{TM}), codeine, and tincture of opium, may be considered in patients with FI exacerbated by loose stools. The most studied medication is loperamide, which improves stool consistency and may also improve anal resting tone [18,19]. It is also relatively cheap and does not require a prescription. A Cochrane review, which sought to compare the efficacy of medications for FI, found that there are no high-quality studies comparing medications, and therefore, none can be recommended above the others [19].

Biofeedback

Biofeedback is essentially physical therapy for the pelvic floor. It is a program led by a physical therapist aimed at retraining the pelvic muscles, improving sensory awareness, and individualizing treatment for problems such as FI or pelvic outlet dysfunction. While it does require a commitment on the part of the patient to undergo weeks of treatments, it is a nonsurgical option that may be quite helpful and is a definitive treatment for some patients with FI. The best patients to undergo biofeedback are those with mild or moderate incontinence who have failed or are not good candidates for medical treatment [20]. Though there are very few large studies of the efficacy of biofeedback, it has been shown to be beneficial to many patients without imposing morbidity [21,22]. Studies have found that around 70%–80% of patients with FI show improvement with biofeedback in nonrandomized trials [23–25]. However, one study found that less than half of all patients referred for biofeedback actually completed the treatment, largely due to the lack of convenient access to a treatment center [23]. It has been shown that the willingness to complete all recommended biofeedback sessions is the strongest independent predictor of success [26]. If available, it may be a safe and convenient solution to mild FI.

Table 94.1 Treatment Options for Fecal Incontinence (109)

Category	Treatments
Nonsurgical therapy	Fiber Medications Biofeedback
Sphincter repair	Overlapping anterior sphincteroplasty Postanal repair
Sphincter augmentation	Injectable materials Radio-frequency energy
Sphincter replacement	Artificial bowel sphincter Dynamic graciloplasty Magnetic anal sphincter
Stimulation	Sacral nerve stimulation Posterior tibial nerve stimulation
Fecal diversion	Antegrade continence enema Stoma

Biofeedback programs are led by physical therapists and are centered around pelvic floor exercises and retraining. One to several sessions per week are conducted for a number of weeks, though there is no single treatment regimen that is routinely followed. Pelvic floor exercises alone may improve symptoms of FI, when compared to additional therapies [27]. These exercises may be done at home or in the presence of the physical therapist. Other adjunctive treatments may be utilized, including digital feedback, manometric testing, ultrasound guidance, electrical stimulation, or anal balloons. Many studies have found that the addition of manometric monitoring, digital feedback, or electrical stimulation may improve the results of biofeedback [27–29]. Anal manometry may also be used to monitor the treatment effect, which has been shown to be durable at 1 year after finishing therapy [30,31]. The type of biofeedback offered is dependent on the individual physical therapist and the patient level of comfort with various treatment modalities. The main advantages of biofeedback are that it may avoid surgery in patients with mild FI and does not interfere with any future surgical treatment options.

SPHINCTER REPAIR

Overlapping Anterior Sphincteroplasty

Overlapping sphincteroplasty is done to restore the integrity of the sphincter complex and was historically the gold standard treatment for FI. Eligible candidates have a thin anovaginal septum or a palpable sphincter defect, confirmed with an anal ultrasound. However, it is important to note that not all sphincter injuries result in FI [32]. Nonetheless, the majority of overlapping sphincteroplasties are performed in women with a history of prior vaginal deliveries [33]. Other related risk factors for FI associated with a sphincter defects are third- or fourth-degree tears during delivery, forceps-assisted vaginal delivery, and multiple prior vaginal deliveries [34]. The suboptimal long-term durability of sphincteroplasty was the impetus for the development of the many new treatment options. Short-term results show that about 50% of patients have excellent function and over 70% of patients have good function [35]. However, long-term, durable success is seen in less than 50% of patients [36–42]. Even though FI scores may show worse function with time, patients often report durable improvements in quality of life for many years after overlapping anterior sphincteroplasty [36,39]. Additional treatments should thus be based on patient symptoms, rather than on follow-up physiological testing.

The most common form of delayed sphincteroplasty is the overlapping anterior sphincteroplasty. With the patient in the prone jackknife position under general anesthesia with a roll under the hip, a curvilinear incision is made over the perineum. With cephalad dissection, anterior scar will be encountered in place of the sphincter complex. Lateral dissection is then undertaken to identify the edges of the external anal sphincter. The scarred edges are grasped with an Allis clamp, after which the dissection continues laterally, following the course of the external sphincter, until the edges are mobile enough to be reapproximated. Care must be taken to not dissect too far laterally, to avoid injury to the pudendal nerves bilaterally. The levator muscles and internal anal sphincter are imbricated, after which the ends of the external sphincter are then overlapped for 1–2 cm and sutured together using a delayed absorbable suture. A finger in the anus is used to confirm that the new muscle bulk is snug but not too tight as to cause evacuatory outlet dysfunction. The incision is then closed in layers, with the medial portion left open for drainage. Patients must avoid straining and hard stools in the postoperative period, which may lead to early failure of the repair.

Postanal Repair

Although posterior anal sphincter repair is not commonly performed, it is occasionally utilized in conjunction with anterior sphincteroplasty or perineal rectosigmoidectomy. The reasons one may choose to perform a postanal repair alone or in conjunction with an anterior sphincteroplasty are iatrogenic posterior injury after an anorectal procedure or in the setting of multiple sphincter defects due to trauma. It may also be used for neurogenic incontinence or to avoid anteriorly located scar tissue in a patient who has previously undergone an anterior sphincteroplasty. Postanal repair does not improve on the durability of anterior sphincteroplasty and may in fact have inferior results compared to anterior sphincteroplasty [43,44]. The technique is similar to an anterior sphincteroplasty. A curvilinear incision is again made, but posterior to the anus. Overlap of the external sphincter edges is performed after lateral dissection is performed to attain adequate mobilization of the sphincter. While technically similar to anterior sphincteroplasty, postanal repair should be reserved only for patients with documented and specific posterior sphincter defects. Otherwise, overlapping anterior sphincteroplasty is the gold standard approach for sphincter repair.

AUGMENTATION

Injectable Materials

Injectable materials have been developed to add bulk to the anal sphincter complex. They are injected directly into the anal canal to help keep the anus “closed” at rest. Various materials have been used in animals and humans, including silicone, collagen, adipose tissue, and carbon-coated beads [45]. An injectable material is best used for patients with mild to moderate FI. The benefits are that the procedure can be performed in the office setting and does not require sedation. Though it may require a second treatment to achieve good results, there is little morbidity and the procedure is generally well tolerated. Currently, the injectable material of choice is dextranomer in hyaluronic acid gel (NASA/Dx) or Solesta$^{\mathrm{TM}}$. There is increasing literature on this injectable in particular in recent years. Numerous cohort studies have found that about 50% of patients who undergo NASA/Dx injection have a 50% reduction in FI episodes [46–48]. A randomized sham-controlled study of NASA/Dx reported an average reduction in CCIS from 16.8 to 12.8 [49]. While this is an improvement, it may still leave the patient with residual moderate FI. There are no randomized trials comparing NASA/Dx to other injectable materials. Complications from the injections are rare but bleeding, abscess, and pain have been reported [46–49]. Most studies report follow-up of less than 2 years, though longer-term outcomes are currently being studied.

As mentioned previously, NASA/Dx injection may be performed in the office without sedation. The patient is placed in the lithotomy or prone jackknife position. The material is injected in four quadrants, with 1 mL of NASA/Dx injected in each quadrant, about 5 mm proximal to the dentate line to avoid pain. The material is injected into the submucosa at a 30° angle. The needle is left in the submucosa for 30 seconds to ensure that it thickens slightly and would not leak out of the injection site. An anoscope is used to directly visualize the dentate line and injection site. The patient is monitored for a short period after the procedure is completed to rule out a reaction to the material or bleeding from the injection site. If there is poor response to the treatment at the time of follow-up, as assessed by the CCIS and/or quality-of-life scores, a repeat injection may be performed or alternate treatment modality considered. An injectable used in combination with a bulking agent, namely, fiber, may be most helpful for patients with incontinence secondary to leakage of liquid stool.

Radio-Frequency Energy

Radio-frequency energy application is another way to augment the anal canal without major surgery. The therapy, known as the SECCA® procedure, is used in the setting of mild or moderate FI that has not responded to medical management. The procedure was developed after a similar procedure was shown to be effected for the treatment of gastroesophageal reflux disease (GERD) at the gastroesophageal junction. The Stretta® procedure for GERD is effective and durable up to 10 years at reducing reflux scores and improving quality of life [50,51]. It may be helpful even in the presence of a sphincter defect in patients who are unwilling or not candidates for sphincter repair, though the defect should be less than 30°. In contrast to the injectables, the SECCA procedure induces collagen and muscle restructuring, thus producing a stronger and thicker sphincter complex to help control incontinent episodes. While the durability of radio frequency for FI is not yet known, the study with the longest follow-up found that the majority of patients in the cohort had a least 50% improvement in symptoms at 5 years [52]. Most other cohort studies have also demonstrated significant improvement in fecal incontinent episodes, and some found significant improvement in quality-of-life scores [53–55].

Radio-frequency energy delivery requires conscious sedation and so is performed in the endoscopy unit or the operating room. It is an outpatient procedure. The SECCA device includes a clear anoscope, which is marked with a ruler and contains four retractable curved needles. The device is deployed in each quadrant four times, starting at or slightly distal to the dentate line and moving 5 mm more proximal with each deployment. When the device is deployed, the four curved needles penetrate the rectal mucosa and into the internal anal sphincter. Radio-frequency energy is delivered through these needles for exactly 60 seconds per deployment. During activation, the device is attached to a monitor, which measures the tissue temperature and impedance to ensure that no unwanted damage is done to the mucosa or anal sphincter. Auditory and visual feedback from the monitor guides the operator through the procedure and provides feedback on the safety of the treatment. The entire procedure takes about 30 minutes and may be a good alternative for patients wishing to avoid, or who are not ideal candidates for, major surgery for their FI.

SPHINCTER REPLACEMENT

Artificial Bowel Sphincter

The artificial bowel sphincter is a good option for a select group of patients with severe FI. It is a plastic and metal device with three main components—the artificial sphincter, pump device that sits in the scrotum or labus majorum, and fluid reservoir. By filling and releasing fluid from the artificial sphincter, the patient is essentially able to recreate the relaxation of the sphincter complex to evacuate the rectum and have a continent bowel movement on demand. Thus, the patient must be mentally competent and dexterous to operate the device. Currently, the main indication for the artificial bowel sphincter is severe sphincter damage or malformation, whether traumatic, iatrogenic, or congenital. Other options are preferred due to the high rate of complications with the device. In those patients who retain the device, continence is significantly improved in over 75% [56]. Incontinence scores and quality-of-life scores can be vastly improved with the device [56–62]. The artificial bowel sphincter should not be used in the setting of perineal infection, Crohn's disease, irritable bowel syndrome associated with incontinence, or severe constipation [63]. Unfortunately, broader applications of the artificial bowel sphincter for incontinence have been limited by the device's complications. Device failure and infection are the most common complications, leading to device explantation in up to 50% of patients [64,65]. These complications continue to occur long term after many years [64]. Other complications include erosion of the device and constipation. Meticulous surgical technique by an experienced surgeon is essential to minimize the potential complications, though they unfortunately do still occur with the artificial bowel sphincter.

The patient is placed in the modified lithotomy position under general anesthesia. The hair is clipped from the perianal, perineal, and pubic bone areas. Meticulous sterile preparation and technique are employed throughout the procedure. If available, two surgical teams should be used to simultaneously prepare the perineal and Pfannenstiel's incisions. A curvilinear perineal incision is made anterior to the anus. Dissection down to the rectum is performed and then extended laterally and posteriorly. Blunt dissection is required to encircle the rectum, and this is then measured with the cuff sizer to choose the appropriate device size. Once the artificial sphincter, or cuff, is chosen, it is placed around the anal canal and closed. The clear tubing from the cuff is tunneled to the space of Retzius and a trial filling is undertaken. After equilibration, the reservoir is filled and left in the space of Retzius. The second (black) tubing is attached to the pump. A dilator is then used to create a tunnel and a pocket in the labus majorum or the scrotum. The pump is left in the newly created pocket. Care must be taken to ensure that all components of the device are as deep as possible, so as to avoid the risks of infection and device erosion. Once the pump is activated in the clinic after 6 weeks, the patient will begin using the artificial bowel sphincter. At baseline, the cuff is filled with liquid, thus providing the bulk of an anal sphincter and therefore continence. When the patient pumps the device, the fluid leaves the cuff and enters the reservoir. It then slowly refills over a period of about 2–3 minutes, during which time the patient is able to have a bowel movement with good control. This mimics normal sphincter relaxation to allow for rectal evacuation.

The manufacturer of the artificial bowel sphincter (American Medical Systems, Minnetonka, Minnesota) has recently discontinued distribution and support of this device; thus, it is no longer available for implantation.

Dynamic Graciloplasty

Muscle transposition was developed to replace the anal sphincter complex with autologous muscle bulk. Gluteoplasty with bilateral tongues of the gluteus maximus has been described but never gained popularity [66]. The more popular muscle is the gracilis muscle from the leg, which is considered the gold standard for muscle transfer. The gracilis is a useful muscle due to its long length, substantial bulk, and single proximal neurovascular pedicle in most patients. Small series of less than 10 patients were published showing that a neosphincter wrap of gracilis muscle had near perfect success in treating FI [67,68]. In attempts to reproduce this success in larger trials, nerve stimulation, or dynamic graciloplasty, was introduced. Long-term success of dynamic graciloplasty is reported to be between 60% and 75% [68–74]. A multicenter North American trial of dynamic graciloplasty found that function continued to improve and be sustained up to 24 months, and that continence was slower to improve in patients who originally had a stoma at the time of the graciloplasty procedure [74]. Stimulation of the gracilis occurs either with direct stimulation by an implanted lead or temporary stimulation with an external stimulator to retrain the gracilis. Dynamic graciloplasty is not without problems, including infection, pain, and erosion of the stimulator lead [73,75]. Currently, the procedure is not approved for use in North America but continues to be offered to specific patients in Europe and elsewhere.

Graciloplasty is performed with the patient under general anesthesia, but without muscle paralysis. Muscle harvest is done in the modified lithotomy position. The location and course of the gracilis muscle is palpated and marked along the medial aspect of the thigh. Two or three longitudinal incisions are made proximally and distally over the muscle. The insertion tendon is divided near the knee and the muscle is then divided from its deep perforating blood supply. At the medial aspect of the gracilis, meticulous care must be taken to preserve the neurovascular bundle. Confirmation of the identification of the nerve is done through direct nerve stimulation. The muscle is then tunneled medially. Left and right circumanal incisions are made as deeply as possible and the gracilis is delivered into the perineal incision and circumferentially wrapped around the distal rectum to re-create the anal sphincter complex. It is sutured in place to either the ipsilateral or contralateral ischial tuberosity. An electrode is placed in the gracilis muscle and stimulation is achieved with an implantable stimulator, similar to that of sacral nerve stimulation (SNS), which is discussed later in this chapter. Postoperatively, the patient is placed on bed rest in an adduction splint for 72 hours to prevent early failure of the muscle wrap.

Magnetic Anal Sphincter

A newer device has been developed to simplify the concept of sphincter replacement. The magnetic anal sphincter provides anal pressure and baseline tone at rest, which is overcome during pushing to open the anal canal and allow for defecation. It is currently undergoing clinical trials and is not approved for use in North America. The results from a multicenter prospective feasibility trial showed significant improvements in the CCIS from 17 to 8 and better quality-of-life scores [76]. Another study comparing the magnetic anal sphincter to the artificial bowel sphincter found equivalent improvements in incontinence and similar complication rates, but shorter hospital stay and operative time in the magnetic anal sphincter group [77]. While long-term results are not yet available, it appears that about two-thirds of patients are satisfied with the results of the procedure at about 2 years [78]. Complications of the procedure include bleeding, infection, pain, obstructed defecation, device failure, and device erosion [76]. The need for device explantation appears to be lower than that of the artificial bowel sphincter, but the data are sparse in these small trials.

The magnetic anal sphincter is implanted under general anesthesia as an inpatient surgery. An anterior curvilinear incision is made on the perineum. Much like graciloplasty and artificial bowel sphincter procedures, a circumferential tunnel is created around the anal canal with sharp and blunt dissection. The magnetic sphincter is then fit to size by removing or adding magnetic beads to the chain. The chain of magnetic beads is then wrapped around the rectum and secured in place. The tightness of the device is tested using an anal dilator or finger. The device must be snug enough to provide resting tone and continence, but loose enough that the magnets will be overcome by Valsalva maneuver during defecation and not cause outlet obstruction–type constipation. The incision is then closed and the patient is treated with antibiotics in the postoperative period to reduce the risk of device infection. This is a promising procedure that may provide a less complicated alternative to the artificial bowel sphincter and dynamic graciloplasty in the near future.

STIMULATION

Sacral Nerve Stimulation

SNS has markedly changed the treatment of both fecal and urinary incontinence. It has provided an effective alternative for moderate to severe FI without having to access the perineum or anal sphincter complex itself, which is desirable given the infectious complications of some of the treatments discussed earlier. The stimulator is implanted only after a test phase of stimulation is completed. Improvement in FI during the test phase positively predicts overall success of SNS [79]. Patients with prior sphincter repair, current sphincter defects, or known pudendal nerve injuries have all had good success with SNS [80–82]. The mechanism of action of SNS is not clear and appears to be multifactorial. Not only is there direct stimulation of S3 on the anal sphincters, but it also improves the sensation of rectal filling, alters colonic transit, and increases central nervous activity at the level of the cerebral cortex [83–86]. Significant improvements in FI scores have been universally reported in the short and long term, and the majority of studies also show sustained improvements in quality-of-life scores [87–93]. A report by the SNS Study Group found that almost 90% of patients had long-term reduction in incontinent episodes and over one-third had complete continence at 5 years or longer [87]. Infection, pain, and device migration are the most common complications of the procedure, which occur in about 10% of patients [91,94,95]. The SNS Study Group found that about one-third of patients need some sort of device manipulation or removal over long-term follow-up [87]. SNS is one of the few treatments for FI that has been robustly examined for cost-effectiveness and has been shown to be cost-effective in multiple reports [96,97].

SNS is done in two stages—a test phase and implantation procedure. The device consists of a tined quadripolar electrode lead and implantable pulse generator. During the first phase of the procedure, that patient is placed in the prone position in the operating room under light sedation. Using mostly local anesthesia for pain control, the tined lead is introduced into the medial aspect of the S3 foramen via a posterior approach. Fluoroscopic guidance is used to plan the insertion point and assess the depth of the lead. By stimulating the guide wire and then the lead, confirmation of good placement is achieved in three ways: by looking for plantar flexion of the great toe, visualizing anal bellows (inward retraction of the anus), and asking the patient to report stimulation in the perineal area. Once a good response is confirmed, the lead is deployed in position and attached to a temporary external stimulator. The test phase is conducted over 1–2 weeks while the patient keeps a bowel diary. If the patient experiences a 50% reduction in incontinent episodes, the second stage of the procedure is completed. Alternatively, a temporary lead may be placed in the office setting with local anesthesia using bony landmarks to guide placement. If a good response is attained, this temporary lead is again attached to an external stimulator for 3–5 days.

During the second stage, the implantable pulse generator, similar to a cardiac pacemaker, is inserted deep in the gluteal fat, just above the gluteal fascia. If an office-based test phase with a temporary lead had been performed, the permanent tined quadripolar electrode lead is also placed during the second stage of the procedure. The patient controls the intensity of the stimulation and can also adjust which of the four electrodes is being stimulated using the control device. The device needs to be exchanged every 4–5 years to replace the battery.

Posterior Tibial Nerve Stimulation

This novel approach to the treatment of FI is borrowed from the treatment of overactive bladder syndrome and urinary incontinence. It can be thought of as a bridge between biofeedback and SNS, as it is a noninvasive attempt to retrain the anal complex through stimulation of the sacral nerve complex. Patients undergo percutaneous or transcutaneous tibial nerve stimulation in an outpatient setting for 30 minutes at a time for about 12 weeks. A systematic review recently found that both percutaneous and transcutaneous stimulation are effective modalities [98]. The cortical effect of posterior tibial nerve stimulation (PTNS) appears to be durable with time, even after the treatment sessions have ceased. At least, a 50% reduction in fecal incontinent episodes is seen in over two-thirds of patients [98–101]. Long-term follow-up beyond 2 years is not yet known, though it is clear that patients need to undergo monthly treatment to maintain the durability of the response, similar to biofeedback. The fact that this treatment combines the similar multimodal benefits of SNS with the minimally invasive appeal of biofeedback may make PTNS a potentially desirable treatment for moderate FI for many patients who are willing to undergo a full course of treatment.

Currently, PTNS is done in the presence of a physical therapist in an outpatient facility. A surface electrode or needle electrode is placed just posterior and caudal to the medial malleolus of one elevated leg with the patient awake in the lying or sitting position. If a needle electrode is used, the goal is to place it near, but not directly into, the posterior tibial nerve. A ground pad is placed and the stimulator is activated for 30 minutes. Pulse stimulation is performed and correct placement of the electrode is confirmed by visualizing flexion or fanning of the toes and plantar flexion of the foot. Sensory stimulation may also be reported by the patient on the plantar aspect of the foot. The patient typically undergoes 1 or more sessions per week over a course of 12 weeks. Changes in the number of FI may not be noticed immediately and typically occur after multiple sessions. PTNS is not approved for treatment of FI in the United States, but is being used for this indication elsewhere in the world.

FECAL DIVERSION

Antegrade Continence Enema

The antegrade continence enema (ACE), also known as the Malone procedure, is the most commonly described in the pediatric population. It can be helpful in both children and adults, especially in those with colonic dysmotility resulting in overflow FI. This most commonly occurs in institutionalized patients or those with neurogenic bowels due to spina bifida. In this population, the ACE procedure is done in combination with surgical treatment for neurogenic bladder and overflow incontinence [101,102]. It allows for the patient to effectively flush out the colon daily in a controlled setting to avoid the problem of overflow incontinence. There are very few studies that describe long-term outcomes of the ACE in adults with FI. It is also important to note that many patients do not continue to perform antegrade enemas in the long term [103]. In those that do use the ACE, 75% of patients report significant reduction in FI and most have improved quality-of-life scores [104–106]. Problems with the procedure include infection and leakage or stenosis of the access site that may require a revision. Thus, it is a procedure worth considering in a very select adult patient population.

There are many variations of the ACE procedure. In essence, an access point to the bowel is brought to the skin. The distal ileum, appendix, cecum, and even left colon have been used as access points. The appendix is the most commonly used, as it can be inverted at the level of the skin to act as a channel for the irrigation catheter. The procedure should be laparoscopically performed, if feasible, to enhance recovery. After the access point is left fixed to the skin, a catheter is left in place for a few weeks to allow for the site to mature. The patient or caregiver is educated on how to perform intermittent catheterization of the access point. Then, large volumes of water or a bowel cleansing solution are used to flush the colon every 1 to few days. Both water and cleansing solutions are effective and the choice largely depends on patient preference and effectiveness. By evacuating the colon in a timed and controlled setting at home, the patient is able to perform daily and social activities without the fear and inconvenience of overflow FI. While this may seem to be a burdensome procedure, it can afford selected children and adults better hygiene and social independence throughout the day.

Stoma

The only way to completely eliminate the risk of FI is to create a stoma. Patients are often worried about the social stigma and embarrassment of a colostomy or ileostomy and so are often hesitant to proceed, unless the symptoms are severe. It should be considered, though, to be a very well-tolerated option for those with severe incontinence. Unless the patient has impaired colonic transit, a colostomy is preferred over ileostomy due to thicker and more formed stools from a colostomy, which are easier to manage. In the current era of minimally invasive surgery, a diverting colostomy can be laparoscopically created to minimize the morbidities of surgery, including bleeding, infection, incisional hernia, and cardiac or respiratory complications. Anecdotally, many patients with severe FI are very happy once they proceed to colostomy and find it to give them much more freedom in their daily lives. In fact, a study of patients with FI found that patients with a colostomy had significantly higher general quality of life and FI-related quality-of-life scores, compared to those with FI [107]. Others have found that 80% of patients who underwent colostomy for FI are satisfied and state they would choose the procedure again [108]. Therefore, in the event that other treatment modalities have failed, we must not forget to offer this treatment option to patients with severe FI.

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95 Rectal Prolapse and Other Causes of Fecal Obstruction

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DEFINITION AND CLASSIFICATION

Rectal prolapse is a circular invagination of all layers of the rectal wall in a longitudinal direction [1,2]. The prolapsed segments are situated in the aboral intestinal lumen and may protrude outside the anus.

A distinction is made between internal and external rectal prolapse [3–5]. Internal rectal prolapse is also designated as intussusception, a condition in which the intestinal wall folds into itself like a telescope. The prolapsed rectal segments are situated in the ampulla or anal canal and do not protrude externally (Figure 95.1a). Depending on the level, a distinction is made between rectorectal and rectoanal intussusception. External rectal prolapse is the true form of rectal prolapse in the strictest sense. Here, the prolapsed parts emerge through the anus either spontaneously or while straining and are visible outside the body (Figure 95.1b).

Rectal prolapse is often clinically classified into Grades 1–3. Grade 1 corresponds to internal prolapse or intussusception. Grade 2 refers to protrusion through the anal canal while straining. Grade 3 denotes a prolapse externally visible even at rest (Table 95.1). Another classification, the Oxford rectal prolapse score, focuses on internal prolapse and thus on x-ray defecography findings (see Table 95.2) [6,7].

Special forms of prolapse are partial rectal prolapse and mucosal prolapse. Partial prolapse does not involve circular protrusion; only part of the wall slides out—usually the anterior wall. Mucosal prolapse does not involve all wall layers; only the mucosa protrudes, and here too the affected area is usually the anterior rectal wall.

EPIDEMIOLOGY

Rectal prolapse can basically occur at any age. Its annual incidence is approximately 2.5 per 100,000 people [8]. There are two incidence peaks. The first one is seen among children during the first 2 years of life. The incidence among adults gradually increases with age and reaches a second peak in women during the seventh decade of life. Affected men are somewhat younger than women on the average. The incidence is markedly higher in women than men with a female-to-male ratio of approximately 9:1 [8].

ETIOLOGY AND PATHOPHYSIOLOGY

The etiology of rectal prolapse is multifactorial. Risk factors include chronic constipation, obesity, connective tissue or muscle weakness, and in women vaginal delivery and multiparity. The pathogenesis of the disease has not been fully clarified. A number of possible explanations have been proposed. In 1912, the Hungarian surgeon, Alexis Victor Moschcowitz, developed the sliding hernia theory [9]: the hernial orifice is situated in the anal canal at the pelvic floor; the hernial sac is the anterior rectal wall. The theory is supported by typical concomitant features such as an elongated sigmoid colon, a mobile mesorectum, lax lateral ligaments, and pelvic floor weakness. Today, the hernia is considered to be the consequence rather than the cause of the disease. Rectorectal invagination is thus considered to mark the onset of the disease, the earliest phase in the development of complete rectal prolapse. The emergence of cineradiography first enabled Broden and Snellman to radiographically substantiate this theory in the 1960s [10]. This is in keeping with the conical high-pressure zone radiographically detected by Shafik et al. at the rectosigmoid junction [11]. This zone resembling a bottleneck may be regarded as the starting point of invagination. In addition, various neurological changes have also been linked with rectal prolapse [12,13].

The prolapsing tissue narrows the intestinal lumen. In contrast to stenosis, this is a dynamic effect that is augmented by straining during defecation and thus leads to functional stenosis. This typically causes severe defecation disorders that may also be designated as obstructed defecation. Due to secondary pelvic floor and sphincter damage, incontinence usually becomes a predominant problem later in the course of the disease.

SYMPTOMS

Rectal prolapse is associated with a variety of symptoms (Table 95.1). Grade 1 is often completely asymptomatic and in that case has no disease status. However, functional stenosis during defecation can cause abdominal complaints, defecation disorders, a sensation of bulging in the rectum, and thus a feeling of incomplete evacuation. Those affected may have frequent or prolonged defecation times or require digital support during defecation. In Grade 2, many patients additionally experience soiling and mild incontinence symptoms. Patients can touch the prolapsed intestine during defecation and push it back in place. Grade 3 is usually characterized mainly by gross incontinence. Ulceration and bleeding may occur in the prolapsed mucosa. Patients are at risk for incarceration and gangrene [2,14,15].

Patients often have a considerably reduced quality of life and markedly restricted social life [8]. Evacuation is painful and is perceived to be psychologically degrading. Fecal incontinence leads to fear of embarrassing situations in everyday life and thus results in social isolation.

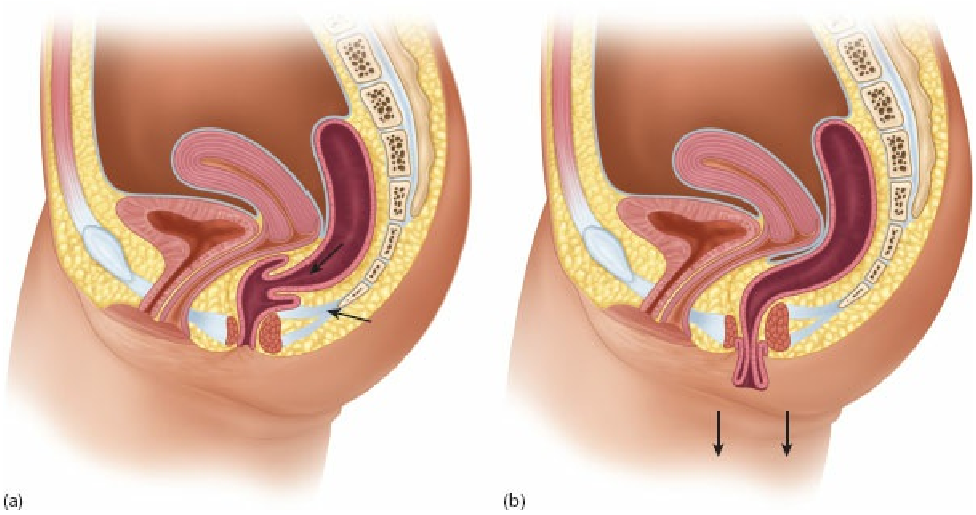

Figure 95.1 (a) Internal rectal prolapse (intussusception) and (b) external rectal prolapse.

Table 95.1 Clinical Classification of Rectal Prolapse

Grade	Definition	Typical Symptoms
1	Internal prolapse (intussusception)	Asymptomatic or impaired evacuation
2	External prolapse during straining	Impaired evacuation, incontinence
3	External prolapse at rest	Incontinence, bleeding, ulcerations, gangrene

Table 95.2 Oxford Rectal Prolapse Score

Grade	Definition
1	High rectorectal intussusception
2	Deep rectorectal intussusception
3	High rectoanal intussusception
4	Deep rectoanal intussusception
5	External rectal prolapse

DIAGNOSIS

Clinical Assessment

Grade 2 and 3 rectal prolapse show the typical clinical picture with circular mucosal folds (Figure 95.2) and can thus be clearly differentiated from anal prolapse with its radial mucosal folds. Prolapse is classified as Grade 3 if present at rest and as Grade 2 if the rectum protrudes only during straining maneuvers [14]. It can usually be pushed out most easily in a squatting or sitting position. Digital rectal examination often reveals reduced resting and squeeze pressure.

Rectoscopy, Manometry, Endosonography

Rectoscopy, manometry, endosonography, and coloscopy are used as complementary measures. They can indicate the extent of prolapse and possibly exclude concomitant diseases [2,16]. Rectoscopic signs may include mechanical irritation of the mucosa and ulcerations (ulcus simplex, typically on the anterior rectal wall). Manometry documents the frequently reduced resting and squeeze pressure. Endosonography can demonstrate alterations or injuries in the anal sphincter, and coloscopy can exclude important differential diagnoses like cancer.

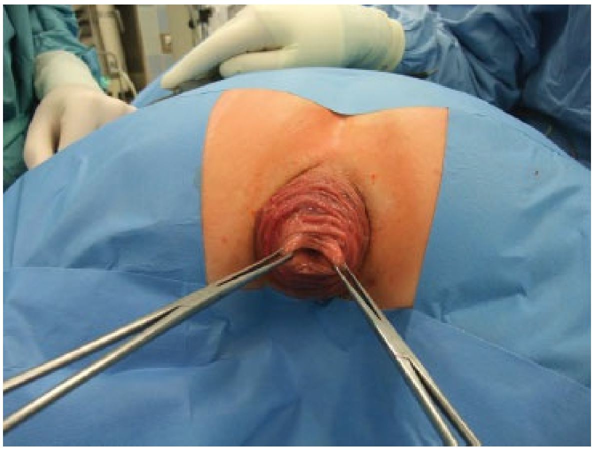

Figure 95.2 External rectal prolapse.

Diagnostic Imaging

Cinedefecography is performed to detect Grade 1 rectal prolapse (intussusception) [2,16]. This dynamic examination during defecation can demonstrate a functional obstruction that only becomes manifest in the defecation process (Figure 95.3a and b). Defecography also enables reliable differentiation from rectocele.

CONSERVATIVE TREATMENT

Depending on the clinical findings, conservative management is possible in Grades 1 and 2. It consists of dietary measures to promote bowel regularity (high-fiber food, plenty of fluids), laxatives, stool softeners, pelvic floor exercises, and biofeedback [14].

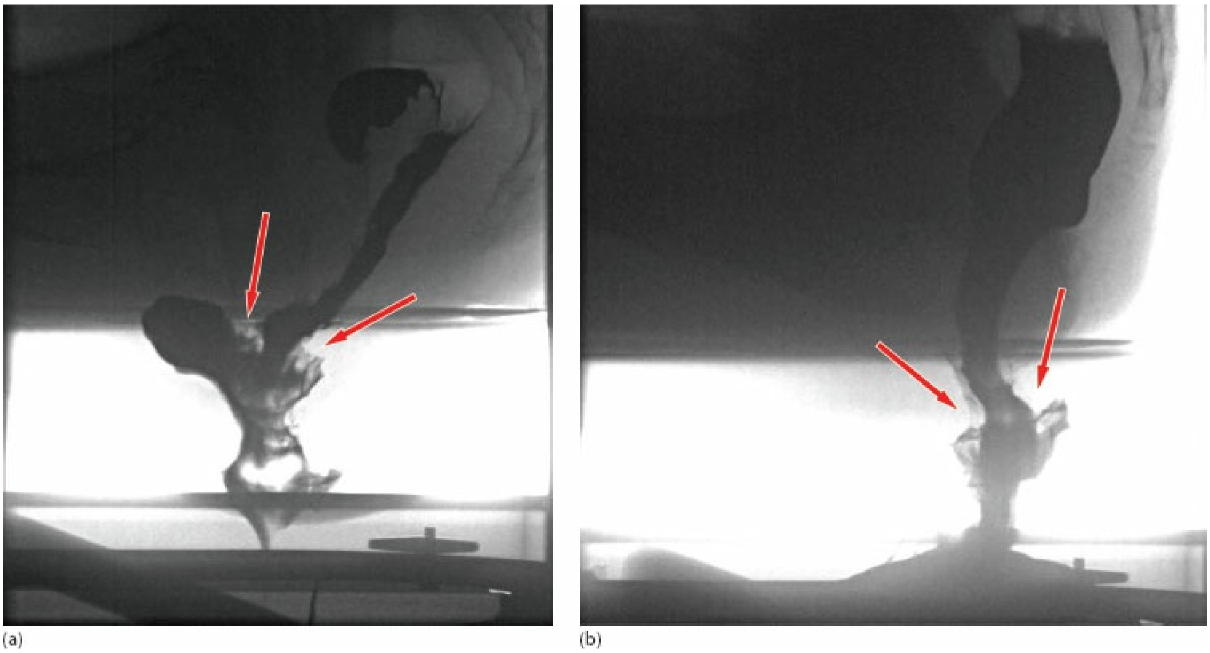

Figure 95.3 (a, b) Two cases with radiographic intussusception (arrow).

SURGICAL TREATMENT

Surgical Indication

The only potentially curative treatment for rectal prolapse is surgery [1]. It does not regress spontaneously or with conservative treatment in adults. Nevertheless, the indication is always dependent on the clinical symptoms and the success of conservative therapy. The general operability of the mostly older patients has to be considered. Intussusception (Grade 1 rectal prolapse) without clinical symptoms may be an incidental imaging finding and is not an indication for therapy [17]. Grade 3 rectal prolapse, on the other hand, is always an indication for surgery, since complications such as ischemia and bleeding may occur if left untreated.

Surgical Methods

There are many different surgical methods for treating rectal prolapse. The aim of all procedures is anatomical correction to improve bowel function and reduce prolapse-related symptoms. However, there are basic differences in the technical implementation of this principle: the surgical approach can be either abdominal or perineal. The abdominal procedure can be performed by either open or laparoscopic surgery [18]. According to the surgical technique, a distinction is also made between bowel fixation (rectopexy), bowel resection (sigmoidectomy), and a combination of the two (resection rectopexy) [1].

There is no gold standard or clear evidence-based recommendation as to which method is most suitable [1]. Relapse rates reported in the literature are mostly lower for abdominal than for perineal interventions. This procedure is therefore recommended particularly for younger and otherwise healthy patients [3,4,19,20]. On the other hand, perineal procedures are associated with lower morbidity and mortality. Thus, they are generally recommended for older and multimorbid patients [4,19]. Some authors have achieved favorable results with laparoscopic abdominal surgery in older people and therefore recommend this type of surgery for these patients [21–23]. Current surgical procedures will be presented in this chapter.

Abdominal Procedures: Rectal Resection and Rectopexy

Abdominal procedures can be performed by open or laparoscopic surgery. Various studies have demonstrated less stress and a faster recovery for patients undergoing laparoscopic interventions. However, these studies have a low evidence level [1].

Sudeck published one of the first studies on rectopexy in 1922. The mobilized rectum was fixed to the presacral fascia with sutures. This method was further developed and modified in various ways. The Wells procedure supplements fixation by placement of synthetic mesh in the presacral space [24]. The Ripstein procedure entails wrapping synthetic mesh around the anterior rectal wall and fixing it to the sacrum on both sides [25]. A newer approach is the Orr-Loygue laparoscopic ventral rectopexy [26]. It is a nerve-sparing procedure, since rectal mobilization and fixation with sutures or synthetic mesh is only performed anteriorly. Though very good results have been published for this method, randomized controlled trials are lacking [27,28].

A procedure that combines rectopexy with resection is the resection rectopexy as described by Frykmann und Goldberg. Very good results have also been published for this frequently applied surgical method [28]. It involves complete circular mobilization of the rectum up to the pelvic floor musculature and resection of the rectosigmoid colon. The rectum is then fixed to the promontory with sutures or by placing synthetic mesh anterior to the sacrum. A lower rate of postoperative constipation had been reported for resection rectopexy than for -pexy without resection [1,19]. However, resection also harbors the risk of anastomotic leak and is thus associated with an increased complication rate.

The material used for rectal fixation also varies widely and includes meshes made from synthetics such as polypropylene, although fixation can also be performed with simple sutures or laparoscopic staples. No clear evidence-based recommendations have been made as to what material is most suitable [1].

Perineal Procedures: Rehn–Delorme, Altemeier, STARR

The Rehn–Delorme procedure involves circular resection of the mucosa of the prolapsed rectum approximately 1 cm above the dentate line. The corresponding muscle layer is unfolded and fixed above the sphincter with single button sutures (Figure 95.4) [1,29]. This procedure can be used for prolapse up to 10 cm long.

The Altemeier procedure entails transanal full-thickness resection of the prolapsed segment. The distal rectal wall is resected approximately 1 cm above the dentate line. The rectum should be proximally mobilized beyond the prolapse. The anastomosis is hand-sutured or mechanically created with a circular stapler [1].

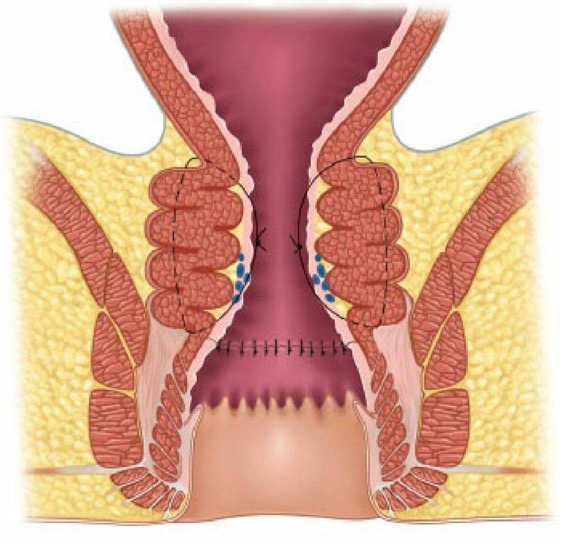

Figure 95.4 Principle of Rehn–Delorme procedure: after isolated circular resection of the mucosa with preservation of the lamina muscularis propria, the corresponding muscle layer is unfolded and fixed above the sphincter with single button sutures.

The STARR operation (stapled transanal rectal resection) is a relatively simple procedure that can be performed for small prolapses with a maximum length of 5 cm. Full-thickness rectal resection is performed here too. The anastomosis is approximately 2 cm above the dentate line. It is important to avoid entrapping any part of the vagina in the staple line, since this may result in necrosis and sepsis [30].

Treatment of Pediatric Rectal Prolapse

Rectal prolapse is usually treated conservatively in small children, since it tends to regress spontaneously by the time they reach the age of 3 [31,32]. Therapy consists of dietary measures to promote bowel regularity and enemas if necessary. Open or laparoscopic suture rectopexy may be performed in rare cases where spontaneous regression does not occur. The rectum is mobilized and fixed to the periosteum of the sacral promontory [33].

COMPLICATIONS AND PROGNOSIS

If left untreated, external rectal prolapse can lead to ulcerations and bleeding. Particularly in Grade 3, patients are at risk for incarceration, gangrene, and sepsis [1]. However, even surgery carries no guarantee of success. Data on complications and relapses vary widely. A complication rate of about 10% and a relapse rate of approximately 6%–15% are reported in the literature [20,21].

The initial complaints—impaired evacuation and incontinence—persist in some patients even after surgery. The literature reports a 30%–40% persistence rate with a higher rate for perineal than for abdominal interventions [20]. Previously masked incontinence may only become manifest after surgical correction of rectal prolapse for impaired evacuation. This means that patients should be informed in detail that their functional problems may not improve even by surgery [4,20].

OTHER CAUSES OF OBSTRUCTED DEFECATION

Obstructed defecation is defined as difficulty in evacuating the rectum despite the urge to defecate [34]. This leads to incomplete evacuation, frequent and prolonged defecation, digital support during defecation, and rectal pain. The most frequent cause is internal rectal prolapse (intussusception), as described previously [34]. Other causes are enterocele, or rectocele. Rectocele involves bulging of the rectal wall, usually anteriorly, due to expansion of the rectovaginal septum. This is often asymptomatic. Symptomatic cases primarily receive conservative treatment as described for conservative management of rectal prolapse. Surgical correction is only performed if relevant symptoms persist despite conservative therapy [35]. Other possible causes of obstructed defecation are neurological disorders such as multiple sclerosis or spinal cord injuries. Treatment is difficult. If possible, the underlying disease is treated, and the patient also receives conservative therapy as described earlier [36,37].

SYNOPSIS

Obstructed defecation is defined as difficulty in evacuating the rectum despite the urge to defecate. The most common cause is rectal prolapse. A distinction is made between internal rectal prolapse (intussusception), where impaired evacuation is the predominant symptom, and external rectal prolapse, which leads to fecal incontinence. The only definitive treatment is surgery. The approach can be either perineal or abdominal. While perineal procedures have a lower complication rate, the relapse rate is lower after abdominal procedures. However, both procedures often fail to improve the initial complaints. Thus, it is necessary to carefully select patients for surgery and provide patients with detailed informed consent. Other causes of obstructed defecation are enterocele, rectocele, neurological disorders, and spinal cord injuries.

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Section IX

Laparoscopy and Robotics

96 Section Introduction: The Role of Laparoscopic Surgery in Urogynecology

Anthony R.B. Smith

INTRODUCTION

The role of laparoscopic surgery in urogynecology is still unclear. This is partly due to a lack of robust evidence supporting the use of the laparoscopic approach to urogynecological procedures and partly due to a lack of training opportunities for both young and older surgeons. The lack of robust evidence of added value for the laparoscopic approach enables those who are resistant to change to maintain their position.

This area has become more complicated by the increased accessibility to robotic surgery, meaning that some surgeons have been able to avoid the difficulties of learning standard laparoscopic surgical techniques by moving straight to robotic surgery.

The chapters in this section provide a comprehensive review of the different laparoscopic urogynecological surgical procedures that have been reported. The term “minimally invasive surgery” has been used for laparoscopic surgery but is misleading because it suggests that the risk of complications is minimized. The potential risks and reported complications of this type of surgery are reviewed and the management discussed.

The role of robotic surgery is reviewed, and the health economics of both laparoscopic and robotic surgery are evaluated.

The vesicoscopic approach to surgery involving the bladder is also covered by a team who have developed the skills to approach such difficult surgery by an alternative route. It is important that such surgery is fully evaluated by teams who have the necessary experience and skills before adoption by others is considered.

97 Pelvic Anatomy through the Laparoscope

Fiona Reid

INTRODUCTION

Knowledge of anatomy is required to perform safe and effective surgery. However, anatomy is usually presented in a format that is not directly relevant to surgeons.

Performing surgery also alters the anatomy as it is traditionally described. There is sometimes a degree of variation in anatomy that is not emphasized in anatomical texts but that can be of significance to surgeons.

The aim of this chapter is to present anatomy in a format that is directly relevant to laparoscopic surgery.

LAPAROSCOPIC ENTRY

The most obvious difference between open and laparoscopic surgery is the method used to access the surgical field.

Insertion of Veress

If pneumoperitoneum is created using a Veress needle, it is commonly introduced at the umbilicus. In theory, it is more effective to introduce the Veress through the base of the umbilicus rather than the inferior margin because the amount of tissue traversed is less at the base, even in obese patients (Figure 97.1).

Adhesions

Brill et al. [1] demonstrated that previous surgery increases the incidence of adhesions of the omentum or the bowel to the anterior vaginal wall. Following a previous Pfannenstiel incision, 27% of patients had adhesions and 55% had adhesions following a previous midline incision below the umbilicus. Therefore, insertion of the Veress at the umbilicus when there is a previous midline incisions could be associated with increased injury to the bowel or omentum. This risk can be reduced by insertion of the Veress needle at Palmer’s point.

Palmer’s point is located in the left hypochondrium within 3 cm of the ribs in the lower margin in the midclavicular line (Figure 97.2). It is important to exclude splenomegaly by palpation. There is no rectus sheath at Palmer’s point so only a single click is felt with the insertion of the Veress through the peritoneum.

Alternative points of insertion of the Veress include midline insertion approximately halfway between the umbilicus and the symphysis pubis. This has the advantage of avoiding potential injury to the great vessels, but the abdominal wall may be very thick in obese patients.

Another alternative is to use the Hasson open laparoscopic entry technique. This may reduce vascular but not bowel injury. This is discussed in more detail in Chapter 102.

Insertion of Ports

The safe insertion of laparoscopic ports requires knowledge of the vasculature of the anterior abdominal wall and the great vessels.

The Great Vessels

Nezhat et al. [2] demonstrated that the cephalocaudal relationship between the umbilicus and the aortic bifurcation varies widely, regardless of body mass index. The position of the aortic bifurcation can range from 5 cm cephalad to 3 cm caudal to the umbilicus. The bifurcation was more likely to be caudal to the umbilicus if the patient is in the Trendelenburg position rather than horizontal. Therefore, most surgeons prefer to insert the primary umbilical port with the patient in the horizontal position.

The aorta bifurcates into the common iliac vessels. The inferior vena cava lies to the right of the aorta and is formed by the joining of the common iliac veins below the level of the aortic bifurcation.

It is this relationship that accounts for injuries to both the right common iliac artery and the left common iliac vein during insertion of a single trocar (Figure 97.3).

Usually, the bifurcation of the aorta is at the level of the fourth lumbar vertebrae; however, it can be between L3 and L5. The vena cava almost always bifurcates below the level of the aortic bifurcation at L5; however, this can also vary from L4 to S1.

These variations are significant to insertion of the primary trocar and dissection of the peritoneum sacral promontory during a sacrocolpopexy.

Insertion of Secondary Ports

The most important structures to identify prior to insertion of lateral secondary ports are the inferior epigastric vessels. The origin of the inferior epigastric artery is from the external iliac artery just before it passes under the inguinal ligament. The origin is approximately midway along the length of the inguinal ligament, and from there, its path is toward the umbilicus. Transillumination will not reliably identify the inferior epigastric vessel. It should be directly visualized; however, in the obese, this can be difficult. The inferior epigastric vessels are found approximately 1 cm lateral to the obliterated umbilical artery (Figure 97.4).

The inferior epigastric vessels lie medial to the deep inguinal ring, which can be identified by following the round ligament to its insertion into the inguinal canal.

The inferior epigastric is a branch of the external iliac artery (Figure 97.5).

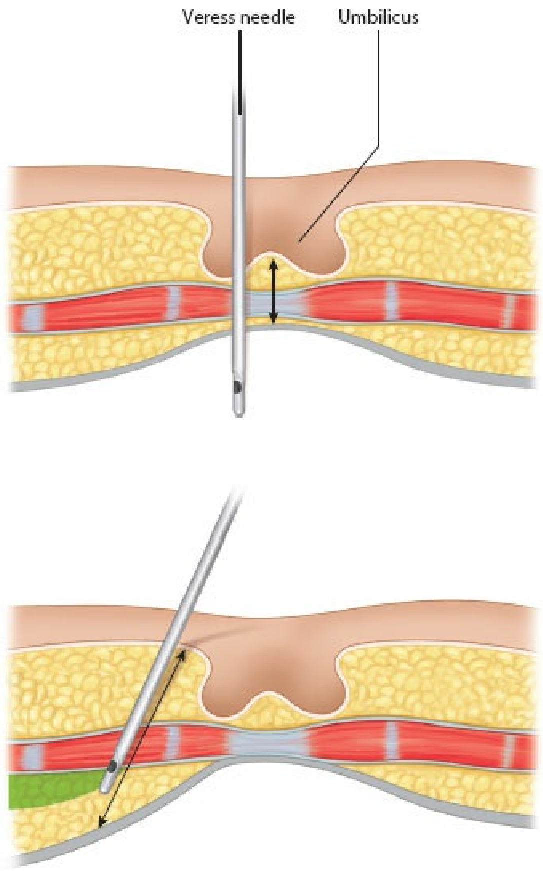

Figure 97.1 Insertion of the Veress needle through the umbilicus.

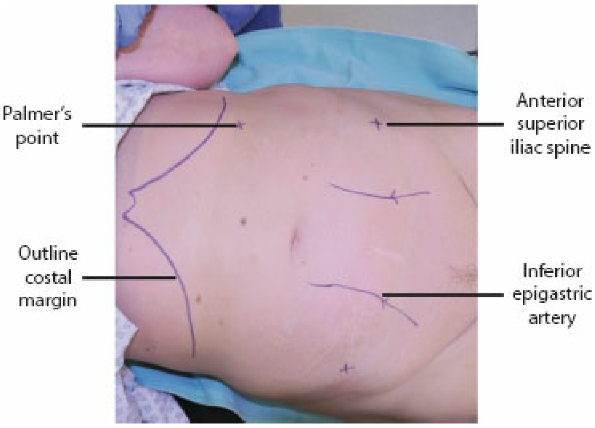

Figure 97.2 Surface anatomy.

Figure 97.2 demonstrates that the flow of blood in the inferior epigastric artery is caudal to cephalad. Hence, if it is injured during secondary port insertion, suturing should be performed caudal to the injury.

The first lumbar nerve divides into the iliohypogastric nerve and the ilioinguinal nerve that traverse the anterior abdominal wall as shown in Figure 97.6. Laparoscopic surgery, by avoiding large abdominal wall incisions, may prevent transection of the iliohypogastric and ilioinguinal nerves, which can lead to cutaneous anesthesia of the pubic region, the inside of the thighs and labia majora, as well as weakness of the muscles of the anterior abdominal wall predisposing to hernia formation.

However, secondary ports placed close to the anterior superior iliac spine may lead to nerve injury during placement or postoperative pain due to nerve entrapment during closure of the port site.

PRESACRAL SPACE

The presacral space begins at the aortic bifurcation and descends to the pelvic floor. It may be entered by pulling the rectosigmoid colon to the left side of the pelvis and incising the peritoneum vertically to the right of the attachment of the sigmoid peritoneum to the posterior pelvis. The dissection begins caudal to the bifurcation of the aorta and proceeds toward the hollow of the sacrum.

Obese patient may have increased fat over the sacral promontory that can make the promontory more difficult to visualize.

In such cases, it may be necessary to use an instrument to feel the edge of the promontory.

The anterior and upper margin of the first sacral vertebrae bulges forward and is known as the sacral promontory (Figure 97.7). Surgeons commonly describe attaching polypropylene mesh to the sacral promontory; however, the attachment is usually cranial to the promontory at the level of the fifth lumbar vertebrae, not the sacrum.

When opening the presacral space, at this level, there is a potential to injure the left common iliac vein that crosses the fifth lumbar vertebrae from left to right to join with the right common iliac to form the inferior vena cava (Figure 97.7).

During laparoscopy, the raised intra-abdominal pressure created by the CO_2 gas can cause compression of the left common iliac vein. This could lead to injury of the vessel during attachment of polypropylene mesh to the spine. To prevent this, surgeons should be aware of the “pillow sign.” When the spine is felt with an instrument, there is a slight softness and a rebound—similar to pressing a pillow (Figure 97.8).

The middle sacral vessels could also potentially be injured during the attachment of the mesh to the anterior longitudinal ligament of the spine as they emerge from under the common iliac vein and descend toward the sacral hollow. Wieslander et al. [3] studied the variation in vascular anatomy of the presacral space in 52 unembalmed females and concluded that although it was possible to identify an avascular area in each cadaver, it was not possible to define a general “safe” avascular zone.

The sympathetic nerve supply to the abdomen comprises two ganglionic trunks and a network of nerves covering the surface of the aorta. The lumbar splanchnic nerves from the left and right trunks unite below the bifurcation of the aorta to form the superior hypogastric plexus. These nerves carry the sympathetic nerve supply to the pelvis. Some nerve fibers pass over the anterior surface of the fifth lumbar vertebrae and may be damaged during the attachment of the mesh to the anterior longitudinal ligament of the spine.

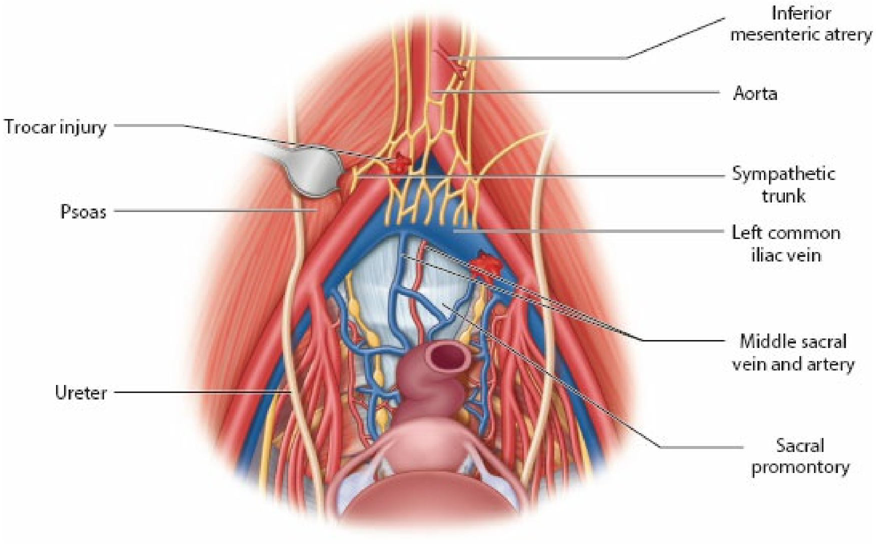

Figure 97.3 Trocar injury to the right common iliac artery and the left common iliac vein.

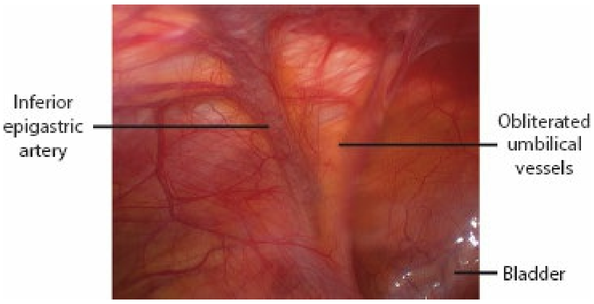

Figure 97.4 Left inferior epigastric vessels.

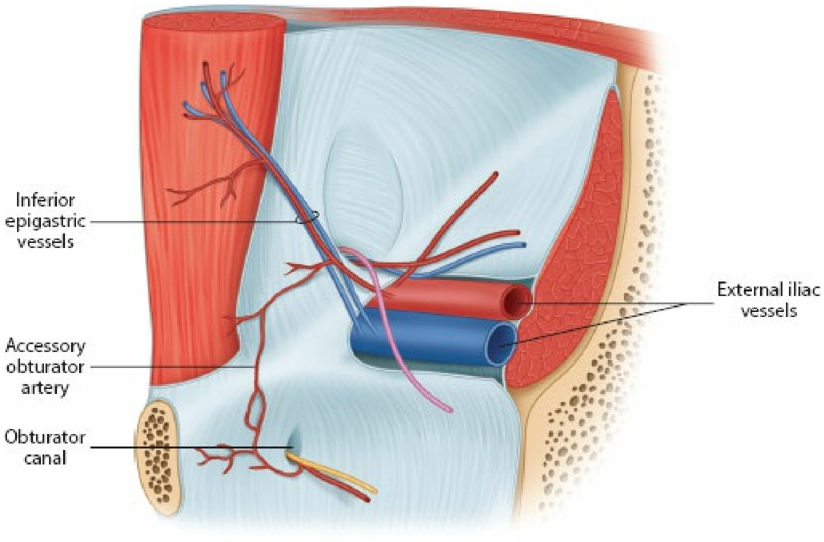

Figure 97.5 Origin of the inferior epigastric vessels

The presacral space is opened during a sacrocolpopexy to attach polypropylene mesh to the spine, and then the dissection is continued caudally to reach the vaginal vault. To the right and lateral to the dissection, the right ureter crosses over the bifurcation of the common iliac vessels and descends along the pelvic sidewall (Figure 97.9).

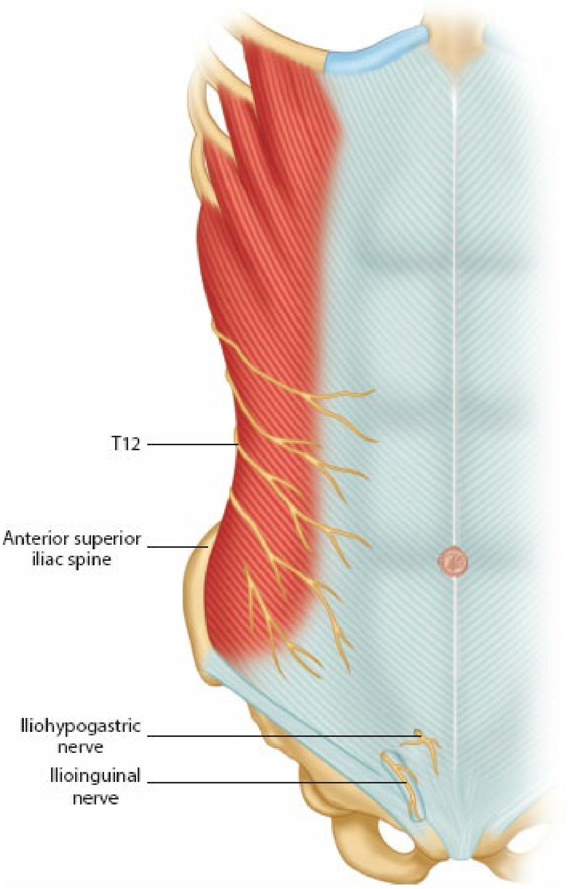

Figure 97.6 Nerves crossing the anterior abdominal wall.

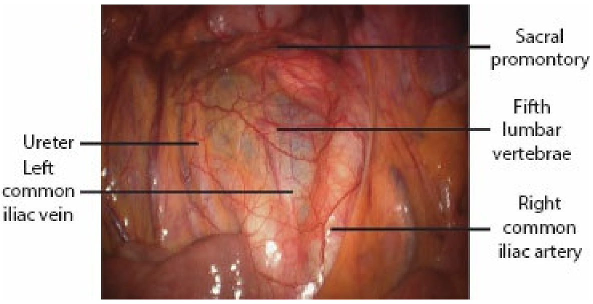

Figure 97.7 Course of the left common iliac vein.

The ureter then passes toward the origin of the uterosacral ligaments. It normally lies only 1–3 cm from the ligament, and this relationship can be altered by endometriosis or previous surgery.

One of the major advantages of the laparoscopic approach is the degree of magnification provided. This is demonstrated in Figure 97.10, showing the peritoneum being opened over the sacral hollow.

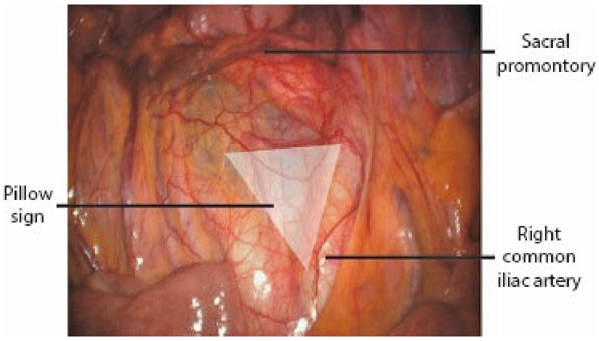

Figure 97.8 Area of pillow sign.

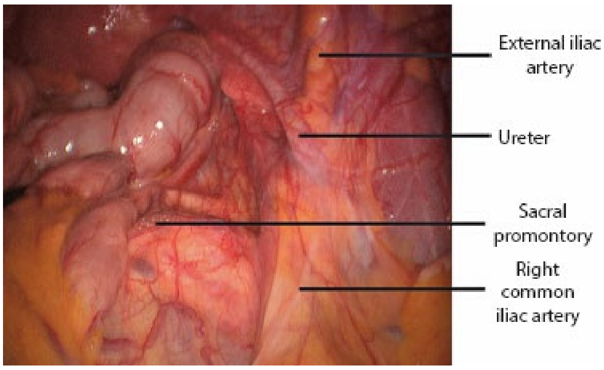

Figure 97.9 Sacral promontory.

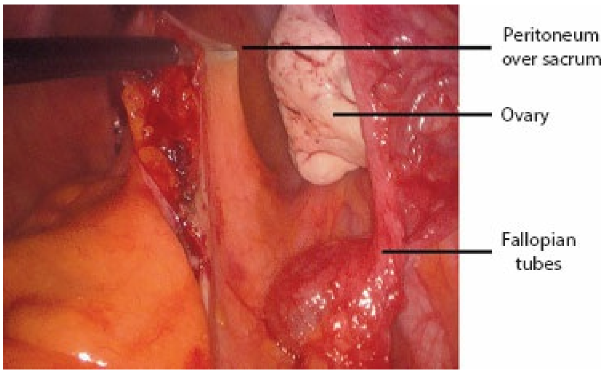

Figure 97.10 Magnification of structures.

RETROPUBIC SPACE: CAVE OF RETZIUS

The retropubic space (cave of Retzius) is a potential space that lies behind the symphysis pubis and in front of the bladder. It is opened to perform both Burch colposuspensions and paravaginal repairs. The sidewalls are composed of the pubic bone and obturator internus muscle. It normally only contains a venous plexus covered with lose adipose tissue (Figure 97.11).

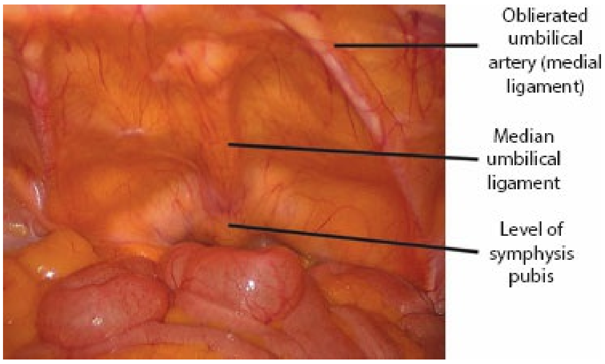
Oblierated umbilical artery (medial ligament)
Median umbilical ligament
Level of symphysis pubis

Figure 97.11 Umbilical ligaments.

The obliterated umbilical arteries are remnants of the fetal circulation. Occasionally, they will remain patent even in adults. They are branches of the internal iliac arteries. The obliterated umbilical arteries can be used as lateral markers for entry into the cave of Retzius; however, if they are not adequately diathermied prior to cutting, they may retract and bleed extensively (Figure 97.11).

There are inconsistencies in textbooks about alternative names for the obliterated umbilical arteries. Some refer to them as the medial umbilical ligaments [4] and others as the lateral umbilical ligaments [5]. The most logical nomenclature would seem to be that lateral umbilical ligaments are the condensation of peritoneum over the inferior epigastric vessels, while the medial umbilical ligaments are equivalent to the obliterated umbilical arteries.

The median umbilical ligament is another remnant of a fetal structure, the urachus. It runs from the dome of the bladder to the umbilicus. It can occasionally remain patent causing a urachal fistula to the umbilicus. All the umbilical ligaments can bleed when surgically divided.

The retropubic space can be opened 2–4 cm above the dome of the bladder. Sometimes, it is helpful to fill the bladder with 200–300 mL saline or methylene blue to enable its margins to be seen. In the midline, anterior to the bladder at the level of the pelvic floor are the urethra and dorsal vein of the clitoris that should be avoided. The space is bound laterally by the obturator canal and the arcus tendineus fasciae pelvis (white line) (Figure 97.12).

The obturator artery is a branch of the internal iliac that runs on the lateral wall of the pelvis to the obturator canal. In about 25% of the population, an aberrant obturator artery arises from the inferior epigastric or external iliac artery. In some cases, both a normal and an aberrant obturator artery are present; the aberrant artery is then called an accessory obturator artery (Figure 97.5).

The superior boundary is the symphysis pubis and the pectineal ligament (Cooper's ligament) (Figure 97.13).

The obturator nerve (Figure 97.12) arises from the lumbar plexus (L2–L4). It enters the true pelvis through the greater sciatic foramen and then runs in the extraperitoneal fat along the lateral wall to reach the obturator canal. It then divides into an anterior and posterior branch to supply the medial thigh muscles.

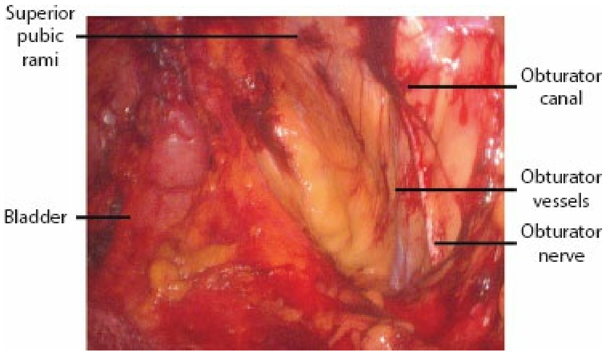

Figure 97.12 Right lateral wall of the retropubic space.

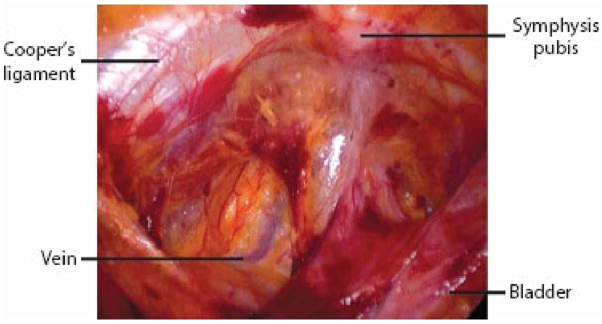

Figure 97.13 Superior boundaries of the retropubic space.

The arcus tendineus fasciae pelvis (white line) is a tendinous arch that originates at the back of the symphysis pubis and runs along the posterior aspect of obturator internus muscle to the ischial spine.

Cooper's ligament (the pectineal ligament) is a strong aponeurotic lateral continuation of the lacunar ligament along the iliopectineal line of the pubis.

ACKNOWLEDGMENT

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98 Training and Accreditation in Laparoscopic and Robotic Pelvic Floor Surgery

Karl Jallad, Marie Fidela R. Paraiso, and Alfred Cutner

DECREASED SURGICAL EXPERIENCE

There is a growing concern that the surgical training of doctors is not sufficient to meet the needs of new graduates [1]. With the advancement of science, newer medical therapies have replaced traditional surgical approaches. Residents and fellows in the United States are now bound to work a maximum of 80 hours per week, reducing the time spent in operating rooms and getting sufficient surgical training. In the United Kingdom, the situation is even more extreme with the European 48 hour week working time directive. Newer technologies are constantly emerging making it difficult for surgeons to become proficient and for hospitals to control credentialing. These are important if patients are to be offered new procedures in a safe operating environment.

All trainees are now expected to be skilled in laparoscopic surgery. Robotic surgery is a requirement in some urological procedures in the United Kingdom and for both gynecology and urology in the United States. Alongside developing new skills, the trainee is also required to attain skills in traditional surgery. Thus, despite reduced hours, the trainees are required to learn a greater variety of skills than in the past. In addition, the length of training has remained unchanged. This has led to the emergence of young graduating surgeons who are not confident enough or ready to operate independently.

In addition, due to medicolegal implications, the concern for OR time, and patient awareness of the medical system, it is now less acceptable to practice on patients [2].

The trend is now shifting toward increased training outside of the operating room by using simulators. The hope is to provide more uniform training and use objective data to grade and certify surgeons. Simulators are accessible to all levels of training, including medical students, residents, fellows, and attending surgeons [3]. They can be used for initial training, and also for evaluation, testing, or recertification purposes.

LAPAROSCOPIC SIMULATION

There are three types of simulators available on the market: box trainers, virtual reality simulators, and augmented reality trainers.

The box trainers are usually plastic boxes built to simulate an abdominal cavity into which real instruments can be inserted [2]. They are relatively inexpensive, provide realistic haptic feedback, and can be coupled with animal or cadaveric material to provide realistic anatomy. However, they require mentors for accurate scoring and do not provide objective performance metrics. There are various models available on the market: the Fundamentals of Laparoscopic Surgery (FLS); Society of American Gastrointestinal and Endoscopic Surgeons, Los Angeles, CA; and eoSim (eoSurgical, Edinburgh, Scotland, United Kingdom). Multiple studies have demonstrated the educational value of the FLS simulator training in surgical residency curricula [4]. At present certification in the FLS is required by the American Board of Surgery for graduating residents though the American Board of Obstetrics and Gynecology has not implemented this requirement. However, a number of institutions require the FLS certification prior to privileging staff in laparoscopic surgery.

In the United Kingdom, all trainees attend a basic surgical skills course, which includes some basic simulator training in laparoscopic surgery, but there is very limited requirement for sign-off. Surgically, the most advanced absolute requirement for all gynecologists is the ability to manage an ectopic pregnancy laparoscopically.

The virtual reality simulators provide a computer-generated environment mimicking real-life scenarios. They facilitate objective scoring without the presence of a mentor and allow for a large number of varied scenarios. However, they are very expensive, require frequent maintenance, and do not exactly replicate haptic feedback of real surgery [2]. Available models on the market are the LapSim® (Surgical Science, Gothenburg, Sweden), LAP Mentor™ (Simbionix™, Cleveland, OH) [5], and MIST VR (Mentice Medical Simulation, Gothenburg, Sweden).

The earliest virtual reality simulators provided no feeling of resistance. Given that surgery relies heavily on the sense of touch and haptics, the virtual reality simulators could not reproduce the more realistic feel provided by the box trainer. With a virtual simulator, one cannot test different suture materials or check the integrity of a knot. However, with improved technology, newer models now mimic real-life scenarios. Despite being more expensive initially, virtual reality simulators do not require a constant change of equipment and supply of suture material. More importantly, virtual simulators eliminate the need to have a supervisor to assess, time, and grade the performance. This is of particular importance in residency programs and surgical training centers where transparency and objective scoring are mandatory.

Newer models on the market now combine both technologies. The augmented reality trainers provide a realistic haptic feedback and objective metric recording; however, they are expensive and are prone to vision tracking system malfunction. Available products on the market are ProMIS™ (Haptica, Dublin, Ireland, and the United Kingdom) and TrEndo (Delft University of Technology, Delft, the Netherlands). With improvement in technology and the advent of new companies, the field of virtual simulators and box trainers is growing exponentially and will undoubtedly play an even more important role in training the surgeons of the future.

A recent Cochrane review to assess the benefits and harm of supplementary virtual reality training of surgeons, with limited laparoscopic experience, revealed that virtual reality training appears to decrease the operating time and improve the operative performance of surgeons with limited laparoscopic experience when compared with no training or with box trainer exposure [6]. However, the authors further discussed the need to perform well-designed trials to assess the impact of virtual reality training on clinical outcomes and the need to control for inherent risk of bias in those studies.

SIMULATOR FOR THE DA VINCI® SURGICAL SYSTEM

The Intuitive Surgical® Skills Simulator that is offered for the *da Vinci Si* Surgical System is based on Mimic's proprietary simulation technology, MSim™. With the growing concern for safety and importance of rigorously preparing the next generation of surgeons, initial training outside of the operating room has become the norm. The dv-Trainer provides an extensive array of various scenarios with a gradual increase in level of complexity. Surgeons performing the tasks are timed and objectively graded with scores compared to experienced surgeons. Simulators provide the residents, fellows, and surgeons flexibility of access to training and more importantly offer a safe environment away from the patients. Multiple studies were performed and demonstrated face, content, and construct validity that is clinically relevant [7,8]. The dv-Trainer is a great introduction to robotic surgery and an invaluable tool to be used for training.

LAPAROSCOPIC SUTURING

Once a surgeon decides to use a simulator, he or she should pick the one that best fits his or her needs. As described earlier, this will depend on the area of deficiency, cost, and location of training. Invariably, one should set goals and objectives and gradually progress from minor skills to complex tasks. It is imperative to train regularly and keep track of progress. One can use a simple notebook and keep track of the time, repetitions, and completed tasks. The more sophisticated virtual simulators have complex computing systems that allow the surgeons and mentors to assess individual or group progress and store valuable information.

In order to perform a complex task like suturing, the apprentice first starts by appreciating depth perception, followed by exploring different instruments and then grasping and touching specific objects. The next step focuses on grasping the needle and learning how to correct its orientation until it is perpendicular to the tip of the instrument. This is a crucial step that the novice surgeon should master perfectly well before attempting more complex tasks. The next step involves grasping the tissue or sample with the nondominant hand and using the dominant hand to drive the needle in. It is imperative to accurately pronate the wrist and enter the tissue at a 90° angle and then gradually advance the needle and supinate the wrist. Once the needle emerges from the tissue, the surgeon should grasp the needle tip with the nondominant hand and gradually release tension off the dominant hand and complete the task. The needle is then transferred back to the dominant hand in the proper orientation ready for another tissue pass. The most difficult task that trainees have to acquire is the ability to operate with both hands working together. This skill is required for all areas of advanced laparoscopic surgery.

ADVANCED LAPAROSCOPIC SKILLS IN MINIMALLY ACCESS SURGERY AND UROGYNECOLOGY

The three main procedures that require advanced laparoscopic skills in urogynecology are sacrocolpopexy, sacrohysteropexy, and colposuspension. The first is a requirement of most modern practicing urogynecologists, whereas the places of the last two have yet to find their definitive place.

Performing these advanced procedures requires advanced surgical skills. These include a knowledge of hemostatic devices, retroperitoneal dissection, and suturing. One has to incorporate fine dissection technique, master extensive intracorporeal and extracorporeal suturing, and have a thorough understanding of pelvic anatomy. Despite the required advanced surgical skills, there is no specific mandatory laparoscopic training for fellows specializing in urogynecology. In the United Kingdom, the subspecialty-training program enables attainment of skills for sacrocolpopexy either open or laparoscopic. However, a more detailed training in laparoscopic urogynecology has yet to be established. This is in marked contrast to other areas or advanced minimal access surgery. It is interesting that there is no political drive to develop training programs despite the recent U.S. Food and Drug Administration [9] and UK Medicines and Healthcare Products Regulatory Agency [10] guidance relating to the establishment of vaginal mesh surgery outside structured training.

Recently, Tunitsky-Bitton et al. [11] developed a model to simulate laparoscopic sacrocolpopexy (Figure 98.1). They measured construct validity by comparing observed masked performances on the model between experienced female pelvic medicine and reconstructive surgeons and upper-level trainees. Experts performed significantly better than trainees in the total score and in every domain of the Global Operative Assessment of Laparoscopic Skills scale. More importantly, the majority of the subjects “agreed” or “strongly agreed” that the model was authentic to the live procedure and a useful training tool [11]. The use of such model could be used in fellowship programs to gradually initiate the trainees and hopefully improve safety, efficiency, and OR time. Given that this is a new and emerging approach to training, further randomized controlled studies will be needed to better assess the potential clinical impact of such models.

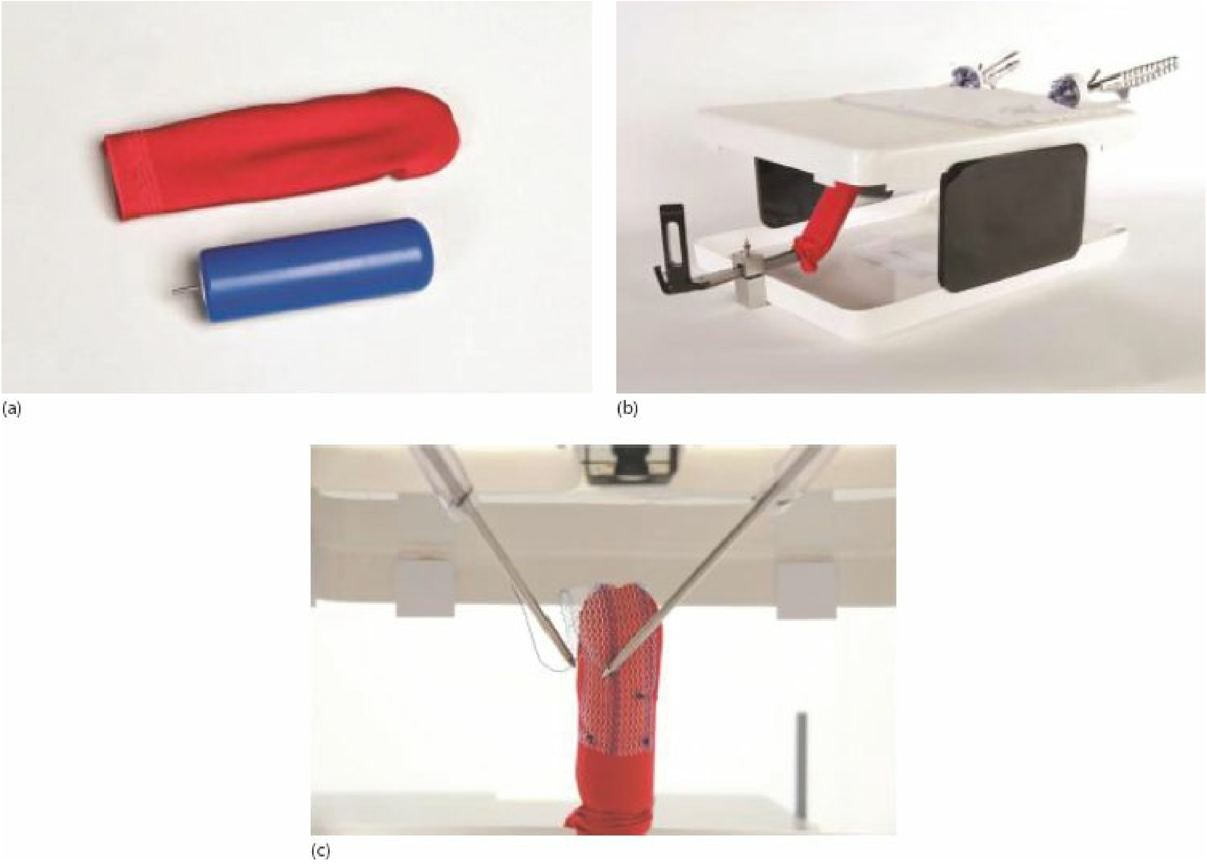
(a)
(b)
(c)

Figure 98.1 (a–c) Simulated laparoscopic sacrocolpopexy.

Simulators can also be used when one has to master the steps to perform a rare procedure. Ureteral anastomosis is a complicated procedure, and even in the busiest centers, fellows will not have enough exposure to become proficient at the end of their training. Tunitsky et al. [12] proposed an authentic and useful simulation model and were able to demonstrate evidence of construct validity. Fellows can now train outside of the OR and perfect their skills in preparation to real-life scenario.

Despite the fact that it is widely accepted that the initial learning and practice of laparoscopic surgical technique should occur in a simulated environment, there is still no available standardized curriculum established by the obstetrics and gynecology, minimally invasive surgery, or urogynecology societies. At present, laparoscopic training still varies widely among our institutions. The American Board of Surgery requires graduates to be FLS certified that greatly helps in standardizing laparoscopic surgical training. At the Cleveland Clinic Foundation in Ohio, fellows in Female Pelvic Medicine and Reconstructive Surgery are expected to train in a dry lab prior to performing a specific procedure on patients. In addition, prior to participating in laparoscopic procedures, all fellows must successfully complete the FLS training program. In order to pass the the FLS training program, the trainee must demonstrate proficiency in performing five laparoscopic skills: peg transfer, precision cutting, ligating loop, and suturing with extracorporeal and intracorporeal knot-tying. To pass the FLS training program, the trainee must demonstrate proficiency in performing five laparoscopic skills: peg transfer, precision cutting, ligating loop, and suturing with extracorporeal knot and intracorporeal knot.

In the United Kingdom, currently, there is no accredited training program, sign-off, or reaccreditation in laparoscopic urogynecology. Anyone who states that they have the ability can perform these procedures. A recent Coroner's verdict in Australia, following an inquest into two deaths following laparoscopic sacrocolpopexy, was critical of the lack of formal accreditation in laparoscopic surgery in some countries. The report from the coroner stated:

> It surprised the Court that elective surgery of the complexity involved in (these cases) carrying as it does a risk of harmful injury however small, can be carried out by medical practitioners whose qualifications and expertise to perform this surgery are in large part based upon self teaching, word of mouth and

reputation but not upon objective assessment of the practitioner's skill as might be evidenced by formal training, examination and certification by a professional institution.

CREDENTIALING

The process of credentialing varies depending on the institution. It is in place to verify that the surgeon can safely complete a procedure as intended and recognize potential complications. It is based on initial training, board certification, and ongoing experience. With the emergence of novel surgical modalities, credentialing now plays an even more crucial role. During their training, residents and fellows in the United States are required to maintain a detailed log of the number of cases they perform. In order for the residents to graduate in obstetrics and gynecology, they need to perform at least 60 laparoscopic cases of which 20 are hysterectomies.

The surgeon seeking privileges to perform laparoscopic surgeries must submit a case list including his or her role (resident, fellow, primary surgeon, etc.) with a brief description of procedures and complications. The surgeon must include a letter from the program director or chair stating whether the candidate can independently and competently perform a specific procedure. The requirement to maintain privileges is usually determined by the chief of a department and its governing body. Depending on the performance, the surgeon might be recertified, monitored, or even requested to undergo additional training and proctoring. The American Association of Gynecologic Laparoscopists (AAGL) recently published guidelines for institutions granting privileges for gynecologic surgery using laparoscopic techniques. The ultimate goal is to provide the highest quality of care and standardize the training and accreditation process.

Robotic surgery has emerged in recent years. While some residency and fellowship programs provide adequate robotic training, most physicians have had minimal exposure. In this situation, initial certification depends on the completion of online training module, completion of at least 2 hours of bedside training for docking and 1 hour of hands-on training with inanimate training aids, demonstration of competency on a robotic simulator, and participation in a live pig lab.

To maintain privileges, a surgeon must perform a minimum of 20 robotic procedures each calendar year. If the surgeon fails to meet the minimum number, he or she would require a proctor on the next case or must achieve a score of at least 85% on robotic simulator.

The situation described relates to the United States and is not currently applicable in the United Kingdom despite a recognized advanced special skills module in urogynecology and a well-established subspecialty-training program.

Minimally invasive surgery is a growing field and is constantly evolving. The use of simulators provides an alternative and safer modality for training. They are now being used for evaluation, testing, and recertification purposes. The ultimate goal is to improve the patient safety, do no harm, and provide the best possible care. A robust system of training, certification, and monitoring should reassure patients that their surgery will be performed by surgeons who have the appropriate skills to complete their surgery to the highest standard.

There is no set learning curve and indeed skill with other laparoscopic operations, and general dexterity skills will have an impact on the numbers required to be competent at these procedures. The trainee who has developed advanced skills such as suturing in the training laboratory will translate these in the operating theater environment. Each trainee will thus have a different learning curve, and perhaps initial credentialing is better being competency based rather than numbers based.

It would appear in line with other, often less complex, operation, that the surgeon carrying out laparoscopic urogynecology should perform a minimum of 20 operations involving retroperitoneal dissection and suturing per year.

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99 Laparoscopic Colposuspension and Paravaginal Repair

Arvind Vashisht and Alfred Cutner

INTRODUCTION

Damage to the urethral sphincter and/or to mechanisms pertaining to its function is believed to be determinants in the pathogenesis of urinary stress incontinence. Undoubtedly, genetic and lifestyle factors that determine connective tissue strength and function are relevant in the etiology of stress incontinence. Pregnancy, childbirth, and in particular vaginal delivery are causative risk factors [1,2], and the condition may often present for the first time during pregnancy or postpartum.

Treatment options will need to take into account the patients' age, comorbidities, and medical and surgical history. Conservative treatment may suffice. The role of a multidisciplinary approach is important. If symptoms are refractory and the woman wishes surgical treatment, there is a range of possible surgical options.

Surgical techniques evolve over time. Maintaining treatment efficacy and reducing morbidity remains key in the evaluation and uptake of such procedures. In many units, the previous gold standard, open colposuspension procedure, has been superseded by midurethral tape surgery, with a drive toward quicker patient recovery. The numbers of colposuspensions performed and surgeons undertaking such procedures have diminished over the past 20 years [3,4]. Laparoscopic colposuspension, the modern-day colposuspension, has persistently had a place in urinary stress incontinence surgery, with those trained in the procedure advocating its use for women who are young, those with significant urethral mobility and anterior compartment prolapse, those requiring other concomitant abdominal surgery to the pelvis, or those with previous failed midurethral tape surgery.

Currently, there is renewed interest in laparoscopic colposuspension. This is due to concerns over midurethral tape surgery and an increasing number of procedures to treat tape-related complications [3]. This resurgence is driven by its efficacy, safety, and patient choice. This chapter will provide a revision of the surgical technique and indications. It will provide an update on the efficacy and morbidity for laparoscopic colposuspension and compare it to other surgical methods.

COLPOSUSPENSION

Although the Burch colposuspension was first described in 1961 [5], the Tanagho modification is now considered the standard method by which a colposuspension should be performed [6]. However, colposuspension is taken to be synonymous with Burch colposuspension, which is neither in the case semantically nor in the reporting of the literature. Colposuspension merely refers to elevating the vagina, or "colpos."

The first report in the literature of a laparoscopic colposuspension was by Vancaille and Schuessler in 1991 [7]. This was not in fact a Burch but rather a modification of the Marshall–Marchetti–Kranz procedure [8]. The authors suspended the vagina with two nonabsorbable 2-0 sutures on either side of the bladder neck to the pubic symphysis as they were unable to clearly visualize Cooper's ligaments. The first actual report of a laparoscopic-modified Burch colposuspension was in 1993 by Liu and Paek [9]. They used two absorbable sutures to elevate the vaginal tissue to Cooper's ligaments.

Variations in Procedure

The various methods of colposuspension described in the literature are shown in Table 99.1. To carry out a modified laparoscopic Burch colposuspension, there are two different methods of entry into the cave of Retzius, either trans- or extraperitoneal. We will later describe in detail the method of transperitoneal laparoscopic Burch colposuspension as carried out in our unit.

The extraperitoneal approach involves accessing the preperitoneal space and dissecting into the cave of Retzius. Either a Veress needle can be placed in a suprapubic site or a cutdown technique with dissecting balloons can be used. In addition, a gasless laparoscopic colposuspension procedure using extraperitoneal balloon dissection followed by a mechanical abdominal wall retractor has been described [12]. Once a pneumo-Retzius has been obtained, the additional ports are inserted. Typically, two operative 11 mm trocars are used just above the pubic hairline and close to either side of the midline, but the procedure can be performed with one suprapubic operating 5 mm port and a 5 mm port for the laparoscope. The colposuspension is then carried out in the same manner.

The advantage of the extraperitoneal approach is reduced risk of injury to intra-abdominal organs and quicker dissection time. In particular, the incidence of bladder injury is reduced. However, it is not possible to inspect the abdominal contents or to carry out additional intraperitoneal procedures at the same time. In addition, the reduced access of this approach and the close port placement makes suturing more difficult. Thus, some authors adopting this approach changed to using mesh and tacks rather than sutures to carry out this type of colposuspension [13].

Apart from the approach to the cave of Retzius, the other variations in the literature relate to the type, number and size of ports, methods used for dissection, type and number of sutures, and whether mesh is used. In addition, there are variations in the type of knots used to elevate the vagina, but these are rarely expanded upon as it is assumed that they are all similar. However, it has been demonstrated in in vitro studies that different methods of knot tying result in different strengths [14,15]. There are also reports of bone anchors, staples, and clips being used to attach the suture to Cooper’s ligaments or the pubic ramus [16–18].

Table 99.1 Different Methods Used to Suspend the Vagina

Author	Year	Method
Vancaille and Schuessler [7]	1991	Nonabsorbable sutures to pubic symphysis
Ou et al. [19]	1993	Hernia mesh and surgical staples
Liu and Paek [9]	1993	Absorbable sutures to Cooper’s ligaments
Carter [22]	1996	Laparoscopic Stamey
Birken and Leggett [20]	1997	Mesh and staples
Breda et al. [21]	1996	Handheld needle
Das [18]	1998	Bone anchors
Kiilholma et al. [10]	1995	Glue
Shoemaker and Wilkinson [11]	1998	Telescopy
el Toukhy and Davies [51]	2001	Tacks
Zullo et al. [48]	2001	Staples
Ross et al. [23]	2002	Bipolar electrochemical energy
Ankardal et al. [50]	2004	Transperitoneal mesh and staples

As well as the standard Burch colposuspension, other methods have also been employed. A technique using mesh to suspend the vagina to Cooper’s ligaments has been described by several authors [19,20]. One or two pieces of Prolene mesh are inserted along the paravaginal fascia longitudinally, 2 cm lateral to the bladder neck on either side, and are fixed to Cooper’s ligaments with staples or tacks. A combined laparoscopic and vaginal approach using a handheld needle has been described [21]. This involves using one suprapubic port to create a pneumocavity in the space of Retzius. Two small suprapubic incisions are made on either side and a suture mounted on a specially designed handheld needle is passed through Cooper’s ligaments and through the lateral fornix of the vagina. The needle is then withdrawn after taking a second bite of the vagina and the vagina is fixed to Cooper’s ligaments with an extracorporeal knot. Carter described another variation, which was described as a laparoscopic Stamey procedure in 1996 [22]. Ross et al. [23] describe a technique using bipolar electrochemical energy to induce shrinkage of the paravaginal tissue causing bladder neck elevation in 94 women. They found that this resulted in 30% shrinkage of the tissue. None of these techniques have been studied in robust, randomized trials and should therefore be regarded as experimental.

Transperitoneal Burch Colposuspension Technique

We will detail the technique that we employ in our unit. Most of the steps are a result of copies and adaptations from the open technique and are subsequently refined over years of experience, many of which remain as yet without a solid evidence base, and some are likely to undergo ongoing evolution.

Preoperative counseling includes a full explanation of the risks of the procedure and the advantages and disadvantages compared to the open procedure. The risks include those of laparoscopic entry and laparoscopic surgery and those of the procedure itself. All women are consented for the possibility of requiring a concomitant elevation of apical support at the time of colposuspension. Preoperative bowel preparation is sometimes advised as it improves visualization of the operative field and reduces contamination in the event of a bowel injury [24]. In certain patient groups, and in particular the elderly or those with relevant medical comorbidities, one should be mindful of using laxative agents due to the risks of exacerbating pre- and perioperative dehydration, with knock on adverse renal function. Most commonly now, we suggest a preoperative bowel enema on the morning of surgery, which is generally equally satisfactory in achieving an empty and compliant rectum for easy mobilization during surgery.

A single intravenous dose of a prophylactic broad-spectrum antibiotic is given (we always use gentamicin providing no contraindications). The patient is prepared for surgery, cleaned, and draped. She is initially placed supine without any table tilt. The legs are placed in a lithotomy position at an angle of 30° at the hips. A size 14 Foley catheter with 10 mL of water in the catheter balloon is placed in the bladder and left on free drainage. We believe this size of catheter to be a sensible compromise allowing relative patient comfort postoperatively and of being of sufficient gauge to ensure free drainage of urine following the inevitable intraoperative manipulation of the bladder and urethra.

Our entry technique follows recommendations as set out in the Royal College of Obstetricians and Gynaecologists Green-top Guideline published in 2008 [25]. We normally use a Veress needle to obtain a pneumoperitoneum. An incision is made in the umbilical region, as it is at this point that the layers of the rectus sheath and peritoneum are fused. The patient is placed supine with no tilt and the needle is first directed toward the sacral promontory, and when the characteristic clicks of passing through the layers are felt, the needle is then directed toward the pelvis. A water test is used to confirm entry into the correct space and the abdomen is insufflated. Insufflation ceases when the preset pressure of 20 mmHg is achieved. The main 11 mm trocar is then placed through the umbilical region. The intra-abdominal pressure is then reduced to 15 mmHg. Where the patient is at high risk of bowel adhesions near the umbilicus from previous abdominal surgery, other sites for first port entry are considered. We use Palmer's point in high-risk cases (the left subcostal area in the midclavicular line) [26,27] (Figure 99.1). Palpation to identify the spleen is carried out prior to insertion of the Veress needle, and a nasogastric tube is inserted to reduce the chance of perforating an inflated stomach [28] (Figure 99.2). Where the patient is very thin, a Hasson entry technique is used to reduce the risk of vascular injury [29]. Some surgeons employ optical ports for first port entry.

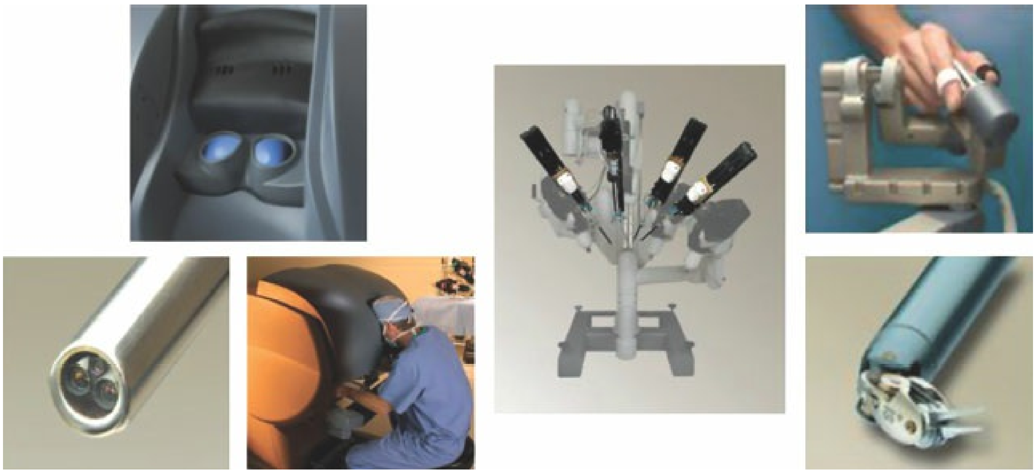


Figure 99.1 Veress needle entry at Palmer's point.

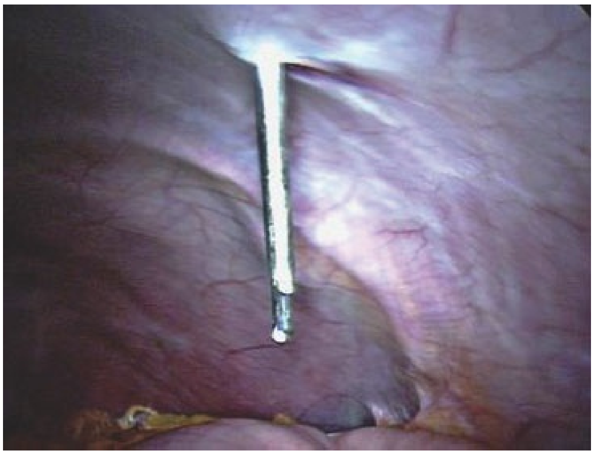


Figure 99.2 Dilated stomach visible in the left subcostal region. To prevent injury to the stomach when inserting the Veress needle subcostally, a nasogastric tube is inserted to deflate the stomach.

Once the laparoscope is inserted, the abdominal contents are examined and the patient placed in a head-down tilt. The placement of additional ports is important. All additional ports must be placed under direct vision to avoid injury to viscera or vessels. Ports should be placed either very lateral or medial to avoid the inferior epigastric vessels [30,31]. They should be placed so that adequate dexterity can be achieved during the operation. For laparoscopic colposuspension, we place two lateral 5 mm ports and one suprapubic 11 mm port. We use 11 mm ports with a variable top for ease of passing sutures into the abdominal cavity. This latter port is often inserted after the dissection into the cave of Retzius only to facilitate suturing: the surgeon can normally comfortably and ergonomically access the surgical space using instruments inserted into the two lateral ports. The lateral ports are placed at least 8 cm from the midline at the level of the umbilicus and inserted perpendicular to the skin to lessen the risk of epigastric vessel injury. We believe this to be the most ergonomically easy for operating in the pelvis. We do not use large ports laterally as these need to be formally closed to reduce the incidence of incisional hernias [32,33]. This closure can increase postoperative discomfort. Due to the size of the suprapubic incision routinely used, we do ensure that the rectus sheath is sutured closed beneath this port site. However, in our experience, this does not cause as much discomfort as deep lateral port closure.

Prior to the colposuspension, the abdominal cavity is assessed. If any additional surgery is required (such as hysterectomy or removal of adnexa), this is carried out prior to the colposuspension. However, the final step of some additional procedures, such as sacral promontory fixation in vault elevation surgery, is carried out after the colposuspension. Elevation prior to the colposuspension makes the latter more difficult to perform chiefly because of the ensuing reduced vaginal mobility on the (now well-supported) vaginal apex and proximal vaginal walls.

The bladder is initially filled with 300 mL of saline (this can be mixed with methylene blue) to aid identification of the superior edge of the bladder dome. The obliterated median umbilical ligaments are used as markers for entry to the cave of Retzius. They are incised 2–4 cm cephalad to the bladder dome (Figures 99.3 and 99.4). The cave of Retzius is dissected toward Cooper's ligaments. The bladder is then drained to enable better access to the paravaginal tissues (Figure 99.5). Dissection is performed with monopolar scissors on 60 W coagulation, or using an ultrasonic scalpel. Both types of energy source enable bleed-free tissue dissection. The dissection should avoid the urethra and the dorsal vein to the clitoris in the midline and the obturator neurovascular bundle laterally. This dissection will expose the pubic symphysis and bladder neck in the midline and Cooper's ligaments and the arcus tendineus fasciae pelvis laterally.

The bladder is retracted medially to allow the colposuspension to be performed. A pledget on a grasper with a marker thread (or a disposable pledget on a stick) is used for blunt dissection (Figure 99.6). Nonabsorbable No. 0 Ethibond® sutures are used for the colposuspension, as it is a permanent suture that has been traditionally used for the procedure. Other surgeons may use a slowly absorbable suture such as polyglycolic acid, with the reasoning that the medium- and long-term success of the procedure depends not on the strength of the sutures per se but the fibrosis they cause. In particular with a permanent suture material, one needs to be mindful of avoiding sutures being placed in the vagina or bladder. One suture is placed on either side at the level of the bladder neck. A second suture is then placed on each side in a slightly more cephalad position (Figures 99.7 and 99.8). A double bite of the vagina is taken with each suture to ensure a good amount of paravaginal fascial tissue is taken and the suture is then placed through the ipsilateral Cooper's ligament. Each suture is tied after insertion on limited tension using an extracorporeal surgical knot. The suture is tied to leave an approximate distance of around 1.5 cm between the ligament and paravaginal fascia. This is thought to give sufficient elevation of the bladder neck and yet still allow satisfactory postoperative voiding. If required, a surgical drain is left in the cave of Retzius. As with most surgery, the decision for leaving a drain will depend on surgeon's preference: we would use a drain if there had been above average blood loss noted during dissection. A cystoscopy is performed with a 120° scope to identify any sutures inadvertently placed in the bladder and to confirm that the ureters are patent by visualizing urine jets. In the unlikely event that sutures are seen in the bladder, these require immediate removal and replacement. We would suggest that visualization of ureteric jets is a good clinical practice and provides surgical reassurance of ureteric function, particularly if a concomitant procedure has also been performed. We have not come across ureteric obstruction during colposuspension, and indeed if ureters are stented during the procedure (for a separate indication such as a concomitant hysterectomy with the need for stent to aid visualization higher in the pelvis), it is apparent that the ureteric path would usually be well away from correctly placed sutures.

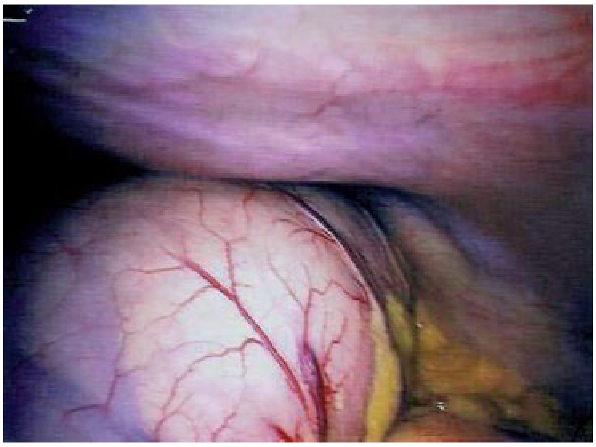


Figure 99.3 The median umbilical ligament is grasped cephalad to the bladder dome after filling the bladder with 300 mL of saline.

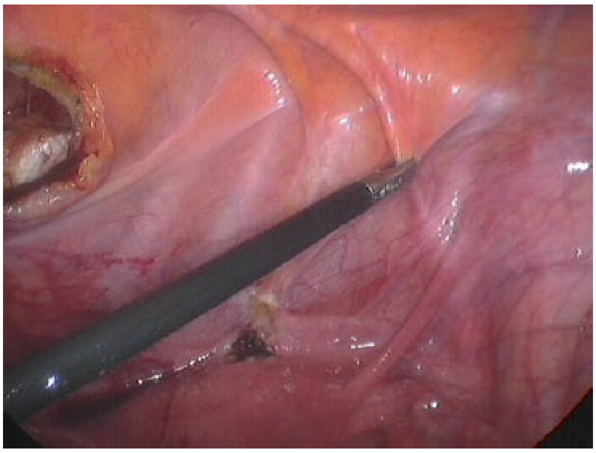


Figure 99.4 An incision is made in the median umbilical ligaments cephalad to the bladder dome to gain access to the cave of Retzius.

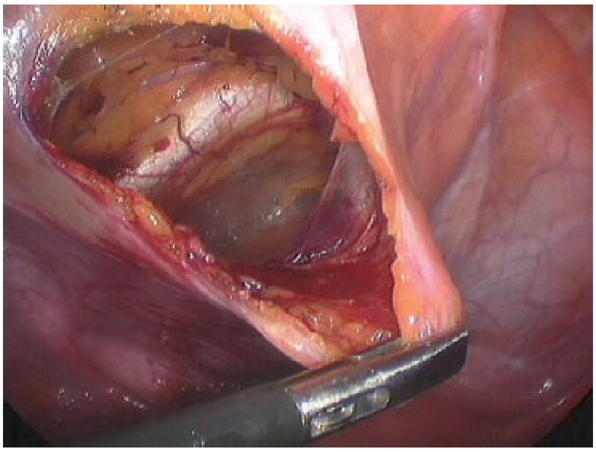


Figure 99.5 The cave of Retzius is dissected, clearly demonstrating the pubic symphysis and Cooper's ligaments.

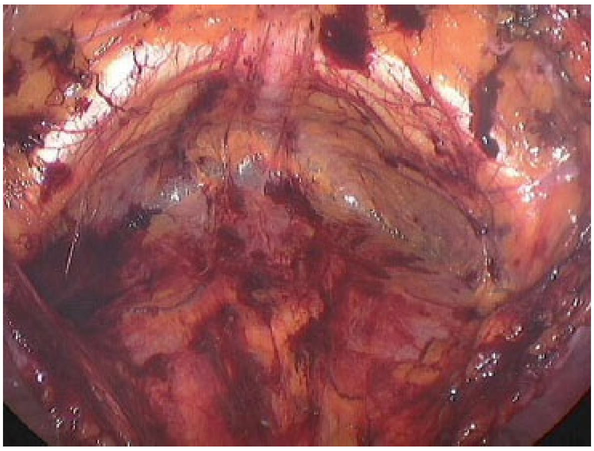


Figure 99.6 A pledget is used to dissect the bladder medially to allow suture placement.

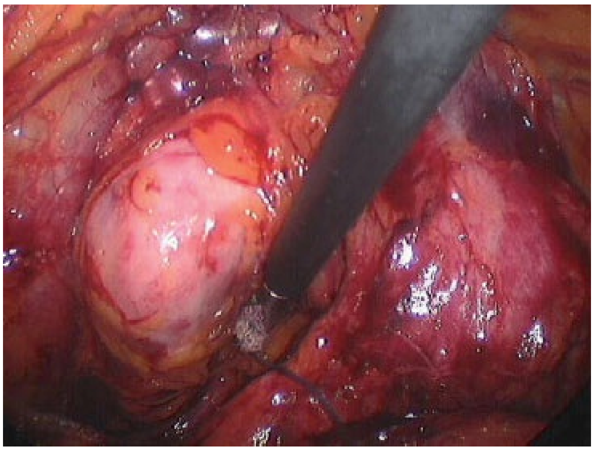


Figure 99.7 The first suture is placed at the level of the bladder neck.

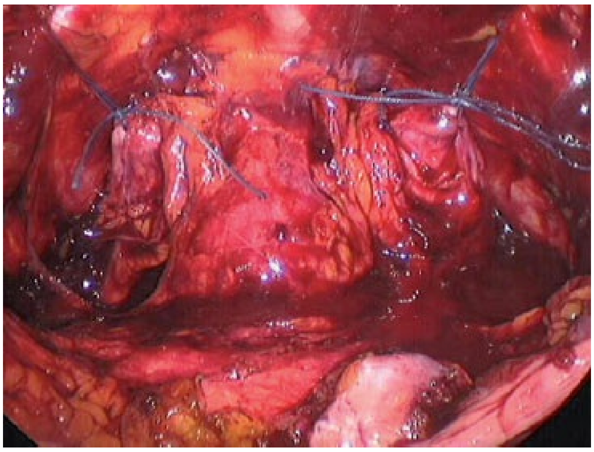


Figure 99.8 The second suture is placed cephalad to the previously placed suture.

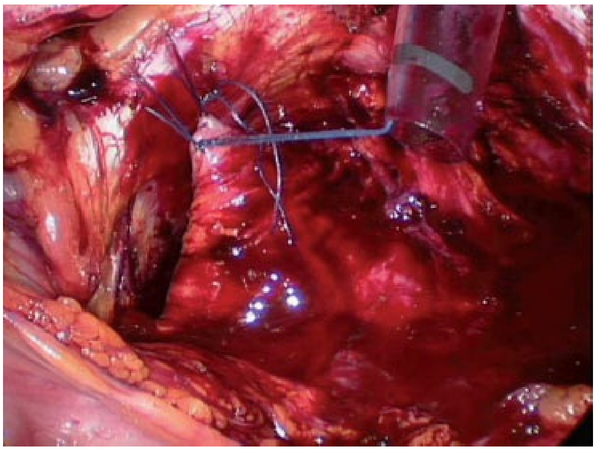


Figure 99.9 The ureter is dissected lateral to the uterosacral ligaments.

If preoperatively there is known to be significant uterine prolapse, then a concomitant laparoscopic hysterectomy and vault suspension or hysteropexy using mesh [34] or a suture is performed [35]. For some women, a hysterectomy may be the most appropriate and requested, but for others, a uterine conservation technique will be employed with a possible lowered morbidity. If it is clear preoperatively that a uterine or vault elevation procedure will be necessary, for ease of surgical access, preparation of the sacral promontory and uterosacral ligaments (or dissection of uterovesical and rectovaginal spaces in the case of a mesh hysteropexy) may be performed prior to the colposuspension (Figures 99.9 and 99.10). The rest of the hysteropexy is then performed following completion of the colposuspension.

At the end of surgery, an indwelling urethral catheter is usually left for 2 days in our unit, although the duration in other units may vary from overnight to 10 days. After the catheter is removed, a trial of void protocol is instituted. The postvoid residual is measured with a bladder scanner after the second void, the results of which determine the need for recatheterization. If the residual is high, the patient is discharged home with an indwelling catheter. An outpatient trial of void is carried out 1 week later. We no longer use suprapubic catheters. The use of bladder scanners and outpatient follow-up has removed the need of clamping and unclamping suprapubic catheters. This has resulted in less discomfort and earlier ambulation. In addition, the suprapubic catheter site can leave an unsightly scar.

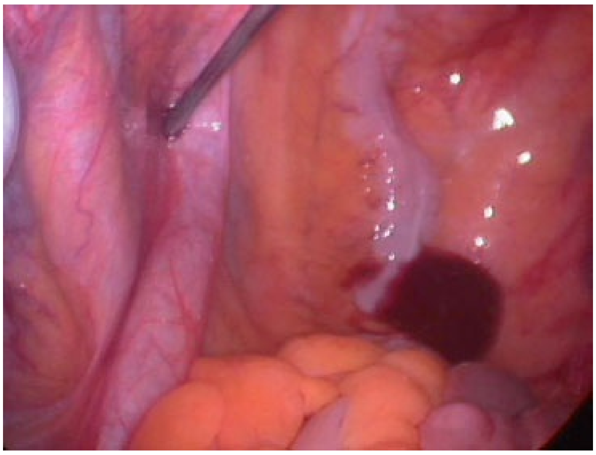


Figure 99.10 Both uterosacral ligaments have been shortened and plicated together in the midline.

Evaluation of the Role of Laparoscopic Colposuspension

In order to appropriately assess the role of laparoscopic colposuspension, a couple of questions need to be addressed: Colposuspension or not? And laparoscopic or not? Within these two questions, several factors need to be taken into consideration.

Open retropubic colposuspension has stood the test of time as a surgical procedure, both in the short and long term [36–38]. It has been shown to be similarly efficacious to traditional suburethral sling procedures [39] and minimally invasive sling procedures [40]. The indications will depend on patient and surgical preference. Due to the obvious increased recovery time and morbidity, particularly associated with the open procedure, the indications for colposuspension have narrowed. It is certainly useful as an option for those women who have significant anterior vaginal wall or bladder neck mobility, for those women undergoing other concomitant abdominal surgery, and for those women with previous failed midurethral tape surgery. Indeed, De Cuyper et al. reported the successful outcomes for laparoscopic colposuspension following failed midurethral tape surgery. In this retrospective study, subjective cure rates of 93% were reported at a median follow-up of 2 years [41]. In addition to this, we believe that there will be an inevitable rise in demand for effective alternatives to midurethral tape placement due to concerns arising from recent media and regulatory body alerts regarding synthetic slings [42].

The debates about laparoscopic surgery have raged since its inception as a surgical technique. We believe that laparoscopic surgery should be considered the same as open surgery but carried out through smaller incisions with longer instruments. The advantages of the laparoscopic approach are better visualization of the anatomy, less postoperative pain, and an earlier return to normal activities [43]. Although there is increased exposure and magnification deep in the pelvis, this is at the expense of less tactile feedback. As with any new procedure, however, there has been healthy skepticism of its merits and careful consideration of its risks. The problems cited have previously centered around efficacy, morbidity, cost, and operative duration. These problems in the early phase of laparoscopic surgery were, in part, explained by the limitations in the optics and the instruments available. Advances in these areas have enabled the surgeon to operate in a more dexterous manner. SynOptics launched the tube camera in 1978 and William Chang invented the first solid-state medical video camera in 1981. The first three-chip camera to be produced giving better clarity of vision arrived in 1989. The S-Video signal was developed in 1992 and the first digital zoom and digital enhancement capabilities were developed in 1999. There have been ongoing steps forward in image clarity with the advent of high definition and 3D technology. The next phase of ultrahigh definition (4K) is on the horizon. Alongside this, instrumentation has advanced to be ergonomically more suitable, further aiding surgical movements. Operating rooms have also been modified, with integrated theaters being developed, allowing the operating surgeon to modify the theater and equipment controls to their own desired settings. This theater environment potentially reduces stress and, hence, may result in enhanced surgical safety [44]. The development of robotic surgery may result in further advances [45] (Figure 99.11). However, as yet, there are no data to suggest any advantages in robotic urogynecology over the laparoscopic approach.

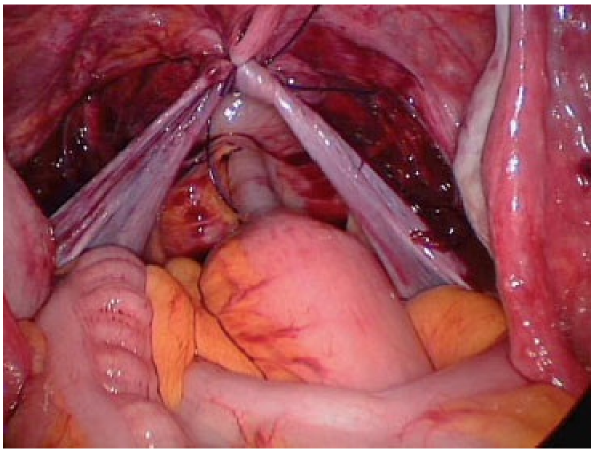


Figure 99.11 The “da Vinci” robotic surgical system.

Many studies have compared open colposuspension to laparoscopic colposuspension with variable success rates reported. Any discussion on laparoscopic colposuspension should be very similar to that of the open counterpart. The reported effectiveness of any of the procedures is reliant on the definitions of subjective and objective improvement and cure rates. Other compounding factors include surgical technique and experience. The requirement to learn new surgical skills for the different operative environment results in a learning curve, which has led some surgeons to develop “shortcut” surgery, and hence, new operations have been devised [46]. These are often given the same name as the traditional counterpart but must be assessed in their own right and should not be considered the same. Most alterations to the traditional approach are due to the difficulty that surgeons have had in learning suturing techniques.

When evaluating operative outcomes, careful consideration should be given to who performs the surgery as well as carefully deliberating which patients are appropriate for surgery. In a review on urinary incontinence, the National Institute for Health and Clinical Excellence (NICE) specified that surgery for urinary incontinence “should be undertaken only by surgeons who have received appropriate training or who work within a multidisciplinary team with this training, and who regularly carry out surgery for urinary incontinence in women” [47]. Despite observing no significant difference in outcome between open and laparoscopic approaches (level 1), the reviewers suggested that laparoscopic colposuspension is not recommended as a routine procedure for the treatment of stress urinary incontinence. Perhaps this was because of the fact that they found level four evidence that the procedure consumes more resources and that there is a longer learning curve for skill acquisition compared to other procedures. The authors reiterated their advice that laparoscopic colposuspension should only be performed by those with experience in performing the procedure, although presumably this advice still holds true for all surgical procedures.

Having established that there is an indication for evaluating laparoscopic colposuspension and having established some ground rules by which it should be assessed, to further evaluate its role, it is necessary to evaluate both the success rate, complication rate, the cost of the laparoscopic approach, and how it compares to other surgical techniques.

Success Rates of Nonsuture Colposuspension

Table 99.1 demonstrated the different methods that have been used to carry out a colposuspension laparoscopically. Apart from the traditional suture method, the main method variation adopted has been the use of mesh and tacks to carry out the suspension.

One randomized trial of 60 women compared suturing and nonsuturing laparoscopic methods. The authors demonstrated a higher objective failure rate at 1 year of 26.9% with the mesh technique compared to 11.1% with sutures [48]. Ankardal et al. [49] similarly demonstrated a statistically significant difference in cure rate using sutures as opposed to that achieved with mesh and staples. There are further studies in the literature that compare the laparoscopic route using mesh to the open procedure using sutures [50,51]. Both studies reported a lower success rate with the laparoscopic approach. However, these studies are in fact comparing two entirely different operative procedures and the results cannot therefore be interpreted as outcome data for all laparoscopic colposuspension procedures.

Success Rates of Laparoscopic Colposuspension

Table 99.2 shows the reported success rates for laparoscopic colposuspension in the literature where sutures were used to elevate the vagina. A variety of different techniques are likely to have been employed, and while most studies report objective cure rates, even within this, there are differences in the objective criteria used. Prezioso et al. using an extraperitoneal approach [52] used patient satisfaction questionnaires and urodynamics to assess outcome. They found a patient satisfaction rate of 90% and a cure rate of 72% at 6 months. The number of sutures placed at the time of the procedure is not clear from the methodology described. A similar cure rate, defined as a negative cough test with a comfortably full bladder, after a mean of 52 months was seen by Hong et al. [53], who also performed surgery by the extraperitoneal approach, placing two sutures 2 cm laterally on each side of the urethra and 2 cm distal to the bladder neck. As is seen with the open technique [37], a diminishing cure rate was seen over time. This is echoed on other studies with long-term follow-up. Barr et al. [69] showed a subjective cure rate of 52% 10 years after laparoscopic colposuspension. McDougall [16] reported only a 30% success rate at 45 months for laparoscopic colposuspension with a nonabsorbable suture compared with 35% for needle suspension. However, it is noteworthy that the suture was attached to Cooper’s ligaments by an absorbable clip in this latter study, perhaps explaining this particularly low long-term success rate.

The most marked difference for technique using sutures is the number of sutures used to elevate the vagina. Persson and Wolner-Hanssen randomized 161 women undergoing laparoscopic colposuspension and showed a higher objective success with two single-bite sutures on each side (83%) compared with one double-bite suture (58%) [70].

Table 99.2 Reported Cure Rates for Laparoscopic Colposuspension with Sutures

Author	No. of patients	Length of follow-up (Months)	Cure rate (%)
Langebrekke et al. [52]	8	3	88
Gunn et al. [53]	15	4–9	100
Liu [54]	132	3–27	97.2
Burton [78]	30	12	73
Su et al. [79]	46	12	80.4
Persson and Wolner-Hanssen [70] (1 suture)	78	12	58
Persson and Wolner-Hanssen [70] (2 sutures)	83	12	83
Ross [55]	32	12	94
Ross [56]	35	12	91
Kung et al. [57]	31	14.4	97
Lam et al. [58]	107	16	98
Liu and Paek [9]	107	18	97.2
Liu [59]	58	22	94.8
Ross [60]	48	24	89
Papasakelariou and Papasakelariou [61]	32	24	90.6
Lee et al. [62]	48	26	93.8
Nezhat et al. [63]	40	30	91.9
Burton [77]	30	36	60
Fatthy et al. [81]	74	18	87.9
Üstün et al. [105]	23	18	82
Huang and Yang [85]	82	12	89
Zullo et al. [48]	30	12	89
Cheon et al. [82]	47	12	85
Kitchener et al. [86]	123	24	80
Bunyavejchevin and Wisawasukmongchol [64]	21	60	76
Dietz and Wilson [65]	50	12	74

Yang et al. [66]	116	12	95
Prezioso et al. [67]	96	6	72
Hong et al. [68]	68	52	72
Barr et al. [69]	139	120	52

Complications

Major complications reported following laparoscopic colposuspension include urinary tract injury, bowel injury, major vascular injury requiring transfusion, and abscess in the space of Retzius. In the longer term, failures of the procedure requiring repeat surgery, de novo detrusor overactivity, voiding difficulty, pain, urethral obstruction, fistula, or posterior compartment prolapse may occur as for the open procedure.

Buller and Cundiff [71], in their review of 1867 patients, report an overall complication rate of 10.3%. The bladder dome was the most commonly injured site and was repaired laparoscopically in the majority of cases. The lower urinary tract is injured in 2%–3% of cases of laparoscopic colposuspension and paravaginal repairs [24,72]. This reported rate is lower than the 10% reported with the open procedure [73]. Intraoperative diagnosis of urinary tract injury is the main factor associated with decreased morbidity [74]. Small bladder injuries can be managed by catheterization, but if greater than 0.5 cm, they should be closed laparoscopically in one or two layers with an absorbable suture.

Where mesh has been substituted for sutures, different additional complications can occur. Kenton et al. have reported two cases of women who presented with complications following laparoscopic colposuspension with Prolene mesh and tacks. Both women had tacks removed retropubically from the bladder and retropubic space and no tacks were seen in Cooper’s ligaments in either patient [75]. In both cases, postoperative cystoscopy was not performed at the time of the colposuspension.

Disadvantages

The main disadvantage of the laparoscopic approach is that the surgeon must possess adequate minimal access skills to perform the procedure competently. It would appear that the modifications introduced in order to overcome the difficulty of suturing in the cave of Retzius, result in lower success rates. To quote the NICE, laparoscopic colposuspension “should be undertaken only by surgeons who have received appropriate training.” This very truism has blighted the uptake of laparoscopic colposuspension, hampered, in part, by inadequate training facilities and archaic theaters. There is a steep learning curve in laparoscopic surgery and this has resulted in fewer laparoscopic colposuspensions being performed. This is likely to be corrected by the stepwise improvements in training opportunities, particularly with plans for the development of laparoscopic urogynecology teaching modules to become incorporated as part of subspecialist training, and the ever evolving developments in theater setup and design.

As with all surgical procedures, adequate surgical audit is of paramount importance in the monitoring of efficacy and complications. For surgeons, NICE has recommended an annual workload of at least 20 cases of each primary procedure for stress urinary incontinence, and surgeons undertaking fewer than 5 cases per annum are advised to do so with the support of a clinical governance committee. These recommendations, in part, account for the relative centralization of specialist techniques like laparoscopic colposuspension; although with some of the changes detailed earlier including improvements in training, theater facilities, and patient demand, there may be a wider uptake of the procedure. There is now a general acceptance of the merits of minimal access surgery among most gynecologists and, therefore, a growing acknowledgment by hospitals of the need to embrace this form of surgery and optimize the clinical setup in order to realize all the potential benefits of laparoscopic surgery.

Laparoscopic Compared with Open Colposuspension: Success Rates, Complications, and Recovery

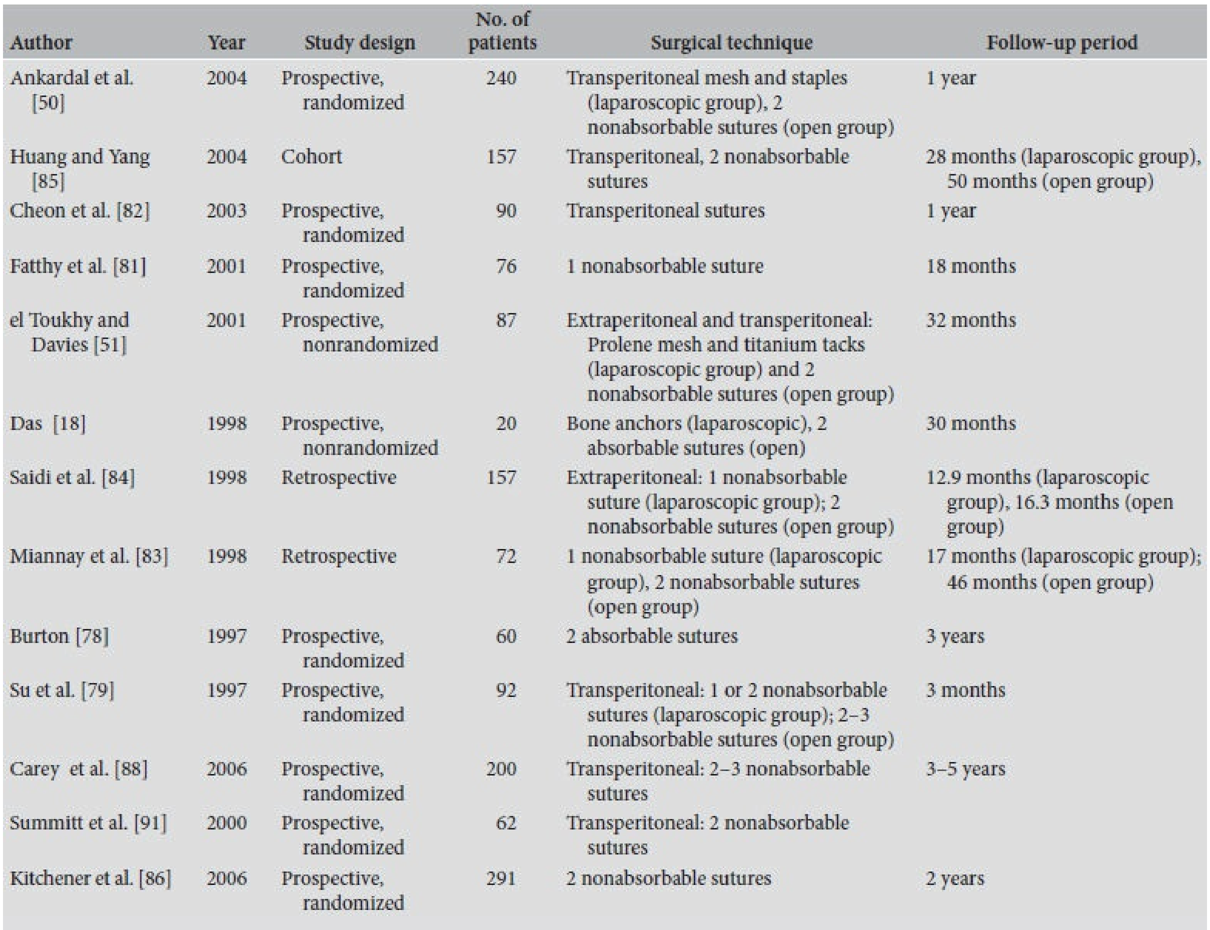
Table 99.3 shows the methodology of studies comparing the laparoscopic approach to open colposuspension. The ideal study would be a prospective randomized study, where both study arms employed the same surgical technique but differed only in their mode of abdominal access. No study achieves this and as with many comparative pelvic floor surgical studies, there is an array of techniques and outcome data employed, which partly explains the disparate findings. That being said, surveying the available evidence to date, the most reasonable conclusion is that the outcome following open and laparoscopic colposuspension is similar. This is apparent from randomized control studies, meta-analysis, and a recent Cochrane review [76].

Burton randomized 60 women to laparoscopic or open colposuspension using two absorbable sutures on either side for both techniques. He reported a lower cure rate at 1 year with the laparoscopic approach compared to the open approach (60% versus 93%) [77]. Similarly, at 3-year follow-up, the results of the laparoscopic group continued to be worse than the open group [78]. However, the author had only performed 10 laparoscopic procedures before the study and absorbable sutures were used. In addition, in the laparoscopic arm, a 12 mm needle was used, and this may have resulted in an inadequate bite of tissue for suspension. The study has not been published in a formal peer-reviewed paper, making further evaluation of the findings difficult.

Su et al. [79] investigated 92 women randomly assigned to the laparoscopic or the open route. They included in the open group those patients who were unwilling to undergo the laparoscopic route after randomization. In addition, 14 women in the laparoscopic group had a laparotomy for hysterectomy immediately following colposuspension. They found less blood loss in the laparoscopy group, similar operating time but lower success rate at 1 year compared to the open group (80.4% versus 95.6%). The follow-up period was variable, and in the majority of cases, only one suture was placed in the laparoscopic group compared to two or three sutures in the open group (placing one suture laparoscopically has been shown to have inferior cure rates to when two sutures are employed [70]). The complication rate in the open group was higher than in the laparoscopic group (17.4% versus 10.8%). This study was included in the systematic review comparing both approaches by Moehrer et al. [80]. The review found that the risk of a positive stress test at follow-up was significantly less in the open treated group. However, when a separate analysis was performed, excluding the study by Su et al. due to some of the aforementioned methodologic flaws, the higher objective cure rate reported with the open approach was no longer significant [80].

Fatthy et al. [81] showed a similar success rate for open and laparoscopic approaches. Cheon et al. [82], in a randomized study of 90 women comparing open and laparoscopic colposuspension, reported similar objective cure rates at 1 year (86% versus 85%). Three further retrospective studies showed similar success rates at 1 year between the laparoscopic and open routes when nonabsorbable sutures were used in both arms with less analgesia, shorter hospital stay, and earlier return to work as seen in the laparoscopic group in two studies [83,84]. The third study compared the anatomic result of the two procedures by assessing the bladder neck position with postoperative ultrasound and found no difference in resting, straining bladder neck position, and urethral mobility at 1 year postoperatively [85].

Table 99.3 Methodology of Studies Comparing Laparoscopic Colposuspension to Open Colposuspension



Author	Year	Study design	No. of patients	Surgical technique	Follow-up period
Ankardal et al. [50]	2004	Prospective, randomized	240	Transperitoneal mesh and staples (laparoscopic group), 2 nonabsorbable sutures (open group)	1 year
Huang and Yang [85]	2004	Cohort	157	Transperitoneal, 2 nonabsorbable sutures	28 months (laparoscopic group), 50 months (open group)
Cheon et al. [82]	2003	Prospective, randomized	90	Transperitoneal sutures	1 year
Fatthy et al. [81]	2001	Prospective, randomized	76	1 nonabsorbable suture	18 months
el Toukhy and Davies [51]	2001	Prospective, nonrandomized	87	Extraperitoneal and transperitoneal: Prolene mesh and titanium tacks (laparoscopic group) and 2 nonabsorbable sutures (open group)	32 months
Das [18]	1998	Prospective, nonrandomized	20	Bone anchors (laparoscopic), 2 absorbable sutures (open)	30 months
Saidi et al. [84]	1998	Retrospective	157	Extraperitoneal: 1 nonabsorbable suture (laparoscopic group); 2 nonabsorbable sutures (open group)	12.9 months (laparoscopic group), 16.3 months (open group)
Miannay et al. [83]	1998	Retrospective	72	1 nonabsorbable suture (laparoscopic group), 2 nonabsorbable sutures (open group)	17 months (laparoscopic group); 46 months (open group)
Burton [78]	1997	Prospective, randomized	60	2 absorbable sutures	3 years
Su et al. [79]	1997	Prospective, randomized	92	Transperitoneal: 1 or 2 nonabsorbable sutures (laparoscopic group); 2–3 nonabsorbable sutures (open group)	3 months
Carey et al. [88]	2006	Prospective, randomized	200	Transperitoneal: 2–3 nonabsorbable sutures	3–5 years
Summitt et al. [91]	2000	Prospective, randomized	62	Transperitoneal: 2 nonabsorbable sutures	
Kitchener et al. [86]	2006	Prospective, randomized	291	2 nonabsorbable sutures	2 years

In the Medical Research Council (MRC) colposuspension trial, 291 women were recruited in 6 centers in the United Kingdom [86]. Of the 144 women allocated to laparoscopic surgery, 11 received open surgery and 2 had no operation. Of the 147 women allocated to open surgery, 1 had laparoscopic surgery and 3 had no operation. On an intention-to-treat analysis at 2 years, the objective outcome (1 hour pad test) showed 80% cured in the laparoscopic group (85.4% data available) and 70% cured in the open group (79.6% data available). The subjective outcome ("perfectly happy/pleased," question 33 in the Bristol Female Urinary Tract Symptoms questionnaire) showed 55% cured in both the laparoscopic and the open group. These results demonstrated that, in the hands of experienced laparoscopic surgeons, laparoscopic surgery does not produce an inferior cure rate to open colposuspension.

The long-term efficacy of both laparoscopic and open colposuspension has been reported. Morris et al. [87] concluded that the laparoscopic approach gave a significantly higher objective cure rate after a median follow-up of 6 years. Carey et al. found no difference in self-reported stress incontinence between the two operative routes, 3–5 years following surgery [69,88]. Barr et al. [69] performed structured interviews at least 10 years following surgery, and the authors reported a deterioration in subjective cure rates (defined as no urinary leakage in last 6 months) from 71% and 67% at 6 months to 48% and 32% at 10 years for the laparoscopic and open procedures, respectively. Again, no statistical difference was noted between the two surgical approaches.

As well as objective and subjective cure rates, authors have evaluated differences in operative time, length of hospital stay, and return to normal activities, between the two operative routes. In the study by Fatthy et al. [81], the laparoscopic approach took 17 minutes longer (the same as the MRC trial) with nearly 200 mL less blood loss, 40 hours less hospital stay, and return to light work 23 days earlier. Carey et al. [88] reported a shorter operative time for the open technique (44 versus 85 minutes). In contrast, Su et al. [79] reported shorter operative time with the laparoscopic approach, although less suturing was employed. The studies by Fatthy et al. [81] and Su et al. [79] both reported longer hospital stay after open compared to laparoscopic colposuspension. Cheon et al. [82] and Carey et al. [88] reported no significant difference. The latter group did, however, report a significantly quicker return to normal activities in the laparoscopic arm of patients. It is noteworthy, however, that length of stay in hospital and time of return to work are also strongly influenced by local and cultural issues as well as surgical morbidity.

Tan et al. [89] identified 16 studies, published between 1995 and 2006 comparing the results of laparoscopic and open colposuspension for patients with stress urinary incontinence. Analysis was performed on 1807 patients, of whom 861 (47.6%) underwent laparoscopic and 946 (52.4%) underwent open colposuspension. They concluded that the former is associated with a similar subjective and objective cure (continence) rate compared to the open operation. It is also associated with a lower operative blood loss, earlier postoperative recovery, and an earlier return to work.

There have been Cochrane reviews evaluating the colposuspension procedure [76,90]. In the most recent review published in 2012, 12 trials were included [49,78,79,81,82,86–88,91–94]. In the analysis comparing open with laparoscopic colposuspension, a total of 1260 women were studied. As is often the case, pooling data from the studies poses problems as most of the trials employ different criteria to define objective and subjective levels of success. Data were analyzed from all of the studies apart from one [78] (Burton) that included visual analogue scores as outcome data. The meta-analyses of data available at less than 1 year revealed a relative risk (RR) of cure of 0.97 (95% CI 0.79–1.18). Between 1 and 5 years, there was a favoring of open surgery, albeit nonsignificant (RR 0.88, 95% CI 0.75–1.03), and if the Ankardal data [49], which included laparoscopic mesh and staples, were excluded, there was a much more apparent absence of difference in objective failure rates between the two treatment groups (RR 0.95, 95% CI 0.80–1.11). Longer-term data were only assessed in one paper [87], which favored the laparoscopic approach in the 64 women studied, although, again, this was nonsignificant (RR 1.89, 95% CI 0.99–3.59). The authors concluded that patient-reported incontinence rates at short-, medium-, and long-term follow-up showed no significant differences between open and laparoscopic retropubic colposuspension [76].

There were no significant differences in the risk for developing adverse events, in terms of perioperative complications, de novo urge symptoms or urge incontinence, detrusor overactivity, voiding difficulties, or new or recurrent prolapse. The authors did highlight four trials [86,88,93,94] that provided limited evidence of a greater tendency for laparoscopic colposuspension to have a higher rate of bladder perforation (0.6% versus 3%). Ultimately, the authors concluded that laparoscopic colposuspension should allow speedier recovery, and available evidence shows comparable effectiveness with open surgery.

Cost

Differences in costs are difficult to assess as there is a great variation in each country as to how long patients tend to stay in hospital following surgery and there are differing costs of operating time. The laparoscopic approach is generally reported to require longer operating time than the open colposuspension or midurethral sling procedures. The other cited factor against the laparoscopic approach is the increased cost of disposables associated with minimal access procedures. With greater adoption of laparoscopic surgery, there has been a continued drive for industry to produce better and more cost-effective equipment, and there is a growing competitive market for this, which ultimately may further drive down costs with no compromise on quality. It is also important to mention that the cost of sterilization of reusable instruments is rarely if ever allowed for during cost comparisons of techniques.

Dumville, as part of the COLPO (Colposuspension; is Laparoscopic Preferable to Open?) study group [95], compared the cost-effectiveness of laparoscopic colposuspension versus open colposuspension. The health outcome measure for the economic analysis used was quality-adjusted life years (QALYs). This is a measure reflecting both patient's health-related quality of life and mortality into a single index. Interestingly, in this study, both groups had a suprapubic catheter inserted at the time of surgery, and both groups were subjected to a particular postoperative trial of void regimen. This is likely to have influenced the length of inpatient stay and may have inadvertently minimized the actual differences between the two study arms in terms of length of hospital stay. Despite this, the laparoscopic group had a reduced mean length of stay in hospital and a reduced number of outpatient and GP appointments during follow-up. The total theater costs for the laparoscopic group were, as expected, markedly higher than the open surgery group (£944 versus £464), mainly due to the longer theater time used and the extra equipment required for the laparoscopic surgery. The total cost of laparoscopic surgery at 6 months of follow-up was higher than the total cost of open surgery (£1805 versus £1433), with a differential mean of £372 (95% CI 274–471). At 24 months, however, those who underwent laparoscopic surgery had higher QALYs compared with those who underwent open surgery. There had been a shorter inpatient stay and fewer postoperative visits. After 24-month analysis, the authors concluded “the laparoscopic approach might be a cost-effective alternative in the medium term, provided that there are no major cost implications from treatment failure compared with the open group.” There is very little evidence that the failure rates of the two procedures are so disparate after 2 years for the laparoscopic approach not to be cost-effective at this time interval.

Kohli et al. [96] reported a retrospective 2-year cost analysis of laparoscopic colposuspension with sutures compared with open colposuspension. They found that the laparoscopic approach was more expensive than the open approach ($4960 versus $4079). This reflected the high hourly operative room charges in North America as the laparoscopic group took on average 44 minutes longer operating time. The postoperative care costs were lower in the laparoscopic group. Persson et al. reported that a laparoscopic colposuspension is cheaper than [97] a TVT in Sweden (€1273.4 versus €1342.8) despite the TVT procedure being performed in less time. In contrast, a more recent Swedish study reported that the TVT procedure generated a lower direct cost than colposuspension, either by the open or laparoscopic approach [98]. Other studies have similarly confirmed the greater expense of the laparoscopic route compared to midurethral surgery [99].

Laparoscopic Colposuspension versus Tension-Free Vaginal Tape Procedures

With the advent of midurethral tape procedures, it is pertinent to evaluate the performance of laparoscopic colposuspension compared with these even more minimally invasive procedures. To address this issue, Dean et al. performed a systematic review identifying seven trials from the Cochrane Incontinence Review Group’s Specialised Register of Controlled Trials [100].

Of the seven studies [97,101–106], three were published as abstracts and one used Prolene mesh and tacks. This latter study found similar cure rates at 6 weeks following surgery, with the TVT arm taking less operative time, shorter hospital stay, and earlier return to work [106]. One patient in the laparoscopic group required a laparotomy to remove the tacks inadvertently placed in the bladder, as they were too difficult to remove laparoscopically. One-year data from the same study showed that the success rate of the TVT as defined by a negative stress test was 85.7%, but the laparoscopic colposuspension group success rate had fallen to 56.9% [107]. In a longer-term follow-up study, the same authors showed superior subjective and objective cure rates with TVT compared to the laparoscopic mesh colposuspension procedure [108]. The authors also concluded “if cases that were lost to follow-up were regarded as failures, the intention-to-treat analysis found no difference between the groups.” Of note, however, as discussed earlier, the mesh procedure is not synonymous with a standard colposuspension, and the findings of the Valpas papers should not be simply translated to the laparoscopic suture colposuspension technique. The use of sutures, irrespective of surgical approach, is seen to be better than the use of mesh [49].

None of the other studies analyzed by Dean et al. showed a significant superior treatment effect with either approach. When pooled results were used, the overall objective cure (a combination of a negative clinical stress and pad tests) rate was statistically higher for TVT when compared with laparoscopic colposuspension (using sutures or mesh) (RR 1.16, 95% CI 1.07–1.25). Interestingly, when the authors excluded the study by Adile et al. [101] due to methodological flaws, no significant difference between the two treatments was seen.

When urodynamics was used to objectively assess clinical outcome, again no difference was seen between the two operations. Reported differences in de novo urgency were conflicting in the studies, and the numbers of women with voiding dysfunction following different surgery were too small to satisfactorily analyze. With respect to morbidity, there were no statistically significant differences in the perioperative complication rates between laparoscopic colposuspension and TVT procedure (RR 1.07, 95% CI 0.64–1.79). The cited benefits of laparoscopic colposuspension over the open procedure were echoed for the TVT procedure over laparoscopic colposuspension. There was a shorter hospital stay by a mean of 1 day and a quicker return to normal activities. In addition, laparoscopic surgery took significantly longer than the TVT surgery by an average of 20 minutes.

Jelovsek reported longer-term data comparing TVT and laparoscopic colposuspension. A total of 72 patients were enrolled. Over a median follow-up time of 65 months, no differences were seen in patient-reported urinary incontinence or bothersome stress urinary incontinence symptoms. Of subjects in the laparoscopic Burch group, 88% reported that if they had to do it all over again, they would choose the same treatment versus 79% in the TVT group [109].

The favorable outcomes seen with midurethral slings are an encouraging development for the treatment of urinary stress incontinence. The balance has shifted toward midurethral tapes as the first-line treatment. Notwithstanding this, the merits of a colposuspension remain, and judicious use in appropriate patients ensures that a range of treatment choices is available.

CONCLUSION

Colposuspension avoids placing a permanent tape under the urethra, thereby reducing concern about the possibility of future tape erosion. Current evidence suggests that laparoscopic colposuspension performed with sutures is as effective as the open approach and the TVT procedures. The use of mesh, tacks, or staples and only one suture appears to reduce the success rate. The laparoscopic approach is associated with a quicker return to normal activity than the open procedure.

Perhaps the recent controversies associated with the placement of vaginal mesh will stimulate the rebirth of the colposuspension in its modern-day form, and a growing number of pelvic floor surgeons will be able to include it in their repertoire of anti-incontinence procedures. Each of the many available techniques offers its own set of advantages and disadvantages, and one single procedure is unlikely to offer a universal panacea. Any successful anti-incontinence procedure should take into account patient symptoms, medical comorbidities, and the presence of other pelvic floor problems. The ability to choose from a range of surgical techniques will inevitably optimize treatment for the individual woman.

The laparoscopic approach requires the surgeon to be competent in minimal access surgery skills as well as urogynecology. We believe that efforts should now be directed toward improvements in training and theater environment, both of which can act as either facilitators or barriers to surgical uptake. Long-term success rates remain the challenge for all anti-incontinence procedures.

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100 Laparoscopic Sacrocolpopexy

Marcus P. Carey

INTRODUCTION

The use of laparoscopic sacral colpopexy (LSC) to treat pelvic organ prolapse has increased in recent years coinciding with a dramatic decline in transvaginal mesh use as a result of recent Food and Drug Administration warnings [1]. In the United states, the number of LSC procedures performed for prolapse exponentially increased during the 10 years from 2003 to 2012 [2]. Among urologists in the United States, in 2012, 70.1% of sacral colpopexies were performed by laparoscopy.

The main limitation of laparoscopy for the treatment of pelvic organ prolapse is the relatively small number of surgeons with sufficient laparoscopic and reconstructive pelvic floor surgical skills to perform these procedures safely and successfully. This underscores the importance of introducing LSC into urogynecology and female urology training programs [3].

Approximately 300,000 women undergo surgery for pelvic organ prolapse in the United States each year [4]. In 2010, around 196,000, 70,000, and 34,000 women underwent native tissue vaginal repairs, transvaginal mesh repairs, and sacral colpopexy procedures, respectively, for pelvic organ prolapse [4]. In a study of women from a large U.S. health maintenance organization, it was reported that by the age of 80 years, 11.1% of women had undergone surgery for pelvic organ prolapse or urinary incontinence, or both [5]. Within 4 years of the primary surgical procedure, 29.2% of these women required repeat surgery for recurrent prolapse or stress incontinence [6]. Younger patients (age less than 60 years) and women with higher grades of prolapse (pelvic organ prolapse quantification [POPQ] stages 3 and 4) are more likely to experience recurrent prolapse after vaginal repair [6,7]. The prevalence of vaginal vault prolapse following hysterectomy is approximately 10% [8]. However, estimates of the prevalence of posthysterectomy vault prolapse vary markedly from 0.2% to 43% [8–10]. Vault prolapse occurs in equal numbers following abdominal and vaginal hysterectomy [11,12].

The high rate of failure with vaginal surgery to treat vaginal vault prolapse led to the development of the abdominal sacrocolpopexy (ASC) procedure. This approach employs the retroperitoneal interposition of a suspensory prosthesis (synthetic, autologous, allograft, or xenograft) between the vaginal apex and the sacrum. ASC was originally described by Huguier in 1957 and later by Lane in 1962 [13,14]. Snyder and Krantz [15] described the attachment of the prosthesis along the full length of the rectovaginal septum. Addison et al. [16,17] described the broad attachment of the prosthesis to both the upper anterior and posterior vaginal walls. Randomized trials comparing the ACS procedure with transvaginal sacrospinous ligament fixation to treat vaginal vault prolapse demonstrated a trend toward the ACS being the more effective procedure [18–20]. In addition to the high success rate reported with the ACS procedure, other advantages include the preservation of vaginal capacity resulting in maintenance of coital function, the use of synthetic material resulting in durable support, and the use of the synthetic graft on both anterior and posterior vaginal aspects providing for balanced support of the various vaginal sites and an acceptable vaginal axis. Significant problems associated with the ASC operation include de novo postoperative stress incontinence, intraoperative hemorrhage, dyspareunia, mesh erosion, and use of a laparotomy incision [14,15,17,21–23].

LSC was first described by Nezhat et al. in 1994 although Wattiez et al. claim to have first performed this procedure in 1991 [24,25]. In addition to treating posthysterectomy vault prolapse, LSC has been used concomitantly with laparoscopic total and subtotal hysterectomy for uterovaginal prolapse. The proposed advantages of the LSC over the ASC include

1. An enhanced view of the pelvic and intra-abdominal anatomy compared to the abdominal approach
2. The avoidance of a major laparotomy incision
3. Less postoperative pain, shorter time in hospital, and reduced risk of wound complications

4. A quicker return to normal activities

The LSC takes advantage of the known high success rate of the traditional ASC combined with the benefits of laparoscopic surgery. The LSC should be performed in an identical manner to the ASC with the only difference being the smaller laparoscopic incisions.

ANATOMIC CONSIDERATIONS

Following hysterectomy, the upper third of the vagina (including the vault) is supported by two mechanisms:

> *Direct* support for the vaginal vault is provided by the parametrium (cardinal and uterosacral ligaments) and paracolpium fibers. These fibers act like suspensory ligaments and arise from the fascia of the piriformis muscle, sacroiliac joint, and lateral sacrum and insert into the lateral upper third of the vagina.
>
> *Indirect* support for the vaginal vault is provided by the levator plate, formed by the fusion of the right and left levator ani muscles between the rectum and coccyx.

Vaginal vault prolapse occurs as a consequence of failure of these direct and indirect supporting mechanisms. This is likely to involve weakness of the muscular pelvic floor and suspensory fibers of the parametrium and upper paracolpium [26,27].

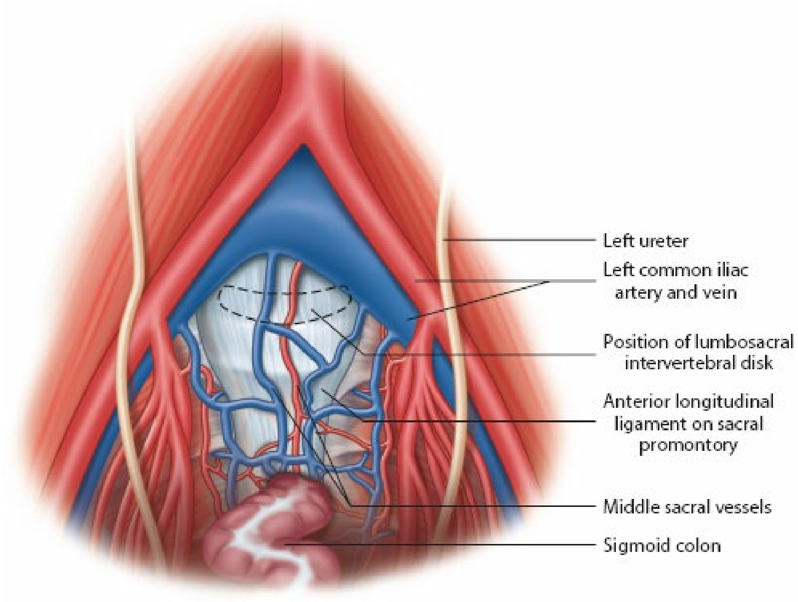
Recent work evaluating the fibromuscular composition of the vaginal wall in women with and without enterocele failed to demonstrate any focal "defect" of the vaginal muscularis [28]. Based on these anatomic considerations, it is not surprising that a site-specific endopelvic fascial repair approach to the treatment of a vaginal apical defect is likely to carry an unacceptably high failure rate [29,30].

For women with vaginal vault prolapse, surgical repair should generally be directed toward restoring vault support and a normal vaginal axis. These anatomic considerations lend credibility to the concept of the ASC and LSC procedures.

Anatomy of the Sacral Promontory

The presacral space is bounded superiorly by lumbosacral intervertebral disk and laterally by the right common iliac artery and left common iliac vein (Figure 100.1). The right ureter is identified coursing in the right lateral aspect of the presacral space. The sacral promontory and presacral space are usually covered by the sigmoid colon. The sigmoid colon at this point is attached to the peritoneum, which is reflected over the left psoas major muscle and iliacus muscle. Once the sigmoid colon is retracted to the left side, the sacral promontory is easily identified. The presacral space and sacral promontory are accessed by gently lifting up the peritoneum directly over the sacral promontory and performing a midline longitudinal incision. This approach into the presacral space will avoid damage to the right common iliac artery and left common iliac vein. The middle sacral artery and vein are easily identified lying directly on the middle aspect of the sacrum. The middle sacral artery originates as a single branch from the posterior aspect of the aorta. The middle sacral vein arises from the vessels emerging beneath the common iliac veins and drains into the inferior vena cava. Some women have an extensive venous plexus in the presacral space, and damage to these vessels can result in dramatic hemorrhage. The middle sacral artery gives off small branches that run laterally on the sacrum to either anastomose with the lateral sacral arteries or directly supply the ventral sacral nerve roots. Damage to these fine vessels can result in bleeding and ischemic injury to the ventral sacral nerve roots.

The hypogastric plexus of nerves descends into the pelvis anterior to the bifurcation of the aorta, enters the presacral space between the common iliac arteries, and is anterior to the middle sacral artery and vein. This plexus carries the autonomic nerves of the pelvic viscera. Extensive damage to this plexus of nerves may result in bladder, bowel, and sexual dysfunction. When performing a LSC procedure, careful dissection is recommended in order to reduce the risk of nerve damage. After entering the presacral space, the anterior longitudinal ligament is exposed by gentle blunt dissection of the presacral tissues over the sacral promontory. Sharp dissection and the use of ablative techniques to access the anterior longitudinal sacral ligament should be avoided. When securing the prosthetic material to the sacral promontory, the surgeon should avoid excessive use of sutures or stapling devices onto the sacral promontory. When performing a LSC procedure, the author uses only one or two sutures to secure the prosthesis onto the anterior longitudinal ligament on the sacral promontory (i.e., at the level of the upper part of the fifth lumbar vertebra) and has not encountered a case of mesh detachment from the sacral promontory with this approach.



Left ureter
Left common iliac artery and vein
Position of lumbosacral intervertebral disk
Anterior longitudinal ligament on sacral promontory
Middle sacral vessels
Sigmoid colon

Figure 100.1 The presacral space is bounded by the lumbosacral intervertebral disk above and laterally by the right common iliac artery and left common iliac vein. The middle sacral artery and vein course over the anterior longitudinal ligament on the sacral promontory.

CLINICAL ASSESSMENT AND PATIENT SELECTION

Clinical assessment is undertaken in the usual fashion. This includes obtaining a detailed history with particular emphasis on any symptoms associated with the vaginal vault prolapse, especially urinary, bowel, and coital symptoms. A detailed general and pelvic examination is undertaken. It is important for the clinician to identify all the vaginal defects accurately so that they can be corrected at the time of surgery. The patient should be examined for signs of stress incontinence with the prolapse present and also for any anorectal pathology, including rectal prolapse.

Urodynamic studies should be made available to patients with associated urinary symptoms. Imaging of the pelvic floor and anorectal physiological testing are recommended as indicated.

Indications

Currently, there is no consensus on the exact indications for both ASC and LSC procedures. The LSC is indicated for patients with symptomatic and significant prolapse of the vaginal vault who are considered appropriate candidates for an ASC. This approach is suitable for younger patients wishing to preserve coital function and in whom there are no contraindications to laparoscopic surgery. Walters and Ridgeway [31] recommended "sacral colpopexy with polypropylene mesh (preferably by minimally invasive route) in younger women, those with severe prolapse or recurrences after vaginal surgery, and women with prolapsed, short vaginas". Gadonneix et al. [32] reported that 89% of 46 consecutive patients presenting with multiple compartment prolapse could be treated by LSC.

The LSC procedure should be made available to patients with significant vaginal vault prolapse with no contraindications to laparoscopy. Typically, these women have had a previous hysterectomy and an International Continence Society POPQ classification of stage 2 or greater prolapse at the vaginal vault site [7]. Patients with significant stage 1 vault prolapse are sometimes offered this approach. LSC can also be used in conjunction with a hysterectomy and subtotal hysterectomy to treat marked uterine prolapse of stage 2 or greater in younger women [13,30,33]. LSC treats vaginal vault prolapse as well as high cystoceles and rectoceles when the mesh is extended onto the upper anterior and posterior vaginal walls [34]. On occasion, the LSC procedure with extension of mesh anteriorly and in combination with a laparoscopic paravaginal repair is offered to women with a recurrent cystocele, as this combination of procedures is very effective in treating recurrent high cystoceles.

LSC is a complex operation requiring both advanced laparoscopic and reconstructive pelvic surgery skills. Only surgeons competent in this operative technique should undertake this surgery.

Contraindications

Vaginal operations may be more appropriate for frail women who do not wish to preserve coital function. LSC is not indicated for women with minor degrees of vault prolapse. This procedure is also not suitable for patients who otherwise have a contraindication to laparoscopic surgery. In these women, an ASC or vaginal surgery to treat the vault prolapse should be offered.

Relative contraindications to LSC are

- Extensive intra-abdominal adhesions
- Morbid obesity
- Elderly patients
- Inflammatory bowel diseases (especially Crohn’s disease)
- Immunocompromised patients
- Chronic pelvic pain
- Prior pelvic radiation therapy

Absolute contraindications to LSC are

- Currently taking anticoagulation medication
- Active inflammatory bowel disease
- Current pelvic or vaginal sepsis
- Sacral abnormalities (e.g., sacral agenesis, sacral meningomyelocele)
- Recognized intraoperative bowel perforation
- Inability to safely access the anterior longitudinal ligament on the sacral promontory
- Any contraindication to laparoscopy

SURGICAL TECHNIQUE

A standardized technique for LSC does not exist. Surgery is performed under general anesthesia with muscle relaxation. A major challenge is the achievement and maintenance of adequate surgical exposure of the vaginal vault and sacral promontory. A steep Trendelenburg position, preoperative bowel preparation, avoidance of nitrous oxide anesthesia, and an adequate number of operating ports all facilitate good surgical exposure. Left lateral tilting of the patient can also be employed [35]. Laparoscopic bowel retractors appear to be of limited benefit. Following induction with general anesthesia, the woman is placed in a low lithotomy position using Allen stirrups. The use of Allen stirrups allows the patient to be repositioned during surgery without the need to redrape. Repositioning may be required when concomitant vaginal surgery is undertaken.

Standard techniques are used to introduce a 10 mm operating laparoscope at the umbilicus. Under laparoscopic vision, two ports (for the right-handed surgeon a 10 mm port on the patient’s left and a 5 mm port on the patient’s right) are inserted through the anterior abdominal wall into the peritoneal cavity. In order to avoid injury to the inferior epigastric artery and vein and damage to the lateral cutaneous nerve to the thigh, these ports are sited two fingerbreadths above and two fingerbreadths medial to the anterior superior iliac spine. A further 5 mm port is introduced suprapubically in the midline under laparoscopic vision.

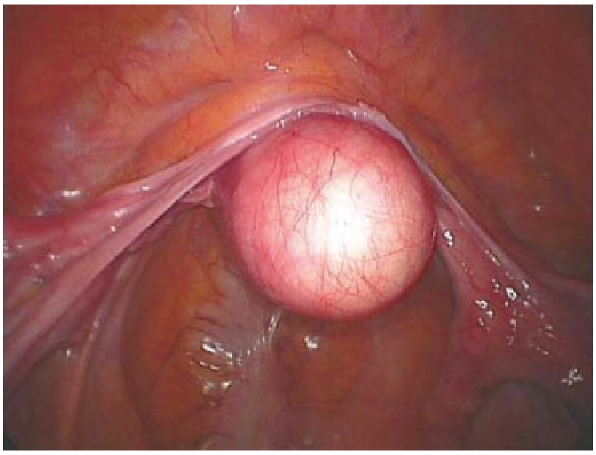


Figure 100.2 The vagina is elevated using a vaginal probe. This facilitates the dissection of the peritoneum, bladder, and rectum off the upper vagina.

A vaginal probe or vaginal elevator is inserted to identify the vaginal vault. With the vagina elevated cranially using the vaginal probe (Figure 100.2), the peritoneum is opened transversely at the vaginal apex. This dissection continues posteriorly into the rectovaginal septum so that the peritoneum is dissected off the upper half of the posterior vaginal wall. At around this point, the rectovaginal septum is entered and the rectum is dissected off the middle and lower posterior vaginal wall. On occasion, dissection can be facilitated by using a rectal probe. This dissection is carried out in the midline and extended laterally on both sides to the medial aspect of the uterosacral ligaments. The uterosacral ligaments are optimally visualized when the vaginal probe is elevated toward the anterior abdominal wall.

The bladder is then dissected off the upper anterior vaginal wall. This dissection continues to approximately the midpoint of the anterior vaginal wall. Dissection is continued laterally toward both the bladder pillars, but generally dissection of the bladder pillars is avoided. This is to reduce intraoperative bleeding and injury to the autonomic nerves to the bladder.

Once the peritoneum has been dissected off the upper vagina, along with dissection of the bladder and rectum, the sacral promontory is identified. Often, the sigmoid colon obscures the sacral promontory and needs to be reflected to the patient’s left. The sacral promontory is usually an easily recognizable and accessible structure (Figure 100.3a). However, in obese patients, the sacral promontory may be difficult to access. Prior to dissection in this region, the right ureter should be carefully identified. The peritoneum over the sacral promontory is grasped and elevated. A vertical incision is made into the peritoneum in the midline to allow entry into the presacral space (Figure 100.3b).

The peritoneum is further dissected in a caudal direction on the right of the rectum and sigmoid colon and below the right ureter into the cul-de-sac to join the posterior vaginal peritoneal dissection. Once this dissection is completed, the tissues in the presacral space over the sacral promontory are carefully reflected laterally so that the glistening white fibers of the anterior longitudinal ligament are exposed (Figure 100.4a). At this point, it is important to carefully identify any vascular structures on the sacral promontory in the midline so that injury to these structures can be avoided when the prosthesis is attached to the sacral promontory. Two rectangular pieces of mesh, a type 1 lightweight polypropylene mesh [36], are then cut to size, the first being 15 × 4.5 cm and the second being 5 × 4.5 cm. The larger piece of mesh is used to support the posterior vaginal wall and vault, and the smaller piece of mesh is used to support the anterior vaginal wall and vault. The larger mesh is introduced into the pelvis through the left 10 mm port. Using delayed absorbable monofilament sutures throughout, this mesh is attached to the posterior vaginal wall with four to six sutures. The smaller mesh is then introduced into the pelvis and attached to the upper anterior vaginal wall with four sutures. Two sutures are placed at the vaginal vault and through both anterior and posterior pieces of mesh. Alternatively, a precut Y-shaped mesh (e.g., Upsylon™ mesh, Boston Scientific, Boston, MA; Restorelle Y™ mesh, Coloplast, Humlebaek, Denmark) may be used.

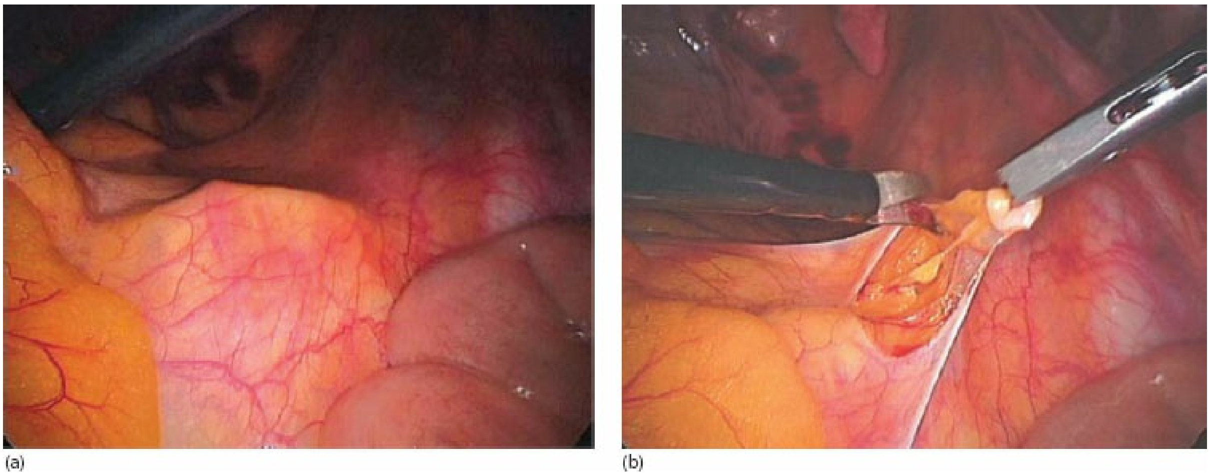

(a) (b)

Figure 100.3 (a) The sacral promontory is easily recognizable and accessible during laparoscopic sacral colpopexy. (b) The peritoneum over the sacral promontory is elevated and a vertical incision is made into the peritoneum in the midline to allow safe entry into the presacral space.

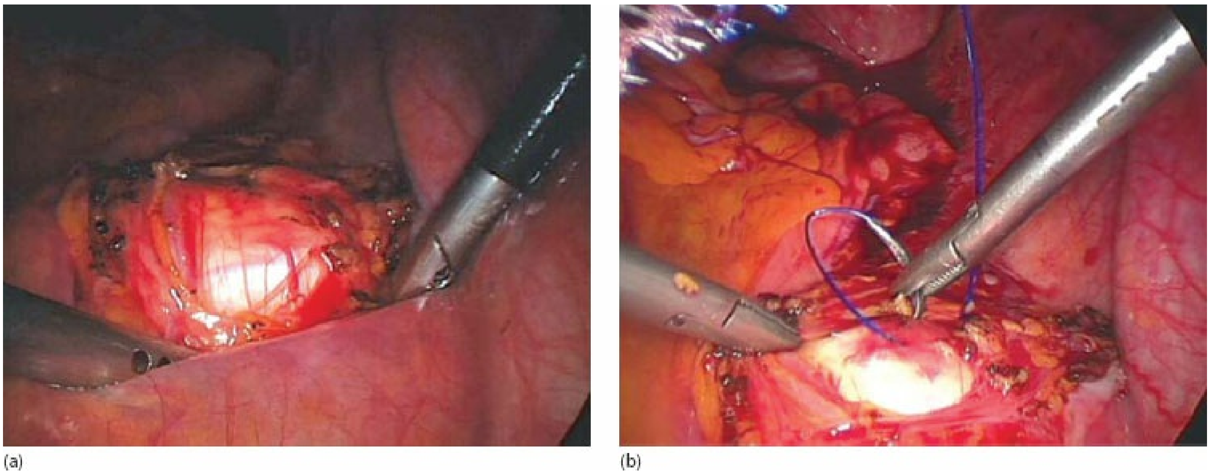

(a) (b)

Figure 100.4 (a) The tissues in the presacral space are carefully reflected laterally exposing the glistening, white fibers of the anterior longitudinal ligament on the sacral promontory. (b) A suture is passed in turn through the mesh and into the anterior longitudinal ligament on the sacral promontory in the midline.

The point of attachment of the mesh onto the sacral promontory is defined. The mesh is fixed to the anterior longitudinal ligament on the sacral promontory without placing tension on the vagina. A permanent suture is passed in turn through the mesh and into the anterior longitudinal ligament in the middle of the sacral promontory, with care taken to avoid injury to any vessels at this site. Occasionally, a second bite into the anterior longitudinal ligament is taken (Figure 100.4b). The suture is then passed again through the mesh and tied, anchoring the mesh onto the sacral promontory. Excess mesh above the knot is excised and removed from the abdomen (Figures 100.5 and 100.6). The peritoneum is closed with a continuous delayed absorbable monofilament suture starting at the sacral promontory. Alternatively, a barbed suture (e.g., 2/0 V-Loc$^{\text{TM}}$, Covidien, Mansfield, MA) may be used to close the peritoneum over the mesh. Closure of the peritoneum completely isolates the prosthesis from the intra-abdominal viscera and contributes to the obliteration of the pouch of Douglas. Occasionally, the pouch of Douglas may remain deep on the left side in which case a left-sided Moschcowitz and Halban procedures can be performed to reduce the possibility of enterocele formation.

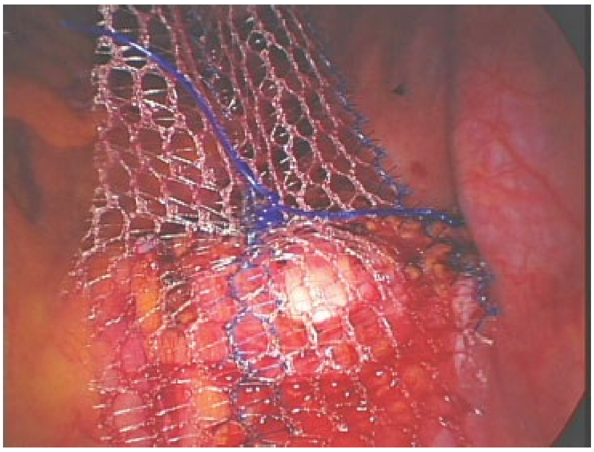


Figure 100.5 Mesh is attached to the anterior longitudinal ligament on the sacral promontory in the midline with a Prolene suture.

Types of Prosthesis

Ideally, the prosthesis used for LSC should be durable over a patient's lifetime, user friendly, and cost-effective and have a minimal risk of complications including erosion, infection, chronic inflammation, tissue contraction, pain, and dyspareunia. A variety of synthetic meshes and biological grafts have been described for both ASC and LSC. There is insufficient research to provide surgeons with answers as to whether synthetic meshes are more durable than biological grafts or whether specific meshes are superior to others with respect to clinical outcomes and complications. In a review of surgery for apical prolapse, Barber and Maher concluded that polypropylene mesh is the preferred graft sacral colpopexy [37].

Surgeons should base their selection of synthetic mesh used for LSC on a thorough understanding of the important biomechanical and biocompatible properties of each available mesh. There is an emerging consensus that lightweight, open-weave, monofilament polypropylene meshes are the most suitable of the existing meshes for use in surgery for pelvic organ prolapse. New-generation meshes specifically designed for pelvic organ prolapse surgery will require appropriate animal and clinical evaluation before being recommended for use in prolapse surgery.

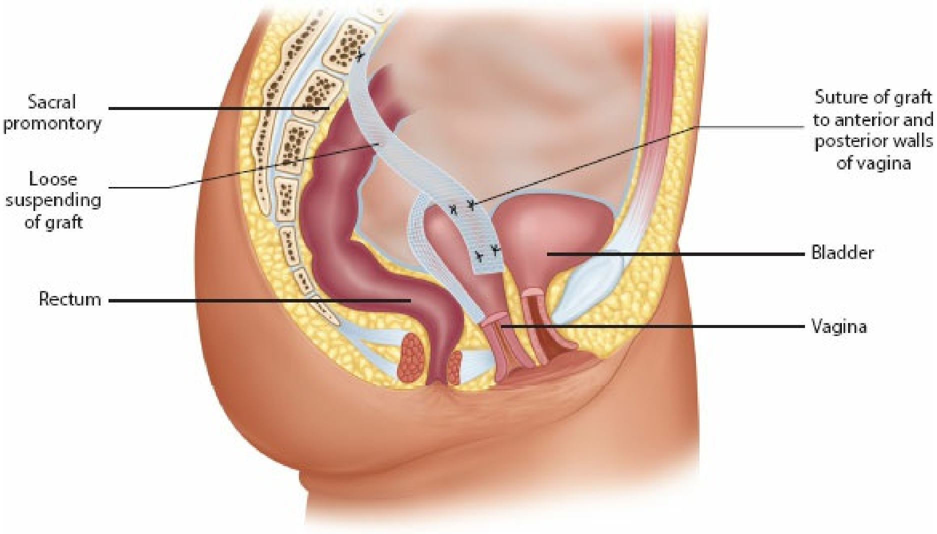

Sacral promontory
Loose suspending of graft
Rectum
Suture of graft to anterior and posterior walls of vagina
Bladder
Vagina

Figure 100.6 Mesh is sutured to the vaginal vault with extension down the upper anterior and posterior vaginal walls. The mesh is then sutured to the sacral promontory without placing tension on the vaginal vault.

Although biological grafts are unlikely to erode, poor durability remains a major concern. FitzGerald et al. [38] reported a high prevalence of prolapse recurrence following ASC using freeze-dried, irradiated donor fascia. At 12 months, after ASC, 43% experienced failure and this increased to 83% at 17 months. Of the 16 women who underwent repeat ASC with mesh, no graft material from initial ASC was identified in 13 (81%) cases, indicating a high rate of graft degradation and resorption. The authors concluded that the use of freeze-dried, irradiated donor fascia for ASC was associated with an unacceptably high failure rate.

Culligan et al. [39] reported on an RCT of 115 subjects comparing porcine dermis with polypropylene mesh for LSC. At 12 months, subjective and objective outcome were similar in both groups. The objective cure rates were 80.7% and 86.2% for porcine dermis and mesh groups, respectively.

Until more clinical information becomes available on the use of biological grafts for ASC and LSC procedures, with the possible exception of porcine dermis, biological grafts should be reserved for specific indications. These indications might include extremely thin vaginal epithelium, replacement for mesh that has required removal, prior pelvic irradiation, and situations of high risk for mesh infection (e.g., bowel resection during combined surgery for genital and rectal prolapse). However, there remains a lack of evidence to support the use of biological prostheses over mesh in these circumstances.

Sacral Promontory Fixation

Various methods of attaching the suspending prosthesis onto the sacral promontory at LSC have been reported. These include sutures, bone anchors, staples, and helical tacks [12,32,34,35,40,41]. There is a lack of research comparing the various methods of fixation of the prosthesis onto the sacral promontory. Due to the technical difficulties involved in laparoscopic suturing with LSC, some surgeons have preferred bone anchors and staples to sutures.

Surgeons have described attachment of the prosthesis to different points on the sacrum. Birnbaum advocated placement of the prosthesis at the level of S3–S4 [42]. Sutton et al. [43] advocated placement of the prosthesis at the level of S1–S2 in order to reduce the risk of massive sacral bleeding. The author’s preference has been to use the anterior longitudinal ligament on the sacral promontory and to attach the mesh with sutures. The sacral promontory is the most accessible point on the sacrum and is particularly well visualized at laparoscopic surgery. Mesh should not be fixed to the lumbosacral intervertebral disk because of the risk of discitis, hemorrhage, and pain from damage to the sensory nerve supply [44]. Superior visualization at the sacral promontory allows the surgeon to avoid damage to vascular structures more easily and to control excessive sacral bleeding than does the hollow of the sacrum. Use of the sacral promontory has no detectable negative effect on the vaginal axis [43].

Robotic Assistance

The use of robotic assistance for laparoscopic sacrocolpopexy is described in Chapter 103.

Perioperative Care

It is the author’s practice that patients be administered a limited bowel preparation in the afternoon of the day prior to surgery. Patients should have an oral intake of clear fluids only during the 12 hour period prior to the commencement of fasting before surgery. Bowel preparation is used in order to improve surgical exposure rather than for anticipated bowel trauma. The potential disadvantages of bowel preparation include dehydration, electrolyte disturbance, patient discomfort, and intraoperation diarrhea. Intravenous broad-spectrum antibiotic therapy and subcutaneous thrombotic prophylaxis are administered with anesthesia induction and continued postoperatively. Handling of the mesh is kept to a minimum. Maintaining hemostasis, liberal use of pelvic irrigation, evacuation of blood from the pelvis, and use of monofilament sutures to attach the mesh onto the vagina are all important measures undertaken to reduce the risk of mesh erosion. At the completion of surgery, cystoscopy may be undertaken to exclude ureteric or bladder injury. Digital rectal and vaginal examination should be performed to exclude the presence of perforating sutures.

Following discharge from hospital, patients should avoid strenuous activity for 3–4 weeks. By this time, the mesh will have become incorporated into the tissues and patients can then resume activities of normal daily living. Patients should avoid sexual intercourse for at least 6 weeks following surgery. Pelvic floor exercises may be recommenced any time after surgery [45].

CONCOMITANT LAPAROSCOPIC HYSTERECTOMY OR SUBTOTAL HYSTERECTOMY

The principles of LSC may be applied to uterovaginal prolapse by combining LSC with either laparoscopic total hysterectomy or subtotal hysterectomy (Figure 100.7). A recent review of LSC performed concomitantly with supracervical (subtotal) hysterectomy reported an anatomic success rate of 90%–100%, subject success rate of 80%–95%, and mean reoperation rate of 3% [46].

CONCOMITANT ANTI-INCONTINENCE SURGERY

Urodynamic assessment is appropriate for women with symptomatic stress incontinence and vaginal vault prolapse. If urodynamic stress incontinence is demonstrated, then concomitant anti-incontinence surgery, in addition to the LSC operation, is indicated. Laparoscopic colposus-pension or a midurethral tape procedure—for example, the tension-free vaginal tape (TVT) operation—can be employed. Occasionally, a transurethral bulking agent is indicated for women with a rigid urethra and, typically, previous failed anti-incontinence surgery. The simplicity and demonstrated effectiveness of the TVT procedure makes this an attractive option over the laparoscopic colposuspension procedure. In a randomized trial of 72 women, Paraiso et al. found the TVT procedure to result in significantly greater objective and subjective cure rates for stress incontinence than laparoscopic Burch colposuspension [47]. This finding was supported by Valpas et al. [48]. Furthermore, the opposing vector effect of combining LSC with laparoscopic colposuspension may result in persistence of postoperative stress incontinence.

The role of anti-incontinence surgery for occult stress incontinence during surgery for pelvic organ prolapse remains the subject of ongoing debate. Nygaard et al. [22] emphasized the clinical challenge of patients with occult stress incontinence and vault prolapse. A systematic review by Maher et al. was unable to determine whether or not “potential stress urinary incontinence detected on reduction of prolapse prior to surgery is best treated with formal continence surgery at the time of prolapse surgery, rather than being left untreated” [20]. Misrai et al. reported the development of de novo stress urinary incontinence in 13% women after LSC. In this study, 53 women without preoperative stress urinary incontinence or occult stress incontinence were assessed [21].

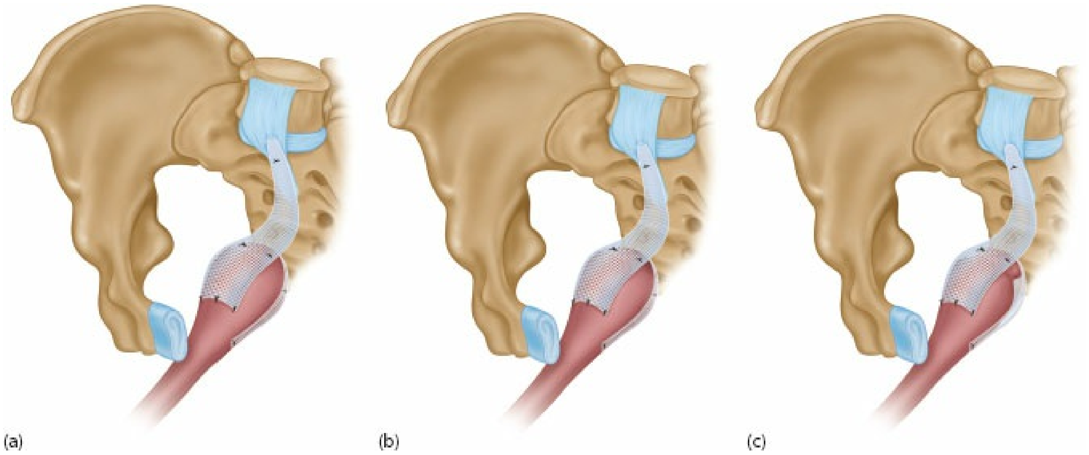


Figure 100.7 Three types of laparoscopic sacral colpopexy (LSC). (a) LSC for posthysterectomy vault prolapse. (b) LSC used in conjunction with laparoscopic total hysterectomy. (c) LSC used concomitantly with laparoscopic subtotal hysterectomy.

Based on the current knowledge, the decision to offer concomitant anti-incontinence surgery during LSC is up to the clinical judgment of the surgeon after a careful discussion with the patient. The author gives patients the option of a concomitant TVT procedure or laparoscopic colposuspension during the LSC procedure when occult stress incontinence is present. Patients should always be warned of the possibility of persisting or de novo urinary incontinence developing following LSC, whether or not anti-incontinence surgery is also performed. The prevalence of de novo postoperative urinary incontinence is approximately 15%–18% [49].

RESULTS

To date, only a small number of studies on LSC have been reported [12,13,24–30,32,40,41,50,51]. All studies report high success rates and low morbidity with the LSC procedure. However, the different study methodologies employed make the outcome data difficult to collate. It is difficult to draw any conclusions about the long-term outcomes for LSC due to a lack of a standardized technique, wide variation in the definition of outcomes, and lack of control for potential confounders, especially concomitant surgery. In some series, the majority of subjects underwent laparoscopic sacral hysteropexy (LSH) rather than LSC [13,32,34]. The surgical outcomes in these studies did not differentiate between LSC and LSH.

Higgs et al. [12] reported on 140 consecutive cases treated by LSC of whom 103 were available for long-term follow-up [12]. This is the largest case series of LSC reported to date with a median follow-up of 66 months. A prior vaginal hysterectomy had been performed in 48% of cases and prior abdominal hysterectomy in 52%. Prolene mesh was used in all cases and fixed to the sacrum by either sutures or staples. Concomitant surgeries included laparoscopic colposuspension (37.8%), paravaginal repair (19.4%), vaginal repair (19.4%), rectopexy (3.8%), anal sphincter repair (1.9%), and transurethral collagen injection (1%). The average age of the patients was 58 years and the mean duration of surgery was 145 minutes overall and 107 minutes if LSC was the only procedure. Review was conducted independent of the surgeon. Of the 140 women, 66 were available for follow-up examination and 92% (objective success rate) of these demonstrated good long-term vault support. A total of 103 women completed follow-up questionnaires and the subjective success rate was 62% with 64 of the 103 women reviewed reporting no “presence of a lump.”

Rozet et al. [13] reported on a large case series of 363 women treated by either LSC or LSH with mesh interposition between 1996 and 2002. Of the 363 cases, 97 (26.7%) underwent LSC (82 women had posthysterectomy vault prolapse and 12 underwent combined LSC and hysterectomy). The other 266 (73.3%) cases underwent LSH with mesh interposition. A polyester mesh, silicone coated on one side, was used with anterior and posterior mesh extensions. The mesh was sutured onto the sacral promontory and the peritoneum closed over the mesh. This study reported outcomes for the whole group and a subanalysis of patients who underwent LSC was not performed. A concomitant TVT procedure was performed in 163 (45%) cases, all of whom demonstrated the signs of stress incontinence preoperatively. The average age of the 363 subjects was 63 years and the average operating time 97 minutes. The prevalence of recurrent prolapse was only 4%.

Sarlos et al. reported on a 5-year follow-up study of 68 subjects treated by LSC. Complete anatomical cure (i.e., stage 0 prolapse in any compartment) was reported in 83.8% of subjects with a 3.5% reoperation rate. Subjective cure was reported in 95.3% of subjects [52].

Comparative Studies

Paraiso et al. [53] compared 56 women with 61 women treated by LSC and ASC, respectively, in a nonrandomized, observational study. LSC required a significantly longer mean operating time than ASC (269 versus 218 minutes). However, LSC was associated with significantly less blood loss and a shorter hospital stay. In the LSC group, 11% of subjects required “further procedures for the pelvic floor, excluding injections” compared with 5% in the ASC group. Similar complication rates were observed in both groups.

Klauschie et al. [54] compared the anatomic and perioperative outcomes for 43 women treated by LSC with 41 women ASC in a nonrandomized, retrospective, observational study. At 1 year, the mean improvement in the POPQ C-point from baseline was similar in both groups. The baseline to 1 year C-point improvement was 7.73 and 7.81 cm for the LSC and ASC, respectively.

Geller et al. [55] compared the short-term (6 weeks) outcomes of robotic LSC with ASC in a nonrandomized, retrospective, observational study. Of the 178 subjects treated, 73 and 105 underwent robotic LSC and ASC, respectively. The mean operating time was longer for robotic LSC than ASC (328 versus 225 minutes) but the mean blood loss was less for robotic LSC (103 versus 255 mL). At follow-up, there was a significant, but not clinically relevant, improvement in the median POPQ C-point score for the robotic compared to the abdominal group (−9 versus −8 cm, $p = 0.008$).

Marcickiewicz et al. [56] compared 60 women with 51 women treated by LSC and vaginal sacrospinous colpopexy (VSC), respectively, in a nonrandomized, observational study. The operating time was significantly longer for the LSC group (median: 129 minutes) compared to the VSC group (median: 62 minutes). Complications and days in hospital were similar in both groups. The median follow-up period was 33.6 and 28.4 months for the LSC and VSC groups, respectively. No recurrent vault prolapse occurred in either group, but 25% and 27.4% of subject in the LSC and VSC groups, respectively, had cystoceles at follow-up. In the LSC group, 16.7% of subjects had rectoceles compared with 0% in the VSC group at follow-up.

Anger et al. randomized 78 women to either robotic (robotic sacral colpopexy [RSC]) or LSC [57]. Compared to RSC, LSC took, on average, 24.4 minutes less time ($p = 0.03$). RSC was more expensive than LSC but outcomes at 6 months and complications were similar in both groups.

COMPLICATIONS

Just over 3.7 million women underwent surgery for pelvic organ prolapse from 1979 to 1997 in the United States; this included 31,387 women with laparoscopically performed prolapse surgery. Complications in association with all the various procedures used to treat prolapse occurred in only 5.5% of cases. In women who underwent laparoscopic surgery to manage pelvic organ prolapse, complications were identified in only 6.6% of patients, which is comparable with other prolapse operations. Women treated laparoscopically had a significantly higher risk of pulmonary edema but a lower risk of urinary complications [58].

Higgs et al. [12] reported that immediate and short-term complications of LSC were rare. However, the mesh erosion rate was high at 9%. When the mesh was introduced vaginally, the erosion rate was 20% but only 6% when introduced laparoscopically. The transvaginal introduction of the mesh was performed in 20 cases but abandoned in favor of laparoscopic introduction after the authors noticed a high erosion rate with this technique. The mesh erosion rate reported by Geller et al. following robotic LSC was also 6% [55].

The main complications of LSC reported by Rozet et al. included eight conversions to ASC, three vaginal mesh erosions, two mesh infections, one bowel obstruction requiring bowel resection, and one case of spondylitis. No case of postoperative dyspareunia was reported [13].

In the series reported by Cosson et al., conversion from LSC to ASC was required for 7.8% of cases [33]. One rectal and two bladder injuries were reported. Reoperation for hemorrhage or hematoma was required in three women. A conversion rate of 5% from robotic LSC to ASC was reported by Geller et al. [55].

CONCLUSION

Vaginal vault prolapse following hysterectomy is a challenging clinical problem. The goals of surgery when treating vaginal vault prolapse are

- The relief of patients’ symptoms
- The correction of vaginal vault prolapse by restoring the normal pelvic anatomy where feasible
- The correction of coexisting urinary, coital, and lower bowel dysfunction
- The avoidance of the development of urinary, coital, and lower bowel dysfunction
- The achievement of a durable result, which in some cases may require the use of prosthetic materials

The “best” operation for treating vaginal vault prolapse remains the subject of ongoing debate. In treating vaginal vault prolapse, vaginal, abdominal, and laparoscopic approaches should not be viewed as competing procedures [59]. The choice of operation to treat vaginal vault prolapse depends on many factors: the surgeon’s training and experience will influence the choice of surgery, and a recommendation for a specific operation can only be made after careful clinical assessment and after taking into consideration the patient’s age, medical condition, coital activity, level of physical activity, and a history of failed prior surgery.

Systematic review of the surgical management of prolapse has demonstrated the ASC procedure to be associated with a lower recurrence of vault prolapse and less dyspareunia than vaginal approaches [18–20,22]. However, when compared to vaginal approaches, ASC required a longer operating time and patients were slower to return to activities of normal daily living. LSC should be performed in a similar fashion to ASC. Based on the reported experiences of many surgeons over the past 50 years [22] and upon personal experience of ASC and LSC procedures, the following important principles of ASC and LSC are proposed:

- Careful patient selection
- Appropriate level of surgical experience and expertise
- Use of a biocompatible prosthesis
- A broad area of prosthesis attachment to the vaginal vault and upper anterior and posterior vagina
- Fixation of the prosthesis to the anterior longitudinal ligament on the sacral promontory rather than to the sacral hollow
- Placement of the prosthesis without tension to reduce the risk of postoperative urinary incontinence

From the limited available data, LSC appears to be a highly effective procedure for the treatment of vaginal vault and marked uterovaginal prolapse. The LSC procedure combines the accepted effectiveness of ASC over vaginal operations for vault prolapse with the significant benefits of laparoscopic surgery. These benefits include superior surgical visualization, less pain, and quicker return to activities of normal daily living. The major limitation of LSC is the high degree of laparoscopic and reconstructive pelvic surgical skills required to perform this operation effectively and safely. With continued advances in laparoscopic equipment (including robotics) and more widespread training in advanced laparoscopic surgery, LSC is likely to gain in popularity. Currently, there is a paucity of data on the effectiveness, functional outcome, and safety of LSC. Further prospective studies, including more comparative studies, are required to evaluate the role of the LSC procedure.

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101 Laparoscopic Sacrohysteropexy

Helen Jefferis, Natalia Price, and Simon Jackson

LAPAROSCOPIC HYSTEROPEXY

Hysteropexy should be considered when it is appropriate to offer a surgical remedy for uterine prolapse.

The absolute indication is fertility preservation in women who have not yet completed childbearing. However, this is a small group of patients; most women presenting requiring surgery for prolapse have no desire for further children, indeed the majority are postmenopausal.

In the authors' experience, the other more prevalent indications for hysteropexy include patient request and superior outcome. The latter is a contentious statement; clinical data is still sparse and will be discussed in this chapter. However, when there is loss of apical support, traditional vaginal hysterectomy will not correct defects. This is most readily apparent when women present with procidentia; it is self-evident that hysterectomy will not treat vaginal eversion. If hysterectomy is performed, additional vaginal suspension needs to be provided, usually either by sacrospinous fixation or sacrocolpopexy.

Hysteropexy, in our view, offers a more logical approach, and furthermore avoids vaginal mesh, with the attendant extrusion risk it carries.

THE TRADITIONAL APPROACH FOR UTERINE PROLAPSE

Vaginal hysterectomy has long been the standard approach for management of uterine prolapse, with the first successful planned case being credited to Langenbeck in 1813. While it has served the gynecologist well for many years, its continued use raises some significant questions. Vaginal hysterectomy fails to address the underlying deficiency in connective tissue pelvic floor support [1] that causes prolapse; indeed, the uterosacral ligaments are cut during the operation—it is hardly surprising that recurrent prolapse rates are so high, with rates of up to 40% described in the literature [2,3]. Recurrence can manifest with vaginal vault eversion, or more commonly recurrent enterocoele/cystocele. We know that cystocele commonly arises because of loss of apical type 1 vaginal support [4], and until apical support is established, it will recur. Repeated colporrhaphy may ultimately shorten, narrow, and scar the vagina.

Furthermore, hysterectomy removes a healthy organ which may play a role in patients' individual and sexual identity. It certainly isn't playing a role in their prolapse etiology; uterine prolapse is merely a sign of support failure, not the underlying cause! Vaginal hysterectomy is associated with significant postoperative morbidity. Up to one in four women may develop a vault hematoma following vaginal hysterectomy.

Increasingly, women are requesting uterine conservation [5]. This may be due to the wish to preserve fertility, or due to the belief that female identity is bound up in the female genital organs. It frequently arises after they have researched literature and the internet themselves and become aware that there are alternatives to hysterectomy. The overall rate of hysterectomy as treatment for menstrual dysfunction is also declining significantly.

THE HISTORY OF UTERINE PRESERVING PROLAPSE SURGERY

The concept of uterine preservation surgery for pelvic organ prolapse is not new.

In 1888, Archibald Donald first described the Manchester repair as an alternative to vaginal hysterectomy for patients with uterine prolapse, although this may have been a more useful technique for patients with an elongated cervix rather than a true uterine descent. In 1934, Victor Bonney highlighted the passive role of the uterus in uterovaginal prolapse, telling us it was merely the symptom of underlying poor pelvic floor support [6]. Subsequent surgeons have developed techniques for uterine preservation via a vaginal, abdominal, or laparoscopic approach.

Vaginal Approach

In 1966, Williams [7] described a technique for transvaginal uterosacral–cervical ligament plication and reported on outcomes for 20 women undergoing this procedure, with 3 "failures" encountered within a 6-month follow-up period. His method involved a posterior colpotomy with division of the uterosacral ligaments from the cervix, plication across the midline, and reinsertion into the cervix. The cardinal ligaments are then plicated anteriorly across the midline.

The concept of sacrospinous hysteropexy was first described by Richardson et al. [8] in 1989. The cervix or uterosacral ligament is transfixed to the sacrospinous ligament using either permanent or delayed absorbable sutures. In 2001, Maher [9] reported a small comparison study between sacrospinous hysteropexy and vaginal hysterectomy with sacrospinous vault fixation, with no differences in objective or subjective outcomes at follow-up. Other studies have suggested that sacrospinous hysteropexy has a shorter operative time and reduced blood loss as compared to vaginal hysterectomy [10]. One study also reported less postoperative incidence of overactive bladder symptoms in the sacrospinous hysteropexy group [11]. Dietz et al. [12] describe an increased risk of anterior compartment prolapse following sacrospinous hysteropexy with an incidence of up to 40%. Sacrospinous hysteropexy is the most studied vaginal technique for uterine preservation prolapse surgery; however, in general, the studies assessing it are of poor quality, with small numbers, of short follow-up periods, of lack of controls, and with limited functional outcome data.

The technique of posterior vaginal slingplasty [13] was first described in 2001, using a mesh kit to create "neo-uterosacral ligaments." One prospective comparison study quoted a 91.4% patient satisfaction rate postsurgery [14], but cumulative data suggest a high incidence of mesh complications with up to 21% mesh erosion rate [15].

Abdominal Approach

A number of methods for abdominal hysteropexy have been described, including transfixing the uterus to the anterior abdominal wall and ventral fixation to the pectineal ligaments. Most techniques use the sacral promontory as the fixation point, giving rise to the term abdominal sacrohysteropexy.

Abdominal suture sacrohysteropexy [16] was described as early as 1957, with the uterine fundus being fixed to the sacral promontory with silk sutures. More recent techniques have utilized a variety of synthetic meshes to aid fixation. In 1993, Addison [17] first described a technique for resuspending the uterus to the sacrum using Mersilene^{TM} mesh. Leron and Stanton [18] followed up 13 women undergoing abdominal sacrohysteropexy and found it to be a safe and effective surgery for the management of uterine prolapse.

Roovers et al. [19] reported on a comparison between sacrohysteropexy and vaginal hysterectomy with vault fixation; recurrence was higher in the abdominal surgery group (22%) than in the vaginal hysterectomy group (2.5%). Costantini et al. [20], however, found no subjective or objective difference in functional outcomes when comparing a group of patients undergoing sacrohysteropexy with those undergoing hysterectomy with sacrocolpopexy. Sacrohysteropexy was associated with a shorter operative time and hospital stay, with a reduction seen in intraoperative blood loss. It is difficult to interpret data reporting comparisons between abdominal sacrohysteropexy and hysterectomy due to variations used in surgical technique and differences in mesh type, size, shape, and attachment points.

Laparoscopic Approach

Laparoscopic abdominal surgery has, with very few exceptions, replaced laparotomy in many centers. The laparoscope confers better vision than laparotomy, allowing a magnified, high definition view. Furthermore, the long instruments allow better pelvic access, particularly behind the uterus, than laparotomy confers.

A number of laparoscopic uterine suspension procedures have been described using different methods.

Laparoscopic ventrosuspension proposes suturing the round ligaments to the rectus sheath. The round ligament is not however particularly robust, and perhaps as expected, it has been shown to have poor outcomes, with one case series of nine women reporting recurrent prolapse in all but one patient within 6 months [21]. Chen et al. [22] used mesh to suspend the uterus by attachment to the anterior abdominal wall. While they reported good outcomes, all patients experienced significant pain or dragging sensations over the mesh attachment site. Laparoscopic uterosacral ligament plication was first described by Wu et al. in 1997, with good results in a small case series [23]. Maher et al. [24] modified this technique to include reattachment of the uterosacral ligaments to the cervix and closure of the pouch of Douglas, with an objective success rate of 79% in 43 women at 12 months.

Recently, techniques have focused on using the sacral promontory as a point of fixation. Krause et al. [25] followed up 81 women undergoing laparoscopic sacral suture hysteropexy, placing sutures through the posterior aspect of the cervix, and transfixing to the sacral promontory via the right uterosacral ligament. Objective correction of prolapse was seen in 94% of patients.

Cutner et al. [26] developed the technique of laparoscopic uterine sling suspension. The peritoneum is opened over the sacral promontory and the rectum is reflected laterally. A tunnel is created by blunt dissection underneath the peritoneum from the sacral promontory to the insertion of the uterosacral ligament complex into the cervix on either side. Mersilene tape on a needle is placed through the cervix, through the uterosacral ligaments, and through the peritoneal tunnels on each side before being tacked to the sacral promontory bilaterally to suspend the uterus. This technique aims for the sling to resemble newly created uterosacral ligaments.

Oxford’s experience with hysteropexy has shown that mesh, when attached to the posterior aspect of the cervix, or to the cervical stump following hysterectomy, has a high avulsion rate. We therefore developed a method of complete cervical encirclage (The Oxford Hysteropexy, Price et al. 2010) using a bifurcated polypropylene mesh [27]. Initial follow-up studies [28] show good outcomes with significant improvement ($p < 0.001$) in all parameters of International Consultation on Incontinence Questionnaires-Vaginal Symptoms (ICIQ-VS) and Pelvic Organ Prolapse Quantification (POP-Q) scores postsurgery.

The rest of this chapter looks at the technique of laparoscopic hysteropexy in more detail.

AIMS OF LAPAROSCOPIC HYSTEROPEXY

- To restore and reinforce uterine support by suspending the uterus from the sacral promontory using Type 1 polypropylene mesh. Two strong attachment points are used; the cervix and the anterior longitudinal ligament overlying the sacral promontory.
- To restore vaginal length without compromising caliber.
- By restoring apical support, a reduction in anterior prolapse is seen, consistent with the importance of restoring level 1 support in cystocele repair.
- By restoring apical support, a reduction in enterocoele is seen; low rectocele, however, frequently requires a concurrent vaginal repair.

The theoretical advantage is that this type of repair, by augmenting weak connective tissue with prosthetic prolene, confers stronger apical support resulting in lower recurrence rates. It allows the patient to retain their fertility; and by avoiding vaginal surgery, there is a lower potential for dyspareunia and sexual dysfunction.

TECHNIQUE: THE OXFORD HYSTEROPEXY

The procedure is performed under general anesthesia with the patient supine and in semilithotomy position. A urinary catheter and uterine manipulator are inserted. A four-port laparoscopic technique is used with 10 mm umbilical, two 5 mm lateral, and a 12 mm suprapubic port inserted. After identifying the sacral promontory, the peritoneum is incised with bipolar graspers and monopolar scissors to identify a safe window of periosteum. A peritoneal relaxing incision is then used medial to the right ureter to retract it from the surgical site and extended into the pelvis, lateral to the rectum. The right uterosacral ligament is identified and the peritoneum is opened over this, where the uterosacral ligaments insert into the cervix. A flap of peritoneum is mobilized to facilitate reperitonization. The vesicouterine peritoneum is incised to reflect the bladder away and bilateral avascular windows are created in the broad ligament, lateral to the uterine arteries, at the level of the internal os.

The authors use a bifurcated polypropylene Type 1 macroporous nonabsorbable mesh (ProLite^{TM}; Atrium Medical Corporation), bringing the arms of the mesh through the broad ligament windows. This is transfixed to the anterior cervix using nondissolvable, nonabsorbable polyester 2-0 sutures

(Ethibond®). The mesh is attached to the sacral promontory under moderate tension using two to three 5 mm helical fasteners (Pro-Tack®, Covidien). The mesh is then completely reperitonized using Monocryl® sutures [29] (Figures 101.1 and 101.2). The technique has evolved over time; initially reperitonization was not performed, however after two patients undergoing subsequent laparoscopies were found to have bowel adhesions to the mesh, this adaptation was introduced.

Approximate operating times in the authors' unit are 45–60 minutes, although senior trainees under supervision usually require about 90 minutes.

ANATOMICAL ANOMALIES

The Oxford Hysteropexy is often straightforward; it is less technically challenging than laparoscopic sacrocolpopexy. However, surgery can be complicated by unexpected anatomical anomalies and the surgeon should be aware of these to minimize risk. Less experienced laparoscopic surgeons would be well advised to consent patients for alternative options, such as vaginal surgery, should anatomical anomalies make laparoscopic surgery too challenging.

Sacral Promontory

The aorta and vena cava generally bifurcate above L5; there is a safe window at L5/S1 for mesh fixation (see Figure 101.3). However, low bifurcations are seen relatively commonly and, unless visualized, dissection and promontory fixation can result in great vessel trauma and life-threatening hemorrhage (see Figure 101.4). The left common iliac vein can be particularly difficult to identify as it traverses the lumbar spine. Positive peritoneal insufflation pressure, in combination with steep Trendelenberg tilt, can cause venous emptying and the venous appearances are sometimes not dissimilar to peritoneum (see Figure 101.5).

Fat around the sacral promontory makes dissection more difficult and sacral fat doesn't necessarily correlate with body mass index; many larger patients have an easy sacral promontory and vice versa.

Beware the boggy sacral promontory (*called the pillow sign, on account of the similarity to pressing on a pillow*); when the laparoscopic instruments palpate soft tissue rather than firm sacral promontory, you are either encountering periosteal fat, or low bifurcating great vessels; dissect carefully!

Pelvic Sidewall

There is usually a very safe window between the rectosigmoid medially and the ureter laterally that can be opened and used to bury the sacral mesh tail. However, low iliac vein anomalies can be encountered (see Figure 101.6), so the safe technique is to lift the peritoneum off the pelvic sidewall before incising.

Broad Ligament

There is usually a large avascular window in the broad ligament lateral to the uterine artery that can be safely opened. However, large venous anomalies can occur, and identifying an avascular window can be problematic (see Figure 101.7). *Beware: veins and peritoneum both look blue*!

LAPAROSCOPIC APPROACH

Over recent years, there is ever growing interest in a laparoscopic approach to surgery, with many new techniques being adopted to modify procedures previously performed via the open or vaginal route. One major advantage is the magnified image giving excellent intraoperative visualization of the pelvic anatomy. The other significant advantage is improved access to parts of the pelvis that are difficult to reach via an abdominal incision. In particular, access to the Pouch of Douglas is enhanced at laparoscopic hysteropexy, compared with laparotomy. General advantages of laparoscopic compared to open surgery are reduced hospital stay, reduced need for analgesia, quicker recovery, and minimal blood loss. There is suggestion that adhesion formation is also reduced.

The main disadvantage of laparoscopic surgery is the initial increase in operating time while the surgeon learns laparoscopic techniques. Focused training and use of skills labs and laparoscopic simulators can help to address this issue. As a new generation of surgeons develop, trained from the outset in laparoscopic techniques, such concerns will become obsolete.

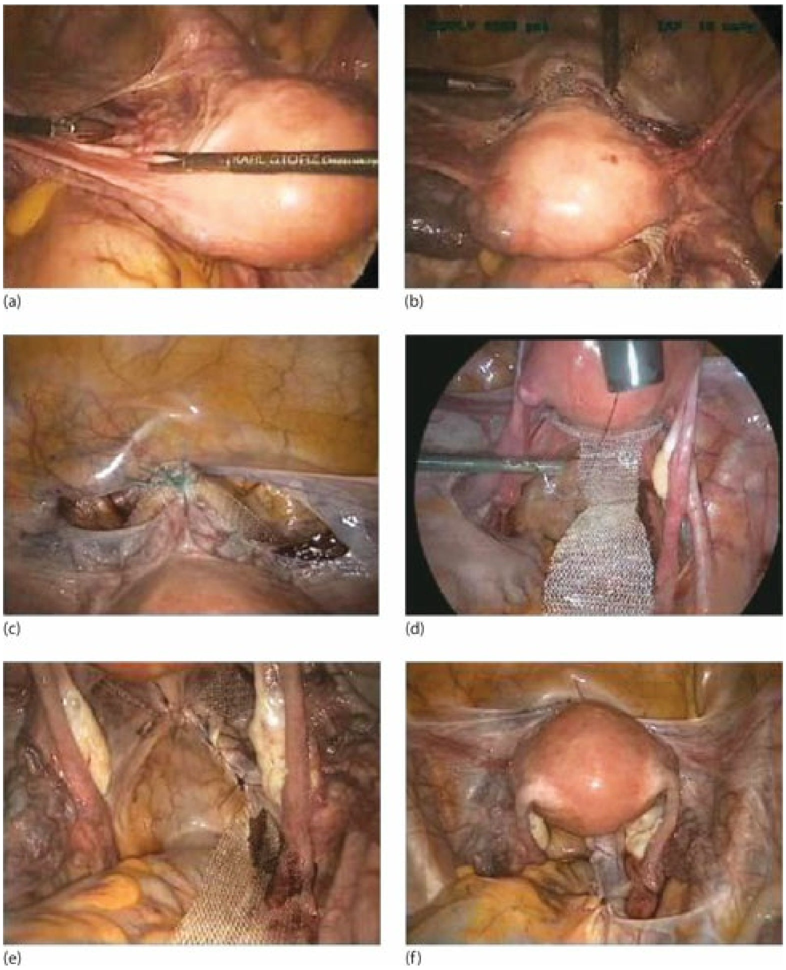

Figure 101.1 The surgical technique of laparoscopic hysteropexy: (a) Opening of the left broad ligament. (b) Mesh inserted through windows in the broad ligament. (c) Suturing of the mesh over the anterior cervix. (d, e) Peritonization of the mesh prior to fixation to the sacral promontory. (f) Mesh is fixed to sacral promontory and peritonization completed. (Reproduced from Price N et al., *Br J Obstet Gynaecol*, 117, 62, 2010. With permission.)

Robotic surgery may also have a place in the future although its benefit in gynecological surgery is still highly debatable; some contend that the learning curve for robotic surgery is quicker than conventional laparoscopic surgery.

Many skilled laparoscopic surgeons, in fact, find that if they are in a situation where open surgery is required, the operating times are slower and visualization of the anatomy is poorer.

OUTCOMES

Outcome data post laparoscopic hysteropexy are sparse. One prospective observational study [28] has reported outcomes following laparoscopic sacrohysteropexy in 140 women. Follow-up time varied between 1 and 4 years. Eighty-nine percent of women felt their prolapse was “very much” or “much” better. There was a significant improvement ($p < 0.001$) in all parameters of ICIQ-VS and POP-Q scores postsurgery. Four percent of women experienced further apical prolapse of which half underwent further surgical intervention. This compares favorably with the risk of vault prolapse following vaginal hysterectomy [30]. One reason for recurrent apical prolapse was the initial mesh either being left too loose or stretching in vivo. This was simply treated by mesh plication (Prolene® or Ethibond nonabsorbable sutures). The authors have now modified their technique and are using a more robust mesh, 5 cm in width compared with a previous 3 cm mesh that was more susceptible to stretch. The rate of serious complications was 4%, and comprised of bowel adhesions (prior to the modified reperitonization technique), broad ligament vascular injury and one pulmonary embolus. Ninety-two percent of women when asked would recommend the operation to a friend.

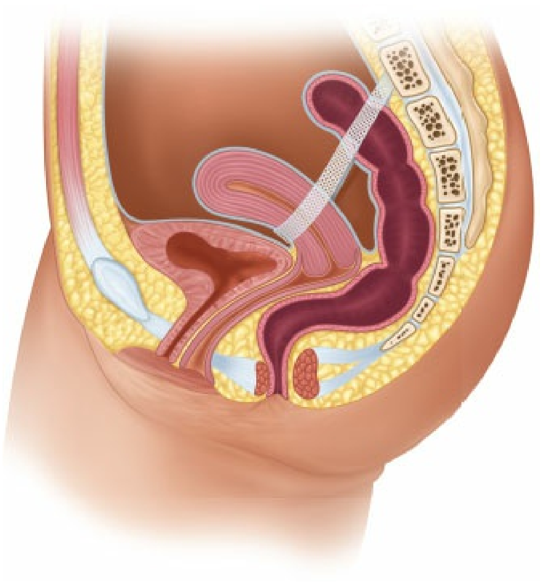

Figure 101.2 Diagram of hysteropexy: the uterus is resuspended using bifurcated mesh.

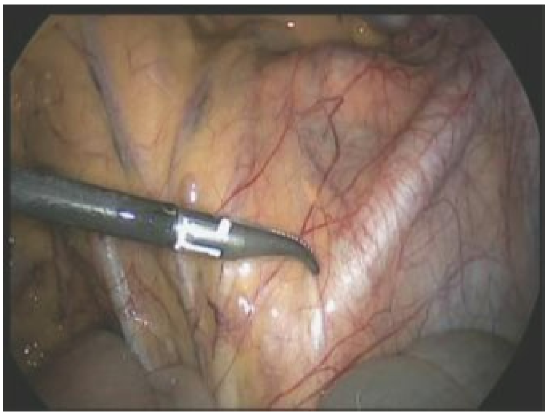

Figure 101.3 Sacral promontory showing normal aortic bifurcation.

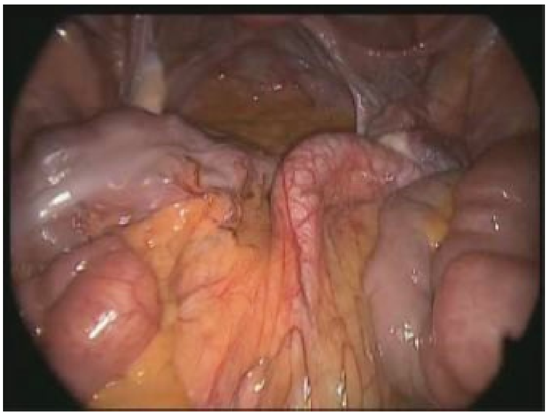

Figure 101.4 Sacral promontory showing low aortic bifurcation.

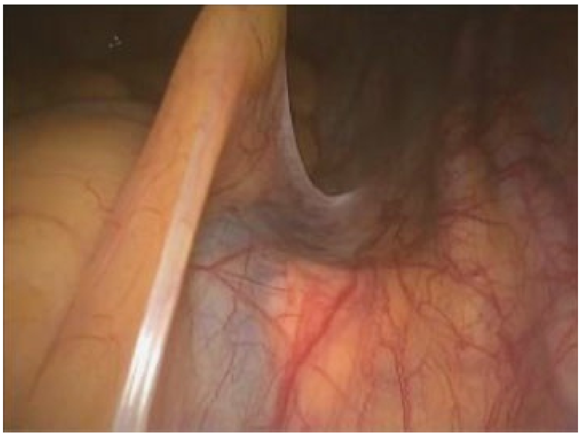

Figure 101.5 Left common iliac vein running over the sacral promontory.

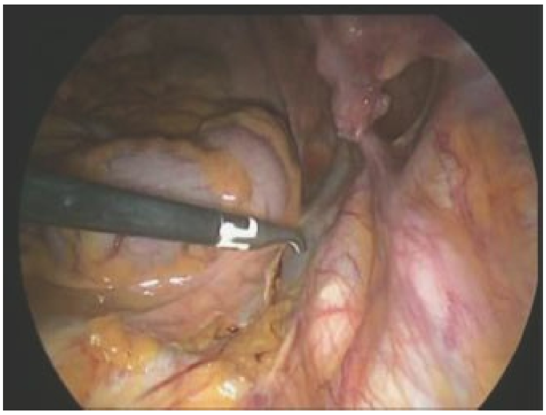

Figure 101.6 Low right iliac vein on pelvic sidewall.

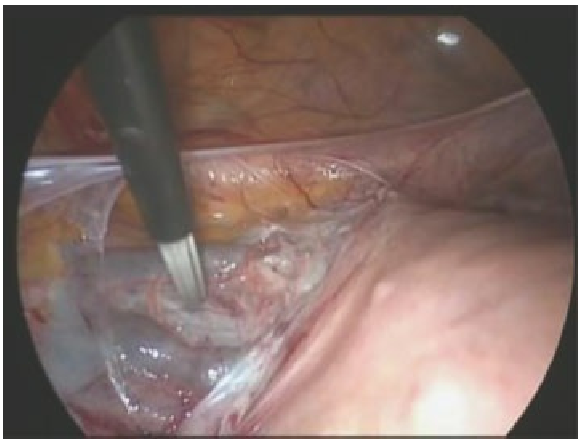

Figure 101.7 Large vein in the broad ligament. A safe window can be found in most cases.

As this is still a relatively new technique, more outcome data over a longer time frame is needed to enable comparison with more traditional approaches. The outcomes of the Vault or Uterine prolapse surgery Evaluation (VUE) study [31] (randomized multicenter trial comparing uterine preservation surgery with vaginal hysterectomy) are eagerly awaited, although the methodology does allow any surgical hysteropexy technique to be incorporated, and this will adversely affect the power of the study.

DISADVANTAGES

Vaginal hysterectomy eliminates the possibility of uterine or cervical pathology, and there are incidences of unexpected pathology being detected at pathological examination of the removed uterus [32]. However, this benefit is less relevant with current advances in minimally invasive treatment of abnormal uterine bleeding. The cervical screening program is reducing cervical cancer incidence, and endometrial cancer classically presents at an early stage with uterine bleeding. Therefore, hysterectomy, to prevent future malignancy, seems irrational and totally unnecessary. There may be some value in screening women listed for laparoscopic sacrohysteropexy with an ultrasound scan before surgery.

FERTILITY FOLLOWING UTERINE PRESERVATION SURGERY

Theoretically, one advantage of sacrohysteropexy is retention of reproductive potential. It may therefore be the preferred approach for younger patients who may not have completed their family. Patients must however be counseled that data for pregnancy outcomes following the procedure are scarce, and the impact of the pregnancy on the surgery and indeed the effect of the surgery on the pregnancy are unknown. With the Oxford hysteropexy, the mesh encircles the cervix and vaginal birth is therefore not possible; in effect, the mesh acts as a cervical suture. There is also concern that uterine blood flow may be compromised as the mesh potentially surrounds the uterine arteries, although it is likely that a rich collateral supply is formed.

Since introducing hysteropexy as our standard approach to uterine prolapse, the authors have been aware of three patients who have subsequently conceived. One patient has been followed through to delivery in conjunction with her obstetrician [33]. Uterine artery Doppler studies at 23 weeks of gestation showed no compromise to blood flow. Serial growth scans showed a normally grown fetus, and the patient underwent elective cesarean delivery at 39 weeks delivering a healthy infant of normal birth weight. The patient has since required surgical correction of anterior vaginal wall prolapse, although obviously it is not clear if this is related to carrying a pregnancy or whether she would have had recurrence of prolapse anyway. The other two patients are in early pregnancy at the time of writing and will be reported on in the near future.

USE OF MESH

The use of Type 1 mesh is well established in pelvic reconstruction surgery with common usage in sacrocolpopexy and mid urethral slings. However, the medical community has become aware of implant complications in recent years; hips and breast implants have been associated with complications that have attracted a high media profile, and in gynecology mesh for prolapse and incontinence is now under intense scrutiny. This has been secondary to a realization that vaginal mesh extrusion rates are higher than previously thought and current media and public attention, in many cases associated with litigation, particularly in the United States and Scotland. The Medicines and Healthcare Products Regulatory Agency (MHRA) [34] and the Royal College of Obstetricians and Gynaecologists (RCOG) [35] have both issued guidance for urogynecologists surrounding the use of mesh in prolapse and incontinence surgery.

Certainly, the use of transvaginal mesh for vaginal prolapse appears to have a relatively high complication rate with the incidence of mesh erosion reported in the literature being 10%–18% [36]. This is secondary to mesh lying adjacent to the vaginal wall, which has been weakened by a surgical incision and subsequent scar. The mesh extrusion rate with an abdominal approach is considerably less, as the vaginal incision is avoided. Sacrocolpopexy mesh extrusion rates of 2%–11% have been reported [37,38]. In the authors’ experience, all of the vaginal extrusion complications seen have been secondary to nonabsorbable sutures (Ethibond), and since switching to absorbable sutures (Monocryl) we have not, in the past 4 years, had any mesh extrusion. There appears to be a lower rate of mesh extrusion associated with an abdominal approach [39].

With the Oxford hysteropexy, the polypropylene mesh does not approximate to the vaginal wall, lying at the level of the internal os. We have not seen, in an 8-year series of more than 500 cases, any vaginal mesh extrusion. Following initial concerns regarding bowel adhesions to mesh, the technique has been modified to completely reperitonize the mesh and subsequent to this modification in 2008, no further bowel adhesions or other mesh complications have been reported.

NICE

The National Institute for Health and Clinical Excellence (NICE) has published guidance for surgeons undertaking uterine mesh suspension procedures, as summarized in the following [40].

- Current evidence on the safety and efficacy of mesh suspension slings for uterine prolapse repair is inadequate.
- This procedure should only be performed by surgeons specializing in pelvic organ prolapse.
- Units carrying out these procedures should have arrangements for clinical governance, consent, and audit.
- Patients should be given clear written information regarding the uncertainty about the safety and outcome of the procedure.
- All cases should be entered onto the British Society for Urogynecology database.

SUMMARY

Uterine preservation surgery is increasing in popularity both with surgeons and patients. Fertility is preserved and this remains the one absolute indication for hysteropexy. Other theoretical advantages include stronger apical support, reduced vaginal surgery, associated vaginal dysfunction and psychological wellbeing, and reduced surgical morbidity. More good quality data are needed to enable clinicians to make evidence-based decisions regarding choice of prolapse surgery. It is to be hoped that the VUE study into different techniques of apical support will inform this debate.

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Prevention, Recognition, and Treatment of Complications in Laparoscopic Pelvic Floor Surgery

Christopher Maher and Nir Haya

INTRODUCTION

Gynecologists have led the surgical specialties in recognizing the benefits to our patients of reduced postoperative pain, hospital admissions, and quicker return to normal activities associated with laparoscopy. Improved optics, lighting, instrumentation, and technology over the last 15 years have seen an explosion in operative general gynecology surgery previously performed via laparotomy. Over the next decade, as laparoscopic suturing techniques are mastered, the laparoscope is likely to play an increasingly important role in female pelvic floor surgery. It is vital while laparoscopic pelvic floor surgery is in its infancy that we are competent in the prevention, recognition, and treatment of complications associated with this mode of access to the abdomen.

In recent years, the rate of complications from gynecological laparoscopy ranges from 4 to 8/1000 [1–3] diagnostic procedures and increases from 4 to 180/1000 operative gynecology surgeries [3–7]. Risk factors for gynecological laparoscopic complications include establishing laparoscopic access [5,6], concomitant laparoscopic hysterectomy [3,8], and surgeon inexperience [4,9].

ACCESS COMPLICATIONS

At least 50% of all reported complications at laparoscopic surgery occur at time of entry to the abdomen [5,6]. The majority of gynecologists prefer the closed (Veress needle) technique to the open technique [1,10]. The major complications related to entry include vascular and bowel injuries and associated postoperative hernia formation.

Open and Closed Technique

Although entry-related complications using the closed approach are uncommon, they can be fatal and occur in 0.31–2.4/1000 procedures [1,4,8,9,11]. Chapron reported that major vascular injuries occurred five times more frequently during the closed technique as compared to the open approach. Of the 44 reported cases in the literature between 1982 and 1997, 82% followed the closed and 17% followed the open technique [12].

A large Dutch review retrospectively compared the open (12,444 patients) and closed access (489,335). They found that the incidence of major vascular was 0.075% using the closed approach and 0% with the open approach ($p < 0.05$). The incidence of visceral damage was 0.083% with the closed technique as compared to 0.048% with the open ($p > 0.05$) [13].

In a randomized controlled trial (RCT), 150 subjects undergoing cholecystectomy were allocated to the open or closed approach. Major complications were reported in 3/75 (4%) of the closed as compared to 1/75 (1.3%) of the open ($p < 0.05$) [14]. The open approach was also significantly faster to perform. In a smaller RCT of 50 patients undergoing laparoscopic surgery, no difference in complications was observed, but the open approach took half the time of the closed approach to obtain access [15].

In contrast, a more recent questionnaire review of Dutch gynecologists reported that the complication rate in those undergoing open laparoscopy was significantly higher compared to those undergoing closed laparoscopy. The complication rate among those undergoing open laparoscopy ($n = 579$) was 1.38% as compared to 0.12% in the closed group ($n = 20{,}027$; $p = 0.001$). While the rate of vascular injuries was the same in both groups, the rates of gastrointestinal, wound infections, and failed access were significantly greater in the open group. The rate of open laparoscopy among Dutch gynecologists was only 2% and was reserved for those with previous laparotomy, those with suspected adhesions, and the very obese or thin. The authors concluded that the closed approach was safer than the open approach. An alternative message is that gynecologists should not perform procedures that they perform rarely in patients at high risk of complications. In our own tertiary referral urogynecology practice, the open technique is used exclusively. In a recent Cochrane review comparing open and closed access for laparoscopic entry, 17 trials evaluated 3040 individuals. Overall, there was no advantage in using any single technique in preventing major complications. Extraperitoneal insufflations and failed entry were both less frequent in the open technique compared to the closed approach [16].

It has been demonstrated that 50% of women with previous midline vertical incisions and 20% with low transverse incisions have some degree of periumbilical adhesions [17]. When there is concern regarding the safety of blindly introducing the insufflating needle at the umbilicus, an alternative site of placement is the left upper quadrant 3 cm below the costal margin in the midclavicular line (Palmer's point, Figure 102.1a). In retrospective audits, no significant complications have been reported with this approach [18,19].

Trocar-Associated Complications

In an attempt to minimize the risk associated with accessing the abdominal cavity, increased attention has been focused on trocar design. The traditional pyramidal trocar (Figure 102.2) cuts through the tissue, and safety shields (Figure 102.2) have been added to minimize the risk to the abdominal wall or of perforation of intra-abdominal vessels or a viscus. The cutting blade retracts into the plastic sleeve after the abdominal wall has been penetrated. The incidence of major vascular injuries from trocars and Veress needle averages around 0.1% [20–22] and remains unchanged despite the use of the safety shield in a large retrospective series reported by Saville and Woods. Bhoyrul et al. [23] reported that 87% of deaths from vascular injuries and 91% of bowel injuries at time of entry involved trocars with safety shields. They concluded that despite the blade retracting soon after entry into the peritoneum, the momentary presence of the blade in the abdominal cavity as seen in Figure 102.3 is all that is required for injuries to occur. Surgeons should not overestimate the level of safety associated with this device.

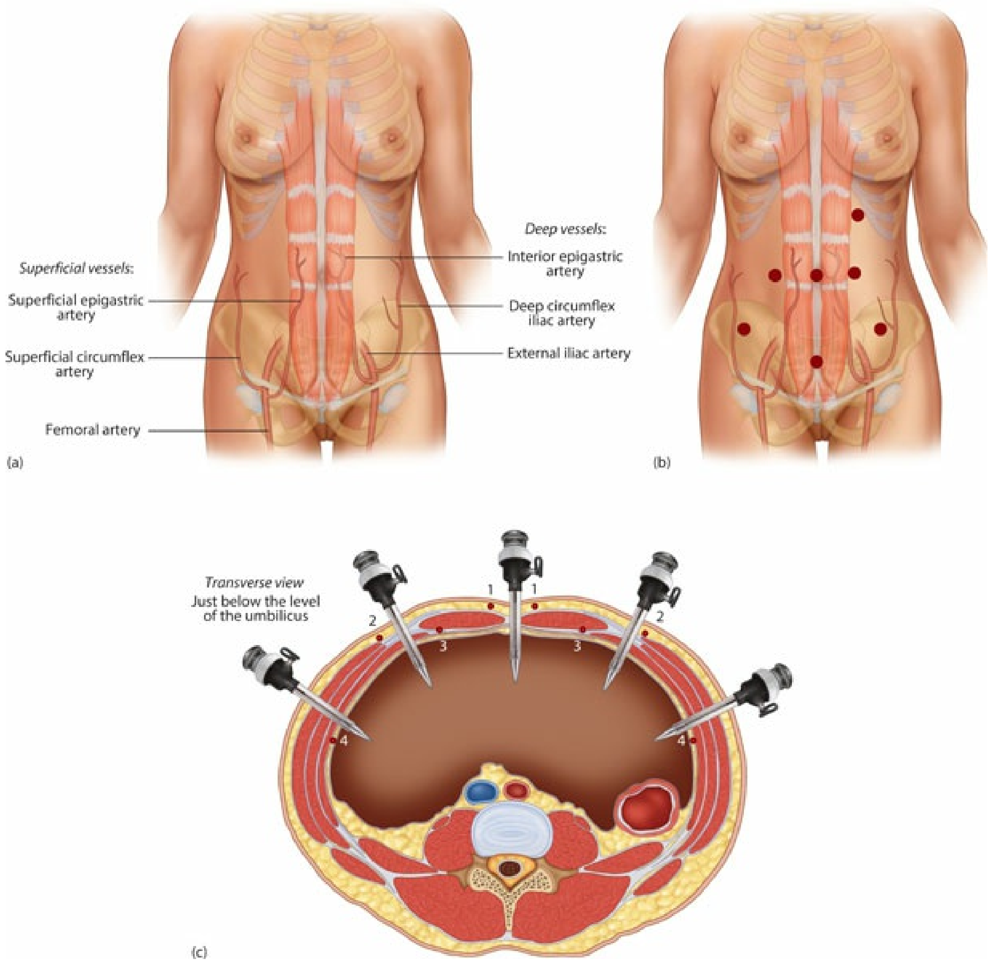
Superficial vessels:
Superficial epigastric artery
Superficial circumflex artery
Femoral artery
Deep vessels:
Interior epigastric artery
Deep circumflex iliac artery
External iliac artery
(a)
(b)
Transverse view
Just below the level of the umbilicus
1
1
2
2
3
3
4
4
(c)

Figure 102.1 (a) Coronial view, anterior abdominal wall vasculature; (b) coronial view, trocar placement sites; and (c) transverse view, trocar placement sites in relation to vessels—(1) superficial epigastric artery, (2) superficial circumflex iliac artery, (3) interior epigastric artery, and (4) deep circumflex iliac artery. (b: Copyright C. Maher/Francis.)

Conical or blunt tip trocars have been designed to minimize the risk associated with bladed trocars (Figure 102.2). They dilate the fascia and muscular tissues, thus decreasing the potential trauma as it enters the abdominal cavity. Conical tips require a greater entry force to the abdomen than sharper pyramidal [24] and leave a defect approximately 50% narrower than the sharper pyramidal [25]. Leibl, in a nonrandomized study, demonstrated that the reduced wound defect following the use of conical trocars was clinically relevant, with incisional hernia being reported 10 times more frequently after the pyramidal as compared to the conical trocar [26]. In a further study, there were no reported injuries to blood vessels of the anterior abdominal wall in the conical group as compared to 0.83% for the cutting trocar [21]. In more recent RCTs, the radially expanding conical trocar (Step^{TM}, InnerDyne, Inc., Sunnyvale, CA) had less cannula site bleeding, reduced pain, less wound complications, and higher patient satisfaction as compared to the pyramidal trocar [27,28]. Munro and Tarnay [29] recently demonstrated that the fascial and muscular defect from a 12 mm blunt trocar resulted in a similar fascial defect to the 8 mm pyramidal trocar and suggested that the fascial defects from 12 mm blunt trocars do not need closing, a view supported by others [27,30].

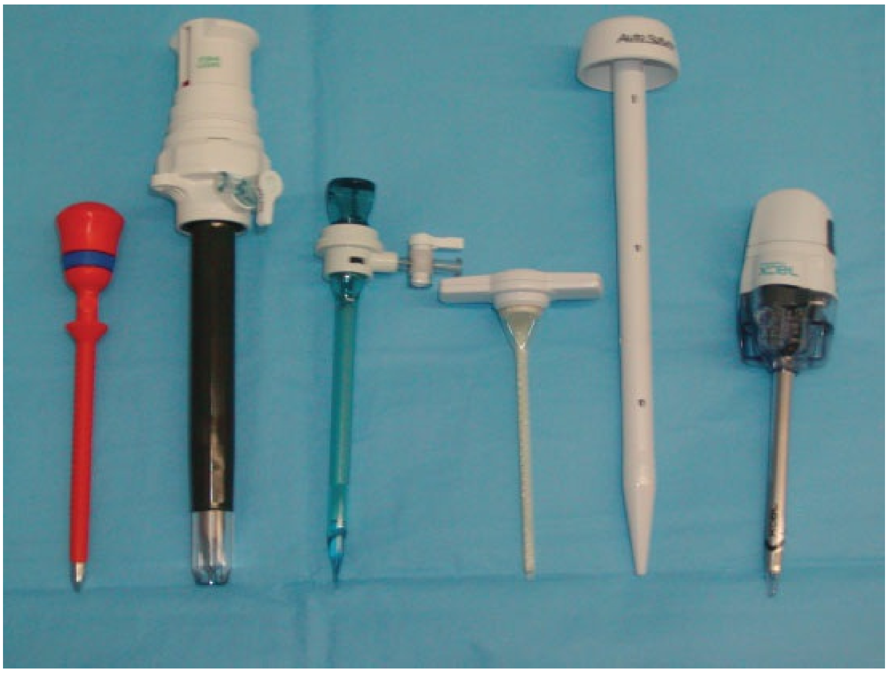

Figure 102.2 A variety of trocar designs. From left to right: pyramidal trocar (E.M.T., Warriewood, New South Wales, Australia), shielded trocar (Versaport, Tyco, Norwalk, CT), conical trocar (Separator, Applied Medical, Santa Margarita, CA), conical trocar (Step, Tyco, Norwalk, CT), and optical access trocar (Courtesy of Optiview, Ethicon, Endosurgery, Cincinnati, OH).

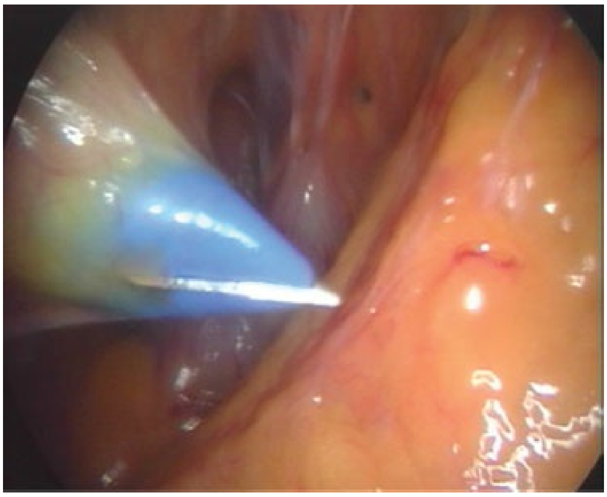

Figure 102.3 Blade of a safety shield trocar, present momentarily prior to retracting, in an abdomen with adhesions.

Optical access trocars (Figure 102.2) are designed to decrease the injury to vessels and viscera by allowing the surgeon to visualize abdominal wall placement during entry. Two optical access systems are available: one utilizes a bladed trocar that strikes the fascia and peritoneum under vision (Visiport, United States Surgical, Norwalk, CT), and the other utilizes a nonbladed trocar where a clear conical tip that is rotated under laparoscopic vision as it rotates through the layers (Optiview, Ethicon Endosurgery, Cincinnati, OH). Video 102.1 demonstrates the technique of a subumbilical optical access entry.

Optical access trocars are designed to decrease the injury to vessels and viscera by allowing the surgeon to identify each layer of the abdominal wall and avoiding inadvertent injuries during entry due to a lack of vision. In a single randomized comparison, direct optical was quicker to perform than both the open [31] and closed [32] approaches without any difference in bleeding or vascular or bowel injuries. In 2013, the same group in a large RCT (n = 228) of obese women (body mass index 30–40 kg/m^2) undergoing benign gynecology surgery again demonstrated reduced entry time and blood loss in the optical access group with a tendency to reduced vascular and bowel injuries as compared to open entry technique [33]. While the superiority of optical access approach compared to alternative entry techniques has been demonstrated, further validation of these outcomes outside of the single research group is required.

An important advantage of laparoscopy over laparotomy is the lower rate of wound complications and hernias. In one study, the incidence of wound infection after open colposuspension was 11% as compared to 1% after the laparoscopic approach [34]. Magrina has estimated that the incidence of trocar hernias after laparoscopic gynecology surgery was 10–100 times lower than laparotomy [35]. He found that the incidence of hernia after laparoscopy ranged from 0.06% to 1% as compared to 13% 5 years after gynecological laparotomy.

The incidence of incisional hernia increases to 3% with the use of 12 mm trocars [36]. It is largely accepted that while 5 mm trocars do not require fascial closure, when bladed trocars 10 mm or greater are utilized, the defects should be closed to minimize the risk of bowel entrapment or incisional hernia. Video 102.2 presents a 56-year-old lady who represented 4 days post–laparoscopic sacral colpopexy with symptoms of small bowel obstruction. The video demonstrates a small bowel entrapped in the 10 mm trocar site. The bowel was able to be reduced with traction from bowel forceps with the bowel mucosa being viable. This trocar defect at the original surgery was closed with 2.0 polydioxanone (PDS) suture. Following this complication, we utilize a trocar site closure device for all 10 mm trocars. The technique is demonstrated in Video 102.3; however, this technique in our experience is associated with increased trocar site pain postoperatively.

Preliminary studies have demonstrated that the blunt trocars will significantly reduce the incidence of trocar site hernia [26], and many believe they do not need to be closed [29,30].

Secondary Trocars

Secondary trocars are required for operative pelvic floor surgery. The correct positioning of these trocars is vital to minimize damage to the vasculature of the anterior abdominal wall (Figure 102.1a and b) and to allow laparoscopic suturing in a safe and biomechanically friendly position for the surgical team.

A thorough knowledge of the vasculature of the anterior abdominal wall is required to minimize and treat perforation of the vessels. The inferior epigastric artery arises from the external iliac artery, passes superior to the inguinal ligament, and travels superiorly and medially to the lateral edge of the rectus muscle. Its position deep to the rectus muscle and superficial to the peritoneum allows for relatively easy localization laparoscopically (Figure 102.4).

The superficial epigastric artery arises from the femoral artery near the inguinal ring and courses medially above the rectus muscle toward the midline. The smallest branch of the femoral artery, the superficial circumflex iliac artery, runs laterally to supply the skin and superficial fascia.

Perforation of the inferior epigastric artery will produce retroperitoneal or intraperitoneal bleeding. Perforation of the superficial epigastric artery will result in intramuscular or subcutaneous bleeding. The deep circumflex iliac artery arises from the external iliac artery opposite the inferior epigastric artery and runs posterior to the inguinal canal to the anterior superior iliac spine where it anastomoses with a variety of vessels. Figure 102.1a demonstrates the course of the anterior abdominal wall vessels.

The surgeon can use transillumination for locating superficial abdominal wall vessels, but intraperitoneal identification is required for the inferior epigastric artery. When the inferior epigastric artery is difficult to visualize, intra-abdominal landmarks can be helpful. It usually arises from the inguinal canal medial to the round ligament and travels cranially lateral to the obliterated umbilical arteries. The lower ports are placed as in Figure 102.1a and b lateral to the inferior epigastric and medial to the deep circumflex vessels. If further trocars are required, they can be sited in the midline suprapubically or at the level of the umbilicus lateral to the edge of the rectus muscle. If a 10 mm trocar or greater is required for introducing mesh, the harmonic scalpel, or the removal of pathology, this is placed either on the side of the surgeon or at the suprapubic site, if utilized.

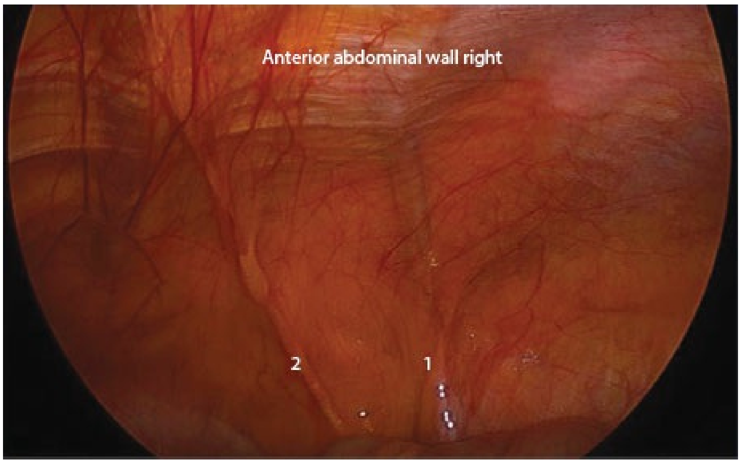

Figure 102.4 Laparoscopic localization of the right inferior epigastric artery (1) lateral to the obliterated umbilical artery (2).

Even after all these preventive measures are employed, experienced laparoscopic surgeons may still be faced with arterial bleeding from the inferior epigastric artery. The offending trocar should not be removed as this denotes the location of the artery that may become difficult to visualize as the hematoma spreads. If the bleeding is recognized early and the inferior epigastric artery can be identified, both ends of the transected vessel can be diathermied with bipolar forceps (Figure 102.5a). If this is unsuccessful, a No. 12 Foley catheter can be passed through the 5 mm trocar and the Foley balloon inflated to 10–15 cm^3 with sterile water. The trocar is then removed over the catheter and firm traction, secured with an umbilical cord clamp overnight (Figure 102.5b). The following morning, the clamp and catheter are removed. If this fails to secure the vessel, a CT-1 needle is passed through the abdominal wall into the abdomen and passed from inside the abdomen to the outside using laparoscopic needle holders and tied both cephalic and caudal to the trocar. The sutures are removed the following morning (Figure 102.5c). Finally, the inferior epigastric vessel can also be secured with sutures introduced through a small abdominal wall incision and two passes of the trocar site closure device (Endoclose^{TM}, Covidien, Mansfield, MA) on either side of the vessel. The suture is then tied above the sheath and the skin incision is closed. This is very similar to the technique utilized for closing large trocar defects in Video 102.3.

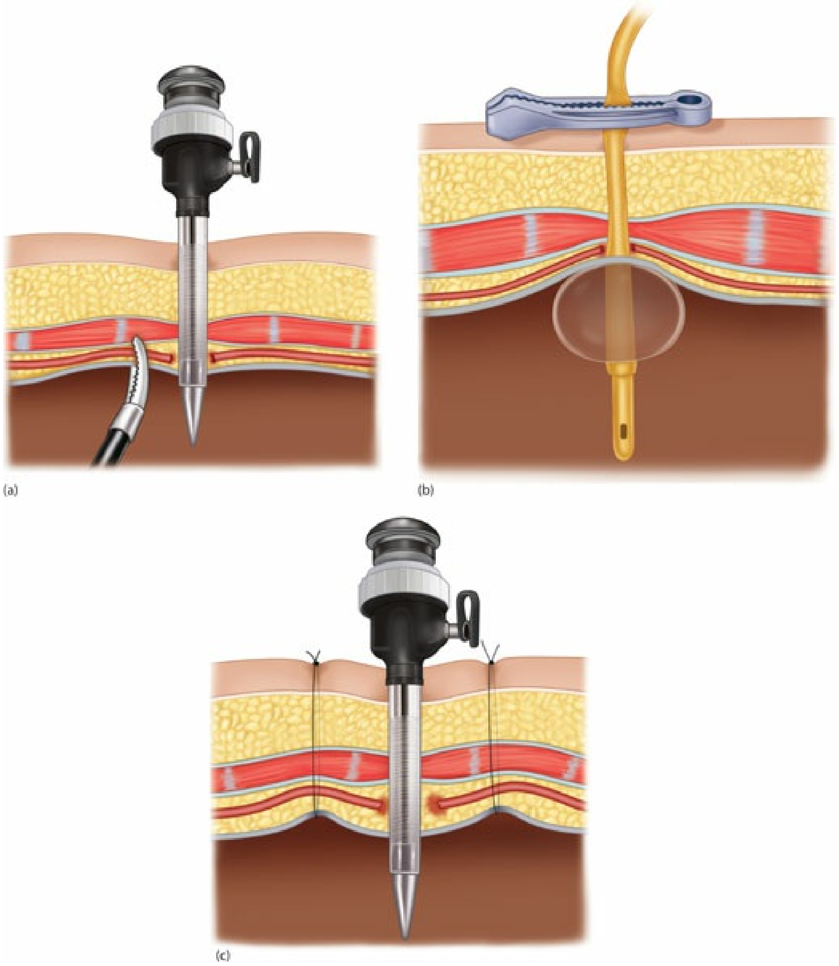

Figure 102.5 Bleeding inferior epigastric artery controlled with (a) bipolar diathermy, (b) tamponade with Foley catheter, and (c) sutures. (c: Copyright C. Maher/Francis.)

BOWEL INJURIES

The incidence of bowel injuries at gynecological laparoscopy varies from 0% to 0.5% [7,37]. Approximately one-half of these injuries occur during entry [3,8,38], and the large and small bowel are equally involved [4,39]. As there appears to be no significant difference in the rate of bowel injuries with either the closed or open approach, little can be done to minimize the occurrence of the injury except that the damage may be more readily detected intraoperatively with the open technique [40]. After reviewing the literature, Magrina calculated that only 43% of bowel injuries at laparoscopic surgery were diagnosed intraoperatively [35]. The mortality rate from bowel injuries in gynecological laparoscopy ranges from 2.5% to 5% [21,41], but this has been shown to increase to 21% in those with a delayed diagnosis of bowel injury [42].

Direct Injuries

If there is a recognized Veress injury to the bowel at the time of surgery and there is no associated fecal spill, it is likely that the injury can be managed expectantly. Although no clear guidelines exist in nine cases of Veress injuries to the bowel treated expectantly, there were no complications [1,8,38]. Trocar damage to the small bowel mandates careful inspection of the whole bowel to ensure no through-and-through injuries have occurred. Simple small injuries to the small and large bowel should be repaired in one or two layers of interrupted sutures, the pelvis irrigated, and antibiotics commenced. Postoperatively, the patient is kept nil by mouth until flatus is passed. Video 102.4 demonstrates a small bowel trocar injury that was identified at surgery. We carefully checked to ensure a through-and-through injury had not occurred and the small bowel was repaired in two layers of interrupted 3.0 PDS as shown. There were no postoperative sequelae.

Electrosurgical Injuries

Electrosurgical injuries are more commonly seen in bowel injuries that are diagnosed postoperatively. Brosens estimated that the average time to diagnosis after needle or trocar injury to bowel was 1.3 days as compared to 10.4 days for electrosurgical burns [42].

Electrical injuries to the intestine are not always diagnosed intraoperatively, or their appearance leads the surgeon toward conservative treatment [43]. It is suggested that burns less than 5 mm in diameter can be treated expectantly [44]. If the area of blanching exceeds 5 mm, it is estimated that the thermal damage may exceed up to 5 cm from the apparent injury and resection should be considered [45].

In patients presenting postoperatively with abdominal pain or bowel symptoms, a computerized tomography (CT) of the abdomen and pelvis with oral and intravenous contrast should be undertaken to assess the integrity of the bowel and urinary system. Alhilli et al. [46] recently reported on a cohort of 205 women who presented within 42 days of gynecology surgery with symptoms possibly suggestive of bowel complications that 38 (18.5%) had bowel injuries. While contrast CT scan definitively diagnosed three cases that were not suspected clinically, the further three cases were not confirmed on imaging demonstrating the value of early consultation with a surgical colleague and early recourse to surgical assessment and management. Damaged bowel must be repaired or resected with or without a temporary colostomy as early as possible to minimize morbidity and mortality. All necrotic tissue should be removed to minimize the risk of abscess formation.

Prevention of Bowel Injuries

The most significant reduction in bowel complications during laparoscopic pelvic floor surgery will arise from preventing damage. The focus of attention should lie on careful adhesiolysis and enterolysis and the detection of injuries intraoperatively rather than postoperatively. A multidisciplinary group of Dutch surgeons recently performed a systematic review on the impact of adhesions in pelvic surgery. They reported on 2565 cases in 16 studies where adhesiolysis was required and reported an enterotomy rate of 5.8%. This rate increased to 8.7% in lower gastroenterology surgery and was 4.8% at gynecology surgery. The rate of enterotomy was also significantly lower if the surgery was performed laparoscopically (1.8%) as compared to laparotomy (8.9%) [47].

During adhesiolysis and enterolysis, sharp dissection with minimal diathermy will be beneficial in preventing inadvertent bowel damage. Careful inspections of the bowel for hematoma or serosal damage that may suggest breaches of the mucosa and the performance of the underwater test, if there is any concern regarding the integrity of the bowel, are all useful in allowing the intraoperative rather than postoperative diagnosis of bowel damage. The underwater test involves holding any area of the bowel suspected of damage under warmed saline looking for gas or bowel leakage. If the laparoscopic pelvic floor surgeon is faced with an abdomen of morbidly dense adhesions, it may be prudent to remember that in a large prospective RCT the vaginal approach to vault prolapse has been shown to be equally effective as the abdominal route [48] and the conversion to the vaginal approach may be the safest approach. At LSC, four (1.5%) bowel injuries in 261 cases were reported. A rectal [49] and colon [50] injury were repaired laparoscopically without sequelae, and two small bowel injuries were diagnosed postoperatively and underwent subsequent laparotomy [51].

Bowel Preparation

Bowel preparation prior to surgery was utilized—first, to remove the bulky intraluminal contents to improve surgical field vision and bowel handling, and second, to decrease the risk of peritoneal and wound contamination if the bowel was inadvertently opened. Neither of these beliefs have been confirmed in RCTs in elective operative gynecology [52] or colorectal surgery [53]. Bowel preparation results in the transfer of fluid and electrolytes to the bowel lumen that may result in hypokalemia and hypothermia and should be utilized perhaps only in those with higher risk of bowel injury such as those with known adhesions or diverticular disease.

Few studies have evaluated gastrointestinal morbidity following sacral colpopexy. In a retrospective review of 390 cases of LSC, Warner et al. reported that the rate of bowel complications including ileus, small bowel obstruction, or bowel injury was 2.3% [54]. The peritoneum was closed over the mesh in this series. In comparison, 1 in 20 women in the colpopexy and urinary reduction efforts trial experienced significant gastrointestinal morbidity after open sacral colpopexy where closure of the peritoneum was optional. Of 322 women in the study, 19 had symptoms of possible ileus or small bowel obstruction; of these, 4 had reoperation for small bowel obstruction, 11 were readmitted for medical management, and 4 had a prolonged initial hospitalization for gastrointestinal symptoms [55]. In a recent publication comparing robotic and laparoscopic approach to sacral colpopexy, again where closure of peritoneum was optional, the rate of small bowel obstruction was 2.6% [56]. The question raised is whether the relatively simple task of closing the peritoneum after sacral colpopexy has a role in minimizing postoperative bowel complications and would be easily answered by a subanalysis of these two papers. Contrary to this, Elneil et al. [57] reported no postoperative bowel complications in a series of 128 cases where the mesh was not buried at time of sacral colpopexy.

LEARNING CURVE AND LAPAROSCOPIC COMPLICATIONS

Improving the laparoscopic experience of the surgeon may prove to be one of the simplest means of minimizing morbidity associated with bowel injuries at gynecologic laparoscopy. Brosens reported that a gynecologist performing less than 100 laparoscopies a year had a five times higher rate of bowel injuries than those performing more than 100 laparoscopies a year [38]. The learning curve associated with LSC has long been considered a barrier to uptake of the technique. Claerhout et al. [58] demonstrated competency based on four outcome measures: complication rate, conversion rate, operating time, and anatomical outcomes achieved after 60 cases. Operating time declined rapidly after the first 30 cases and continued to decline before plateauing after 90 cases. Akladios et al. [59] retrospectively reviewed their first 47 cases and demonstrated a uniform decrease in operating time over the study period; however, the operating time decreased most significantly over the first 30 cases. Similarly, Mustafa et al. [60] demonstrated that during the first 48 cases that operating time decreased uniformly and that mastery was obtained after 30–40 cases. Reassuringly, during studies [59–61] that have evaluated implementation of LSC, no significant change in complication rate was identified during the learning phase; however, given that the significant complication rate is less than 5%, this is not surprising. Skills can be improved in a variety of means including training programs, skills workshops, and operating with colleagues.

INJURIES TO THE BLADDER

Inadvertent cystotomy has been reported in 4% of laparoscopic colposuspensions [62]. In 261 published LSC procedures, 5 (1.9%) inadvertent cystotomies were reported, all of which were repaired laparoscopically at the initial surgery without complication [49–51]. A gas filled urinary bag or blood in the urine means bladder trauma till proven otherwise and warrants careful laparoscopic inspection of the bladder distended to 300 mL and cystoscopy. Cystotomies should be repaired in two layers so that the bladder is watertight at 300 mL. After repair, cystoscopy should be performed with the laparoscope in place, to ensure that there are no other unrecognized injuries and that the ureters are patent.

After a watertight cystotomy repair, the catheter can safely be removed at 4 days [51]. If concomitant continence surgery is performed, the nursing staff and the patient should be vigilant during the trial of void to ensure the bladder is not grossly over distended.

Postoperative cystoscopy is vital to minimize lower urinary tract complications following pelvic floor surgery as it is the unrecognized cystotomy that may cause vesicovaginal fistula [63]. Inadvertent cystotomy can occur during adhesiolysis at LSC: a continuous 2.0 polyglactin suture on a CT-2 needle then closes the defect in two layers. In the first layer, care is taken to ensure that the mucosa and detrusor muscle are included. This layer is inverted during the more superficial closure of the second layer. Problems can also be encountered during the repair of a large cystotomy at the time of a difficult hysterectomy.

URETERIC INJURIES

Ureteric injuries following pelvic floor surgery are reported in 3% of cases [64,65]. The morbidity associated with ureteric injury can be dramatically reduced if identified intraoperatively using postoperative cystoscopy and intravenous indigo carmine [64,65]. If indigo carmine is not clearly visible following laparoscopic pelvic floor repair, the injury is likely to be related to kinking of the ureter in the lateral retropubic space or in relation to the uterosacral/cardinal ligament sutures during sacral colpopexy or vault suspending procedures. Lateral retropubic or vault suspending sutures should be removed one at a time till the ureteric patency is obtained. The sutures are then replaced at a lower level and ureteric patency is again confirmed. If patency is not confirmed with the removal of the sutures, retrograde dye studies and intraoperative urological consultation are required.

Laparoscopic hysterectomy is associated with a 0.7%–1.4% risk of ureteric injury [3,66] that is at least 10 times greater than at vaginal hysterectomy [8]. Most of these injuries are related to clamping, incision, or diathermy damage. Ureteric injuries related to concomitant laparoscopic hysterectomy usually require ureteric reimplantation by urological colleagues. One small study retrospectively compared laparoscopic hysterectomy performed with and without ureteric catheters and suggested that ureteric catheters may decrease the risk of ureteric injury [67]. Just less than 10 minutes was required to place the catheters, but no other prospective evaluation of routine ureteric catheters at laparoscopic pelvic floor surgery is available.

SACRAL BLEEDING

Presacral venous bleeding during LSC is uncommon but potentially life-threatening. The presacral fascia covers and protects the underlying plexus, which consists of venous network both on and beneath the surface of the sacral periosteum as seen in Figure 102.6. Inadvertent manipulation outside this avascular presacral space may tear the fascia and cause damage of underlying thin-walled veins, which are devoid of valves. It is well documented that conventional measures for hemostasis are ineffective in managing presacral hemorrhage [67]. Coagulation and suturing should be avoided because they can aggravate bleeding resulting in significant blood loss.

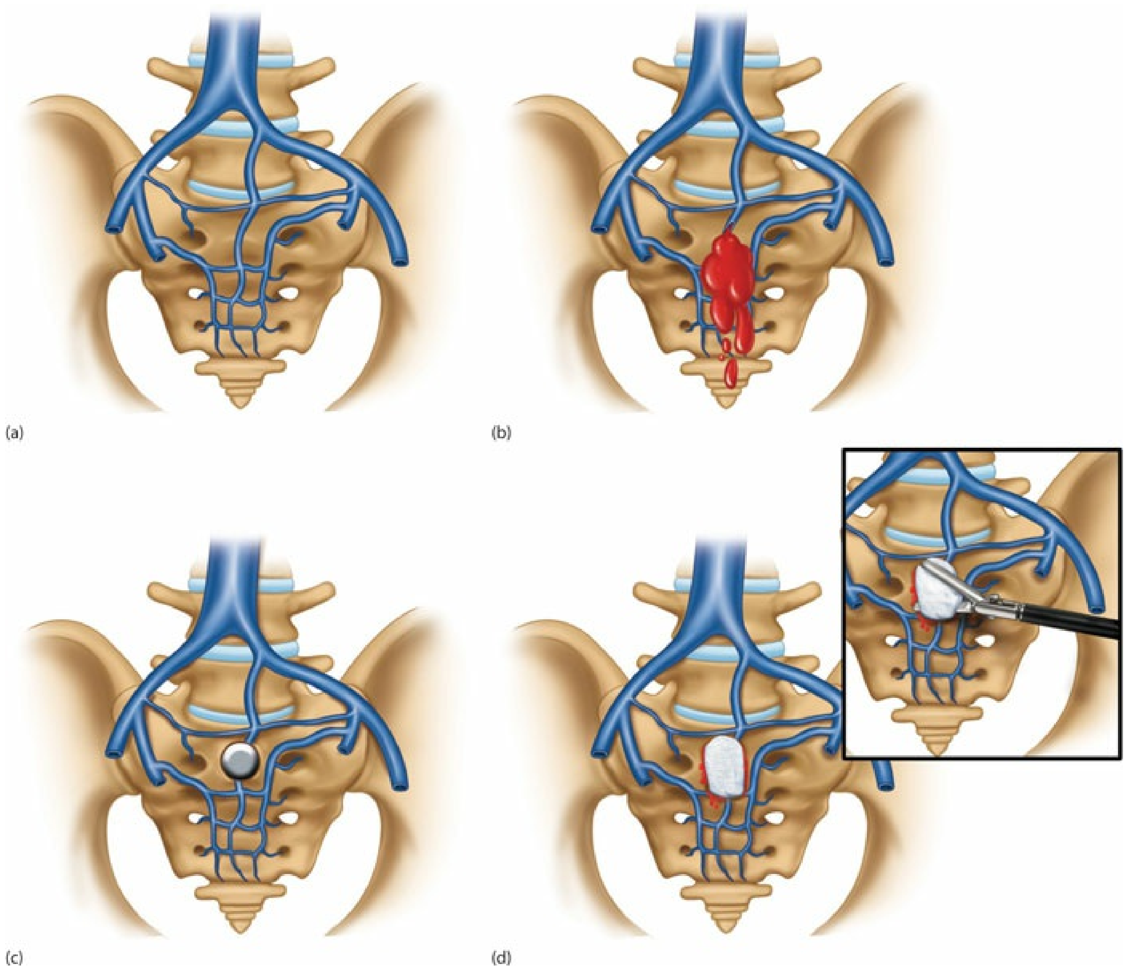

Figure 102.6 (a) Presacral venous plexus (IVC, inferior vena cava; MSV, middle sacral vein), (b) bleeding site with ruptured middle sacral vein, (c) bleeding controlled by insertion of sterile titanium thumbtack, and (d) bleeding site pressed with hemostatic matrix agent.

Surgeons should have a planned approach to this problem, and the author initially applies immediate direct pressure over the bleeding site using small tampon gauze for 5 minutes to temporarily control the bleeding. If bleeding persists, traditionally pelvic packing and the use of sterile metallic or titanium thumbtacks are employed (Figure 102.6c). Packing has the disadvantage of reoperation for removing the packs and risk of rebleeding [68]. More recently, surgeons have reported successfully using a hemostatic matrix agent such as FloSeal (Baxter, United States) or Surgicel Fibrillar (Ethicon, United States) followed by gauze pressure for 5 minutes [68] (Figure 102.6d).

OSTEOMYELITIS/DISCITIS

de Tayrac and Sentilhes recently reported the rate of serious sacral infection following sacral colpopexy to be less than 1% and to be 0.18% after LSC [69]. Although a rare condition, it has been reported after the use of both sutures and tacks into the sacrum and after open laparoscopic and robotic approaches. Potential exacerbating factors include concomitant hysterectomy, mesh exposure, the use of braided sutures or the placement of sutures and tackers deep into the periosteum at robotic sacral colpopexy without tactile feedback [70], and fixation into the L5–S1 intervertebral disc [71]. After cadaveric and CT analysis of the sacrum, Good et al. [71] determined the L5–S1 disc to be the most prominent structure in the presacral space, and insertion of the mesh into the “true sacrum” should be 1.5 cm distal to the S5–L1 disc to minimize serious sacral infections. We perform minimal sacral dissection and simply attach the mesh at the most prominent site on the sacral promontory that appears to compliment Good’s recommendation. Some surgeons attach the mesh to the lower part of the body of the L5 because of easier access.

COMPLICATIONS RELATED TO PNEUMOPERITONEUM

Subcutaneous emphysema arises as carbon dioxide leaks into or is absorbed by subcutaneous tissue. Leaks to the extraperitoneal tissues can occur at entry, with opening of extraperitoneal spaces or through existing undetected hernia. The LSC involves significant retroperitoneal dissection, increasing the risk of subcutaneous emphysema that is usually quite innocuous. Significant or sudden subcutaneous emphysema around the face, neck, and chest must alert to the possibility of mediastinal emphysema. This usually arises from a congenital defect of the diaphragm but can also occur after trauma associated with upper abdominal surgery.

Gas embolism can occur if gas enters the vascular system and usually occurs during or shortly after insufflation. The sudden development of hypotension, bradycardia, or arrhythmias at this time should immediately raise suspicion of gas embolism. While relatively rare occurring in 0.0014% [13], the mortality rate is as high as 28% [72]. The pneumoperitoneum should be released and the procedure abandoned as soon as feasible.

ANESTHETIC COMPLICATIONS

The gynecologist must be aware of the cardiovascular changes associated with operative laparoscopy. Most of the changes are due to establishment and maintenance of pneumoperitoneum or Trendelenburg positioning. Carbon dioxide remains the most widely used distension media but is rapidly absorbed from the peritoneum and may cause hypercarbia and acidosis. Hypercarbia is associated with arrhythmias, increased cardiac output, and decreased systemic vascular resistance. Hyperventilation minimizes the impact of hypercarbia.

Steep Trendelenburg may be required for posterior compartment or vault suspending procedures and results in increased central venous pressure and decreased arterial pressure and cardiac output. Atelectasis and decreased pulmonary compliance can occur but are usually well controlled with general anesthesia, neuromuscular blockade, endotracheal intubation, and controlled ventilation. Both pneumoperitoneum and Trendelenburg position reduce femoral venous flow increasing the risk of thrombotic complications.

CONCLUSION

Laparoscopic pelvic floor surgery affords the surgeon and the patient significant advantages, but complications are related to obtaining access, surgeon inexperience, and associated laparoscopic hysterectomy. The judicious use of open approach or access via the left upper quadrant may be beneficial in minimizing access-related complications. Newer optical entry trocars may serve to decrease morbidity associated with closed or open access techniques. Careful dissection during adhesiolysis and cautious and appropriate use of electrical current will decrease bowel injuries. Vigilance during surgery is required to detect and manage complications intraoperatively, rather than postoperatively. An experienced operating room staff including assistants, scrub sisters, and anesthetists, who are enthusiastic regarding laparoscopic surgery, is vital to minimize complications associated with laparoscopic pelvic floor surgery. Finally, following surgical complication, it is vital to investigate the clinical and surgical decisions that may have led to an unwanted outcome. Video recording of all surgical procedures compliments postoperative evaluation of complications and is recommended as an important measure to improve surgical and clinical healthcare.

VIDEOS

Video 102.1. Technique of optical access subumbilical trocar entry: http://goo.gl/KAjyG5.
Video 102.2. Small bowel entrapment in 10 mm trocar site: http://goo.gl/nJUlt9.
Video 102.3. Device closure 10 mm trocar site: http://goo.gl/qA5mt8.
Video 102.4. Repair of small bowel enterotomy: http://goo.gl/9C2bAw.

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103 The Role of Robotic Surgery

Orfhlaith E. O’Sullivan and Barry A. O’Reilly

ROBOT-ASSISTED SURGERY

Surgical robots were developed to facilitate minimally invasive surgery and to assist surgeons in performing procedures that could otherwise be technically challenging using traditional open or laparoscopic techniques. The development of robotic surgery was aided by the Defense Advanced Research Projects Agency, who funded research into the possibility of a remote surgery program for battlefield triage. In 1999, the first da Vinci® System was introduced to the market, and in 2000 it was cleared by the Food and Drug Authority (FDA) for minimally invasive surgery including urological procedures. Subsequently, in 2005 the da Vinci Surgical System became the only robotic system to be granted FDA approval for gynecological surgery in the United States. In Europe, it has full regulatory clearance and has the Conformité Européenne mark since 1999 [1]. Since gaining FDA approval, the role of the robot in urological and gynecological surgery has increased with many traditional procedures now being performed with a robot assistance, including radical prostatectomy, cystectomy, nephrectomy, pediatric procedures, and stricture surgery [2–4]; within gynecology, these include hysterectomy (for benign and malignant disease), prolapse surgery (sacrocolpopexy/hysteropexy), myomectomy, tubal surgery, and endometriotic and adnexal surgery [5]. It is claimed that robot-assisted surgery is associated with clinical benefits for the patient such as reduced estimated blood loss (EBL), decreased blood transfusion requirements, shorter length of stay (LOS), and reduced perioperative pain and analgesic requirements. The benefits for the surgeon include the potential for greater precision, lower error rates, shorter learning curves, and superior ergonomics than conventional laparoscopy. By December 2012, there were 2,585 da Vinci Surgical Systems installed in approximately 2,025 hospitals worldwide with approximately 450,000 robot-assisted procedures performed in 2012, an increase of approximately 25% compared to 2011 [6].

HEALTH TECHNOLOGY ASSESSMENTS

The idea of a health technology assessment was first conceptualized in the United States in 1967, with the Congressional Office of Technology Assessment being established in 1972 [7]. The general definition of technology assessment used was “a comprehensive form of policy research that examines the short- and long-term social consequences of the application or use of technology.” The Health technology assessments (HTAs) are based on three principles that the assessment: (1) is based on evidence-based knowledge, (2) is all encompassing and interdisciplinary, and (3) is aimed at decision making. This makes them an ideal tool and reference point for systematic reviews of new technology. The HTAs must be performed by an impartial body using evidence-based information on efficacy and comparisons with available alternatives in a timely fashion. Equally, the analysis must be transparent and deal with issues of quality-adjusted life-years and cost–benefit analysis as appropriate to the geographical area served. They are a valuable tool for health care policy making and decision making by governments. In general, the bodies performing the HTA are made up of expert advisors across a broad spectrum of areas in health, finance, and ethics. Recently, five HTAs have been conducted on robotic surgery, in Australia (2009) [8], Belgium (2009) [9], Canada (2010 [10], 2011 [11]), and Ireland (2012) [12]. They concluded that based on the evidence available, the robot-assisted surgery may have a significant impact on many clinical outcomes in patients undergoing hysterectomy. In general, robotic surgery can have an impact on reducing hospitalization costs, but the investment made in acquiring this technology is significant, and institutions that choose to adopt it should make efforts to monitor its costs and outcomes in order to maximize cost-effectiveness within their own center. To decrease costs, centers should maximize caseloads, consider keeping the robot operational for longer durations if possible, and use the technology for multiple indications, particularly those with greater potential impact on important patient outcomes and savings on institutional costs. One of the key advantages of using robotic technology for gynecological procedures is the reduction in surgeon fatigue and the ability to perform complex surgery with a minimal invasive technique.

COST ASSOCIATED WITH ROBOT-ASSISTED SURGERY

This is covered in Chapter 105.

DA VINCI SURGICAL SYSTEM

The first da Vinci Surgical System was a simple three-armed robot with an upgrade in 2003 providing the fourth (retractor) arm. The system consists of three main components: the console from where the surgeon controls the operation, the patient side cart with four interactive robotic arms to which the operating instruments are attached, and the vision system (Figure 103.1). The EndoWrist® instruments used during surgery combines 7 degrees of freedom, with 90 degrees of articulation to provide a range of motion superior to the human hand. It also combines intuitive motion and fingertip control with motion scaling and tremor reduction technology to provide instruments with greater capabilities, and improved surgical dexterity. The latest model the da Vinci Xi Surgical System (2014) allows for more efficient anatomical access with crystal clear 3D-HD visualization. The principle of robotic surgery is that the surgeon operates unscrubbed while seated at the console, from which they are able to view the operating field in three dimensions through a stereoscopic viewer.

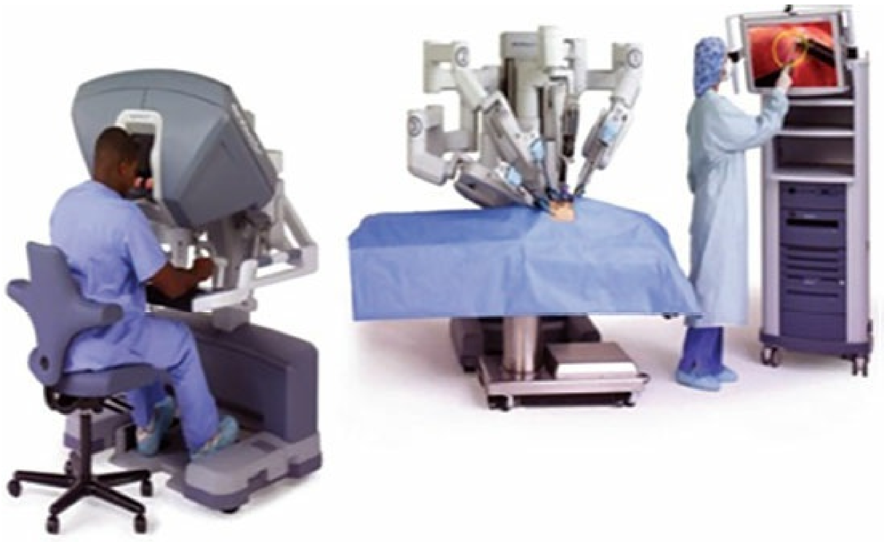

Figure 103.1 The main components of the da Vinci Surgical System. (Courtesy of Intuitive Surgical, Inc., Sunnyvale, CA.)

Robot-Assisted Surgery

The robot-assisted surgery is performed across a large spectrum of surgical specialties; these include cardiothoracic, head and neck, and general surgery, gynecology, and urology.

FEMALE UROLOGY AND UROGYNECOLOGICAL SURGERY

Sacrocolpopexy

The abdominal sacrocolpopexy remains the gold standard for the treatment of vaginal vault prolapse (VVP) despite the introduction of newer techniques such as vaginal mesh kits [13]. It is associated with success rates of 74%–98%, a low recurrence rate, and reduced dyspareunia [14] when compared with vaginal sacrospinous fixation. Laparoscopic sacrocolpopexy has been shown to have similar outcomes with reoperation rates of approximately 6%–7% and a mesh erosion rate of 3% [15]. Furthermore, the conversion rates reduced with increased operator experience [15]. A study by Akladios assessing learning curves in robotic surgery highlighted that once the learning curve is complete, the 1-year cure rate was 98%; however, there was a 20% de novo dyspareunia rate [16]. A recent study on rate, type, and cost of the pelvic organ prolapse (POP) surgery revealed that in France, 38.8% of the POP surgical admissions were for vault repair, of this 56% were for sacrocolpopexy/sacrohysteropexy and the remaining 44% for sacrospinous ligament fixation [17].

Despite the large number of papers published on robot-assisted sacrocolpopexy, there are a limited number of randomized controlled trials comparing laparoscopic with robotic sacrocolpopexy with main end points of operation time, pain, functional activity symptoms, cost, anatomical support, and quality of life [18,19]. There were no functional differences between the two groups, while the robot-assisted approach was associated with an increased cost, increased operative time, and increased pain. This finding of increased pain postoperatively is at odds with other studies, which show either similar or reduced pain scores with robotic surgery [20]. A further study by White comparing three approaches, the robotic, laparoscopic, and single port, revealed no difference in pain, LOS, blood loss, or operating time between the three [20], with the POP-Q scores at 6 months showing good apical support and prolapse reduction. Further studies confirm good functional results using the robot showing it to be efficacious in the management of the VVP [21]. Geller et al. [22] in a retrospective study comparing open with robotic sacrocolpopexy showed the robotic approach to be associated with improved POP-Q C, reduced blood loss, and length of hospital stay. Elliot et al. reported on 30 cases operated on robotically with a mean follow-up time of 24 months. They concluded that robotic sacrocolpopexy was associated with decreased length of hospital stay, a low complication rate, and high patient satisfaction [23]. Gocmen's case series looking at the short-term outcomes over a period of 1 year in 12 cases found there were no conversions to an open procedure and no recurrence. They further stated that the robotic approach may assist the surgeon in dissecting over the sacral promontory [24]. Open sacrocolpopexy is generally associated with greater blood loss, longer hospital stay, delayed return of bowel function, increased postoperative pain, and increased wound complications [25]. A drawback with regard to laparoscopic sacrocolpopexy is the associated technical difficulty in placing sutures [26].

Ploumidis in a retrospective review of 94 cases undergoing robot-assisted sacrocolpopexy with specific regard to complications found one case in which a Clavien grade 3 postoperative complication occurred [27]. Subsequently, there was one case of mesh erosion during a follow-up period of 36 months. Matthews et al. in a prospective study of 85 cases of robot-assisted sacrocolpopexy and robot-assisted sacrocervicopexy concluded these are effective, efficient, and safe procedures. There were two cases of mesh erosion in the robot-assisted sacrocolpopexy group [28]. In 2014, Serati et al. published a meta-analysis and systematic review [29]. The data on 1488 robot-assisted sacrocolpopexies were collected from 27 studies, published from 2006 to 2013. The results revealed objective and subjective cure rates ranged from 84% to 100% and from 92% to 95%, respectively. The conversion rate to open surgery was <1% (range: 0%–5%). Intraoperative and severe postoperative complications and mesh erosion rates were 3% (range: 0%–19%), 2% (range: 0%–8%), and 2% (range: 0%–8%), respectively. They concluded that surgical-related outcomes have improved with increased experience, with an estimated learning curve of about 10–20 procedures. A robot-assisted sacrocolpopexy is a safe and feasible procedure for POP; it allows the execution of complex surgical steps via minimally invasive surgery without medium- and long-term anatomic detriments.

Robot-Assisted Sacrocolpopexy: The Technique

The robot-assisted sacrocolpopexy was first described in 2004 by DiMarco [30] as follows: the procedure combines the use of standard laparoscopy with the da Vinci robotic system. One camera port, two robotic ports, and two standard laparoscopic ports are placed. Standard laparoscopic dissection is used for initial anterior and posterior vaginal mobilization and exposure of the sacral promontory. The da Vinci robot is then docked and used to suture a silicone Y-shaped graft from the vagina to the sacral promontory. The culdoplasty, with plication of the uterosacral ligaments, is then performed, with the final step, retroperitonealization of the graft.

However, over the last number of years with increased surgeon take-up of this technology, the procedure has been modified. In our current practice, the patient is placed in moderate to steep Trendelenburg, and the legs are then placed in the low lithotomy position. Once the positioning is satisfactory, the ports are placed in a W shape with the camera port two fingerbreadths above the umbilicus, the next two ports are placed four fingerbreadths inferolateral to the camera port bilaterally, and the remaining two ports are placed four fingerbreadths superolateral to the preceding two ports

(Figure 103.2). The robot is then docked, the camera arm attaching to the camera port, and the instrument arms subsequently attached and instruments introduced under direct vision. The assistant port is the left superolateral port to facilitate introduction of sutures and ports. Dissection is then performed by the surgeon sitting at the console via the robot, to aid dissection a vaginal and rectal manipulators are introduced (Figure 103.3). The anterior and posterior vaginal walls are mobilized, and following this the sacral promontory is exposed, and a track created to allow the peritoneum to be closed over the mesh. The Y-shaped mesh is then attached from the anterior and posterior walls of the vagina to the anterior longitudinal ligament using permanent sutures, e.g., Gore-Tex. Finally, the peritoneum is then closed over the graft (Video 103.1) [31].

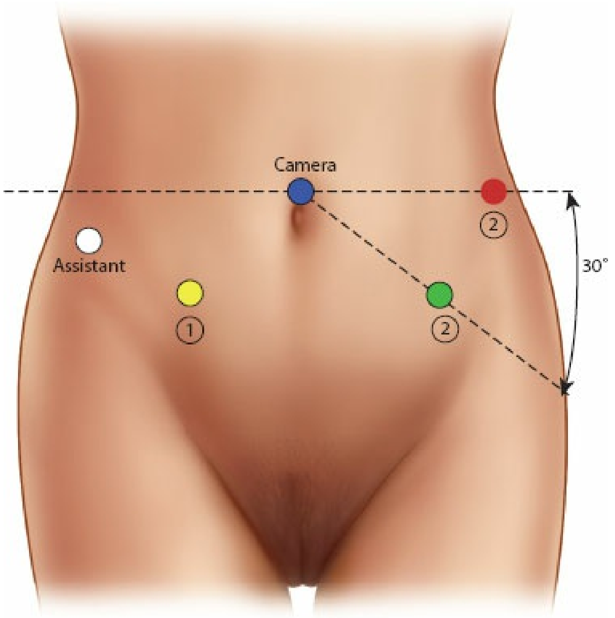

Figure 103.2 Port placement for robot-assisted sacrocolpopexy. (Courtesy of Intuitive Surgical, Inc., Sunnyvale, CA.)

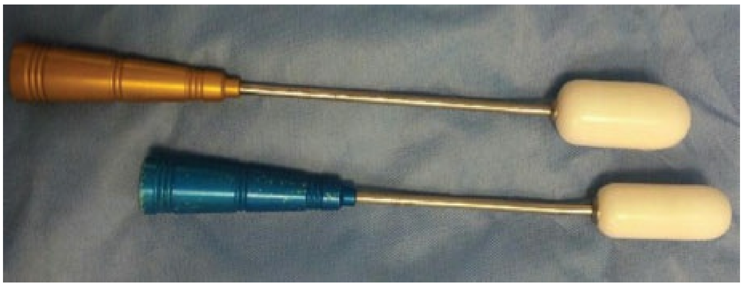

Figure 103.3 Rectal and vaginal manipulators.

Overall robot-assisted sacrocolpopexy is associated with increased operative time compared to the laparoscopic approach [32]. Many publications include training operative times and the operative times for fellows/trainees. While we are aware the learning curves are short, the inclusion of these operative times presents a bias in the times reported. Therefore, to correctly comment on operative times publications should report openly on which times are included. Compared to an open abdominal sacrocolpopexy, the LOS is shorter and the EBL lower, with both approaches having similar complication rates. The evidence available suggests comparable safety and efficacy when comparing robot-assisted to open sacrocolpopexy. The surgical technique used in open/laparoscopic/robot-assisted sacrocolpopexy varies depending on the surgeon across all stages of the procedure. Many papers fail to describe the technique used to perform the surgery, thus making comparison in terms of operation time and outcomes difficult. A consensus is required with regard to the optimal operative technique used to perform a sacrocolpopexy irrespective of approach used.

Hysteropexy

Hysteropexy utilizes many techniques to restore uterine anatomy. Approaches including abdominal, vaginal, and laparoscopic are effective in the management of uterine prolapse where uterine preservation is required [33]. The success rates are similar for all three approaches varying from 87% to 98% [34–36]. Successful pregnancies have been reported following laparoscopic hysteropexy; however, the long-term effects of pregnancy on the surgery are not yet fully appreciated [37]. Lee et al. in their study on the safety and feasibility of sacrohysteropexy for the treatment of prolapse concluded that the surgery was associated with minimal blood loss and had excellent subjective and objective success rates, making it a safe and feasible surgical option in the management of POP where uterine preservation is required [38].

Continent Urinary Diversions

Bladder emptying disorders, which can arise from neurogenic diseases, oncological surgery, or idiopathic causes, are traditionally treated with clean intermittent self-catheterization (CISC). However, in the subset unable to perform CISC, continent urinary diversion (CUD) is an appropriate surgical alternative. The cutaneous appendicovesicostomy initially described by Mitrofanoff in 1980 [39] remains the most commonly performed CUD, followed by the Yang–Monti procedure [40], which uses small pieces of ileum to create a cutaneous ileovesicostomy. These procedures are traditionally performed via lower abdominal incision. Due to technical difficulties, the laparoscopic approaches have failed to achieve widespread adoption. A recently published case series found the robot-assisted approach to be a safe, feasible alternative to both the open and laparoscopic approach in adults [41].

Vesicovaginal Fistula Repair

Another area of urogynecology where the robot-assisted approach has been used is vesicovaginal fistula repair. The robot technology allows a complicated laparoscopic procedure to be performed safely with good results. Vesicovaginal fistulae have been effectively treated using the robot-assisted approach with minimal blood loss, short LOS, and recurrence rates [42,43]. The robot-assisted approach has been used successfully to treat rarer fistulae such as vesicocervical and vesicouterine fistula (1%–4% of urogenital fistulae). Traditionally, these fistulae are surgically managed via an open approach, as they are not accessible transvaginally. The robot aids in the complex dissection and reconstructive techniques required for this type of surgery (Video 103.2) [44,45]. 🎥

TRAINING IN ROBOTIC SURGERY

Traditionally, the surgical apprenticeship relied on the Halstedian model of “see one, do one, teach one.” However, with time it has become evident that this model is inadequate to train surgeons to the highest level without impacting on patient care [46]. The concept of training and surgical education has evolved considerably. Many colleges/boards responsible for the training of surgeons have implemented prerequisites that must be achieved to attain certification to perform surgery. Furthermore, surgeons are required to maintain and update their skills by achieving educational targets. The American Board of Surgeons requires a surgeon to achieve 90 hours of continued medical education credits every 3 years to maintain certification. To facilitate this, the Society of American Gastroenterologists and Endoscopic Surgeons has developed an online university that features journal club, online assessment program, and guidelines. Robot-assisted surgery has created new challenges to ensure proper training and avoid subjecting patients to unnecessary risk. Increased scrutiny of credentialing and medicolegal aspects of robotic surgery have reinforced the importance of training and have led to a number of papers outlining pathways to facilitate this [47,48]. The learning tools for robotic surgery include simulators, dual consoles, robotic courses, and proctoring.

TRAINING COURSES

Training courses on robotic surgery are typically performed using inanimate, animal, or cadaver models. The length of the course varies from several hours to several days, sometimes even weeks in a mini-fellowship situation. The content depends on the attendees at the course. Inanimate exercises offer a cost-effective and robot-agnostic approach to training surgeons [49–51]. They can be designed to target specific (or a subset of) technical skills needed to understand the basic functionality of a robotic system [47,52]. With various levels of difficulty, a continuum of inanimate exercises can guide surgeons of different abilities through their initial learning curves. Inanimate exercises for learning the fundamentals of laparoscopic surgery can be expanded to effectively target robot-specific skills [53]. In order to be useful training tools, inanimate exercises must challenge both specific technical skills of using a robotic surgical system and have validated metrics so that surgeons can accurately track their performance [54].

It is certain that the advent of excellent surgical simulators and structured inanimate exercises has provided tools for novice surgeons to acquire console skills in a safe and structured environment. This will enhance their operating performance and reduce aspects of the learning curve such as operating time; however, the lack of availability of in vivo training opportunities greatly limits the applicability of this method of surgical training [55].

Dual Console

The introduction of the da Vinci Si Surgical System has given surgeons a second robotic console, facilitating collaboration between the proctor and trainee. The mentoring console has two collaborative modes: (1) The swap mode allows the mentor and trainee to operate simultaneously and actively swap control of the robotic arms. (2) The nudge mode allows them to have control simultaneously, sharing the two robotic arms.

Live Surgery and Proctoring

Live case observation remains an important component of a robotic training program [56] and allows the trainee to become familiar with the steps of a specific robotic procedure. Proctoring is defined as direct supervision by an expert during the initial phase of training and the learning curve [56]. It provides a safe environment during the introduction of a new technique and prevents surgeons from performing procedures before they have mastered the technique.

The reality is that simulators, dual consoles, and robotic courses should play an important role in bridging the gap between early surgical skills and effective performance using the robot in a clinical setting without subjecting patients to unnecessary risk. It is also important to have tools that provide an objective means by which to evaluate a trainee's performance in anticipation of their ultimate graduation [57]. Physicians in training can acquire robotic surgery competency. Participants who acquire skills faster regain robotic skills faster after a training hiatus, but, on retraining, all participants can regain equivalent competence. This information provides a benchmark for a simulator training program [58]. One institution has incorporated a graduated program of resident and fellow console involvement based on level of training. They found this approach did not significantly hinder operating room efficiency [59]. However, once acquired, the robotic surgical skills deteriorate without use. In one study, robotic surgical skills degraded significantly within 4 weeks of inactivity in newly trained surgeons [60]. The University of Toronto in a pilot study assessing robotic skill training concluded that the implementation of a multidisciplinary, simulation-based robotic surgery basic skills training curriculum revealed significantly improved basic robotic skills among novice trainees, regardless of specialty or level of training. The competency-based training was associated with significantly better acquisition of basic robotic skills.

LEARNING CURVES

The learning curve associated with laparoscopic sacrocolpopexy has been shown to be linear in nature with the turning point between 18–24 cases in one study [16] and 30–60 cases in another [61].

A recent study assessing the learning curves associated with a robot-assisted laparoscopic colorectal surgery revealed that it consisted of three distinct phases [62]. The first phase or the initial phase occurred over the first 15 cases, during this phase the operating time decreased. The second phase or plateau phase occurred over the next 10 cases; during this phase, the operator becomes more competent with the robotic technology. The third phase or the mastery phase occurred for the subsequent cases. During the mastery phase, the complexity of the cases undertaken increased.

With regard to gynecological surgery, the learning curves reported range from 20 cases for hysterectomy and pelvic lymphadenopathy for endometrial cancer [63], to 50 cases for benign hysterectomies [64], to 10 cases for sacrocolpopexy [65]. The learning curve associated with laparoscopic sacrocolpopexy has been shown to be linear in nature with the turning point between 18 and 24 cases [16]. The robotic approach maintains the benefits of laparoscopy while reducing the technical difficulties [21,23,66].

Knot tying has been shown to be a technical challenge for laparoscopic sacrocolpopexy due to the limited dexterity of the instruments [67]. These challenges are not present in the robot-assisted surgery where studies have shown that due to the instrument grip strength sutures can be tightened effectively [68]. In New York, a study comparing the learning curves for robot versus laparoscopic surgical skills highlighted that with regard to suturing and dexterity skills, the robot allowed for quicker performance than laparoscopy [69]. Ng et al. made the following recommendations to shorten the learning curve. First, have a designated theater team, with no introduction of new members until 20 cases have been performed. Second, patient positioning is of paramount importance and should be standardized for all cases, and finally, familiarization with the instruments sets is required before any deviation is considered [70].

SAFETY IN ROBOT-ASSISTED SURGERY

Problems with Instrumentation

The introduction of new technology brings new challenges especially for the surgeon and the theater team. A recent survey of urologists on intraoperative robot malfunction found that breakdown intraoperatively is uncommon; however, it does occur, highlighting the need to counsel patients and to have a contingency plan. Furthermore, they recommend conventional laparoscopic suturing should be maintained as a requirement on the curriculum, thus allowing the surgery to continue using minimally invasive approach [71]. Murphy et al. [72] in their review reported a device failure rate of 0.2%–0.4%. A report of technical challenges faced by surgeons performing robot-assisted gynecological oncological procedures showed 8% were associated with problems with robotic technology. Of this 8% of cases, 18% involved malfunction of robotic arms, 18% involved light or camera cords, and the remainder included a variety of problems, including malfunction of Maryland bipolar instrument (9%). A further 9% were attributed to power failure requiring rebooting of the robot. Port problems occurred in 18%, and 27% had miscellaneous problems. An estimated average of 25 minutes was added to each case in order to solve the robot-related technological problems. Despite these problems, no cases required conversion to laparotomy. It is noteworthy that the robotic surgeon solved all these problems with the assistance of robotic surgery staff. They conclude that all surgeons performing robotic surgery must become familiar with troubleshooting robotic technology and associated equipment. Failure to do so may add time and technical difficulty to robotic cases [73]. The FDA maintains a database of manufacturer and user facility device experience (MAUDE) where all users of devices report robot malfunctions and their outcomes. In 2008, a review of the MAUDE database identified 168 reported cases of robot malfunction approximately 4.8% of which was associated with patient injury. However, with time the MAUDE database reported incidences of instrument failure have increased with 528 reports of 565 instrument failures over 2 years between January 2009 and December 2010. Friedman et al. divided the instrument failures into five groups depending on the reported failure: (1) wrist or tool-tip failures (n = 285), (2) cautery instrument failures (n = 174), (3) instrument shaft failures (n = 76), (4) cable failure (n = 29), and (5) control housing failures (n = 1) [74]. In general surgery in a single university unit, Buchs et al. recorded a robotic malfunction rate of 3.4% (18/526) over a 7-year period. Instrument failure accounted for 50% (9/18) of cases, 22% (4/18) occurred due to robotic arm failures, 16% (3/18) derived from console errors, the remaining 12% (2/18) failure occurred in the optic unit. Of note, the failure rate decreased with increased operator and team experience [75]. With specific regard to gynecological oncology, Finan et al. reported a technology failure rate of 8.02%. They advocated that surgeons and their team should be specifically trained to troubleshoot for these issues [73].

Neurological Injuries

Patient positioning is of great importance to minimize the potential adversarial outcomes associated with long operative times. In a single unit study, nerve injury associated with positioning during urological robotic surgery had an incidence of 6.6%. It is of concern that 23% of these persisted beyond 6 months. The injury rate was significantly affected by operative time and American Society of Anesthesiologists group. Therefore, patients undergoing long surgeries should be counseled regard the risk of nerve injury especially if they have multiple comorbidities [76].

General Safety

Checklists have been used as an intervention to prevent these failures by promoting a team-working culture, standardizing practice, allowing the detection of potential errors, and improving patient safety as a whole. One example is the World Health Organization surgical safety checklist. Another example, the Healthcare Failure Mode and Effects Analysis (HFMEA) protocol has been widely used across organizations. The HFMEA is a powerful systems evaluation tool developed by the U.S. Department of Veterans Affairs National Center for Patient Safety. It is a step-by-step process that involves the multidisciplinary team in identifying potential causes of error within a system through the use of flow diagrams, hazards scoring, and decision tree analysis. Potential errors are prioritized according to severity, frequency/probability, criticality, detectability, and existing control measures. The final process includes taking steps to implement solutions, minimize errors, and avoid adverse events [77]. In a recent study using the HFMEA, specific hazards were identified, e.g., patient positioning, port placement, robot docking/de-docking, and robotic and laparoscopic equipment checks, which were considered to be important in robot-assisted urological procedures and which are not extensively covered by other checklists [78]. A unit-specific robot-specific checklist was developed with the aim of allowing the detection of potential errors and improving patient safety as a whole.

SURGEON ERGONOMICS

Robot-assisted laparoscopic surgery attempts to overcome some of the limitations of laparoscopic surgery while retaining the benefits of a minimally invasive approach. Specific improvements associated with robot-assisted surgery include better visualization through the use of three-dimensional magnification, availability of tools with 7 degrees of freedom that mimic hand movements along with improved ergonomics, and more intuitive hand–eye coordination when controlling surgical instruments [79–81]. However, this has been achieved at the cost of haptic and tactile feedback, as a result of the instruments not being directly manipulated by the surgeon [82]. It is yet to be seen whether tactile feedback can be achieved through increased sophistication of the computer software.

There is limited primary data available in regard to the effect of using the robotic device on surgeon morbidity and discomfort. A pilot study by Lawson et al. [83] assessed the differences between musculoskeletal discomfort and ergonomic strain in laparoscopic versus robotic surgery for gastric bypass surgery. They found that robotic cases were associated with more discomfort in the neck, while laparoscopic cases were associated with greater discomfort in the upper back and in both shoulders.

Furthermore, analysis of ergonomic positioning during the procedures found that laparoscopic surgery was associated with poorer ergonomic positioning of the upper arm, lower arm, wrist, and wrist twist, while robot-assisted surgery scored lower for trunk positioning. A recent study assessing the ergonomics of the surgeons’ physical workload during both laparoscopic and robot-assisted procedures found the physical workload and the perception of effort were greater for laparoscopic procedures. During the standard laparoscopic procedures, there was a greater physical activity in the trapezius and dorsolumbar muscles. Mental stress was identical for the two groups, while the heart rate was significantly raised in the standard laparoscopy group confirming greater physical expenditure [84].

However, the ability to generalize based on studies for specific surgical indications is limited, as the advantage of robotic-assisted surgery significantly depends on the type of the procedure [81]. The EBL was reported as lower in the robot-assisted group compared to open surgery. This may be secondary to the improved visualization achieved using the robot and subsequent improved surgical precision.

The traditional limitations on laparoscopic surgery performed with straight-stick instruments have been superseded by the EndoWrist instruments in robotic-assisted surgery. These allow for a wider scope of practice and manipulation. Furthermore, robot-assisted surgery is associated with improved visualization thus allowing for improved surgical precision, which could account for the associated reduced blood loss when undertaking complicated surgical cases.

With obesity increasing throughout the developed world, patient habitus often precludes them from laparoscopic surgery. However, they may have robot-assisted surgery performed with similar benefits. More complex procedures can be undertaken robotically than with traditional straight stick surgery. Obesity is traditionally associated with an increase in perioperative morbidity and mortality [85]. Buchs et al. [86] in perioperative risk assessment of 884 patients undergoing robot-assisted surgery found a BMI of >30 did not influence morbidity or mortality. Eddib et al. studied the effect of morbid obesity on outcomes in robot-assisted gynecological surgery. They found that morbid obesity did not appear to be associated with an increased risk of morbidity. Furthermore, while morbid obesity is associated with an increased procedure time, it had no effect on outcomes. Therefore, robotic surgery offered an ideal approach, allowing minimally invasive surgery in these technically challenging patients, with no significant increase in morbidity [87]. Robotic surgery may provide benefits in terms of wound infection and conversion rates [88]. Comparing the laparoscopic and robot-assisted approach in obese patients, there was no difference in outcome, a longer operating time and reduced LOS [89,90]. Studies have shown a fourfold higher conversion rate with the laparoscopic approach in obese women undergoing hysterectomy compared with nonobese women [91]. Body surface area has been shown as a predictor for conversion during laparoscopic colorectal surgery [92]. However, robot-assisted hysterectomy has not been shown to have a higher conversion rate in obese women [93]. Many authors allude to the potential reduction in surgeon strain with regard to surgery in the obese patient; however, no specific studies have been published.

CONCLUSION

The robot-assisted surgery aims to offer the benefits of minimally invasive surgery, such as reduced postoperative pain, shorter hospital stay, quicker recovery time alongside the specific benefits associated with robotic surgery including less technically demanding, shorter learning curve, and ergonomic benefits [31].

There are significant limitations with the quality of the published data analyzing the advantages and disadvantages of robot-assisted surgery. This makes it difficult to know whether the advantages claimed by the protagonists are genuine, and until robust trials are performed, the validity of the claims of benefits to patients and surgeons must be questioned [8–11]. Some of the limitations include a low quality of evidence when the studies were graded according to the National Health and Medical Council hierarchy of evidence [94]. There is a paucity of long-term functional and outcome data associated with robot-assisted surgery and its effect on the patient’s quality of life. Furthermore, there is limited data available for gynecological procedures such as prolapse surgery in the form of sacrocolpopexy/hysteropexy, where only one randomized control trial (RCT) exists. A recent editorial in the *International Urogynecology Journal* highlighted nicely the limitations and difficulties faced when trying to conducted an RCT in robotic-assisted surgery [95].

The robot system may allow minimally invasive approaches to be used where conventional laparoscopic approaches would otherwise not be possible [96]. It also allows for improved visualization and subsequent improved surgical precision.

From the available published literature, most studies conclude that robot-assisted surgery is feasible and technically safe with acceptable early operative outcomes that appear to be comparable to those achieved with open or laparoscopic surgery. However, more robust studies need to be conducted to answer the question of which modality is associated with the greater long-term results.

VIDEOS

Video 103.1. Robot-assisted sacrocolpopexy: http://goo.gl/lnHoCm.
Video 103.2. Robot-assisted vesicovaginal fistula repair: http://goo.gl/zlf3VO.

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104 Vesicoscopy

Philippe Grange and Chrysanthos Kouriefs

INTRODUCTION

Vesicoscopy is an elegant minimally invasive technique applying the principles of laparoscopic surgery to the bladder. The suprapubic percutaneous transluminal route allows a variety of procedures that would otherwise not be accessible via transurethral endoscopic surgery. In this chapter, we will describe our experience with vesicoscopic procedures in female patients and explain the most common indications for such procedures. We will critically discuss the use of vesicoscopy as reported in the literature and conclude with the future of vesicoscopy.

MATERIALS AND METHODS

Our Experience to Date

Between 2007 and 2014, 25 female patients underwent 33 vesicoscopic procedural steps under the same mentoring team at three sites: King's College Hospital, London, United Kingdom, $n = 20$; Polykliniki Ygeia, Limassol, Cyprus, $n = 3$; and Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany, $n = 2$. The age of the patients ranged from 13 to 67 and their BMI from 17 to 60. Vesicoscopy was chosen in congenital, acquired, and iatrogenic conditions including incontinence, ureterovesical reflux, voiding dysfunction, foreign bodies, endometriosis, and ureteric strictures. The intended procedures were ureteric replantation $n = 13$, vesicovaginal fistula (VVF) repair $n = 9$, foreign body extraction $n = 5$, antegrade ureterectomy $n = 3$, bladder diverticulum $n = 2$, and tissue excision, $n = 1$. Vesicoscopy was performed as a standalone approach in 13 patients and in combination with other approaches in 12 cases, with vaginal approach $n = 8$, with both vaginal approach and transperitoneal laparoscopy $n = 1$, and with retroperitoneoscopy in the supine position $n = 3$.

Standard Technique

In cases of antireflux ureteric replantation, the patient is in the supine position; the legs are flat and the arms rest along the body; the urethral catheter is inserted after cleaning and draping to allow intraoperative access. We find it ergonomically comfortable to use a moderate head-down position and whenever possible to sit and work from the left side of the patient. If an assistant is needed, which is not always the case, he or she will sit on the right side of the patient. The imaging screen display stands at the feet of the patient. When it is necessary to access the vagina or urethra, the assistant sits between the patient's legs.

The bladder is distended using CO_2 gas supplied from a standard laparoscopic insufflator connected to a Foley catheter at a pressure setting of 15 mm Hg. Should the patient present with any lower abdominal scar and history of pelvic surgery or if the distended bladder is not palpable, we feel it is appropriate to perform a suprapubic ultrasound scan first. This harmless investigation helps to identify risks related to the presence of a bowel loop, vascular abnormality, or insufficient bladder distension. Translucent visible ports are placed under direct 0° camera vision. The primary 5 mm access port is inserted 2 cm above the symphysis pubis on the midline. A twist and push maneuver splits the successive layers of tissues clearly visible through the translucent blunt tip of the trocar. In the presence of a "Pfannenstiel," we place our port below that incision. Two further 5 mm ports are inserted on either side of the primary port on the same horizontal line, fairly close to each other (Figure 104.1).

The next crucial step consists of suspending the anterior wall of the bladder to the abdominal wall with a single stitch inserted with an "in and out" maneuver on either side of the midline port using a specific reusable or disposable device, releasing and catching back a 2-0 monofilament suture. This prevents the bladder from collapsing if a port is inadvertently retrieved or if the patient suddenly strains on "anesthetics grounds." Once all three ports are in place, the 0° scope is replaced by 30°, inserted into the right port, and stabilized by a motorized camera holder. We work from the two ports, closer to the surgeon.

Combined Procedure with Vaginal Access

We combine the vaginal approach and the vesicoscopic route in procedures such as vaginal fistula repair. The patient is placed in the Lloyd-Davis position. At the “vesicoscopic end,” little differs from the generic access apart from the screen display standing at the right leg of the patient. At the “vaginal end,” the surgeon sits between the patient’s legs and should ideally have an ancillary screen display at the head of the patient (Figure 104.2).

Combined Procedure with Retroperitoneoscopy in Supine Position

We combine vesicoscopy and supine retroperitoneoscopy in procedures such as ureteric remnant excision. The patient is placed in the supine position with the side to be operated on exactly at the edge of the table, the leg straight, and the arm held above the thorax. The opposite leg is generously flexed to allow the introduction of a semirigid ureteroscope that will help in differentiating the ureter from the surrounding postoperative fibrotic scar tissues. The surgeon is at the left side of the patient for the vesicoscopic step, looking at a screen placed at the patient’s feet. For the ureteroscopic step, the surgeon stands on the right side of the patient looking at a screen placed on the left side of the patient. For the supine retroperitoneoscopic step, the surgeon sits at the side of the patient looking at a screen on the contralateral side (Figure 104.3).

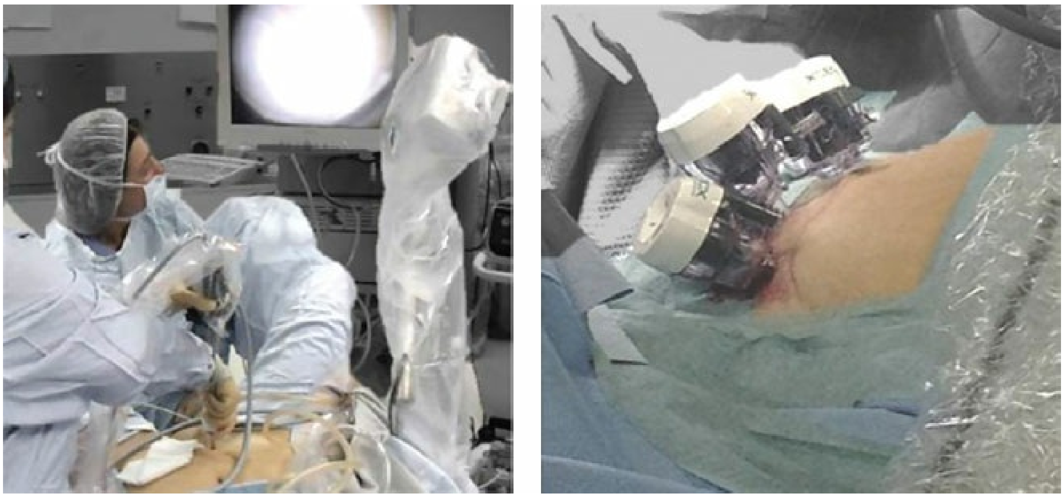

Figure 104.1 Primary port insertion under 0° vision, three ports in place below the Pfannenstiel scar.

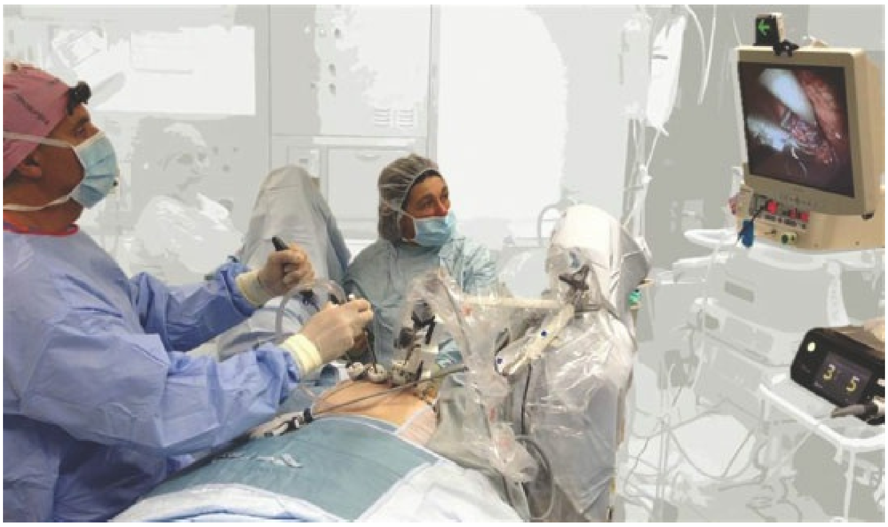

Figure 104.2 Theater choreography for a collaborative vaginal and vesicoscopic approach.

RESULTS

Vesicovaginal Fistula

Nine patients suffering from incontinence related to a complex VVF not suitable for simple vaginal approach underwent a combined vaginal and vesicoscopic repair. The reasons for this choice were narrow introitus, high location, involvement of ureters, and radiation therapy. The detail of the technique is described in a separate publication [1]. The vaginal surgeon, at the beginning of the procedure, obliterates the fistula track by various means to allow bladder distension. When the time comes to excise the fistula tract, he or she gives crucial information on the softness of tissues on palpation, allowing an accurate and complete excision of the fibrotic tissues, which is the key to successful repair. Finally, at the end of the repair, the vaginal surgeon can retrim, mobilize further, and suture the vaginal vault. The vesicoscopic surgeon carries out a resection that should not be restricted by the proximity of the ureter. Whenever necessary, it must be displaced and replanted. This has been the case for three of our patients who underwent one bilateral and two simple antireflux reimplantations (one for stricture, one due to proximity). The generous mobilization of the bladder wall allows the vesicoscopic surgeon to suture well-vascularized tissues without tension in a watertight fashion (Figure 104.4).

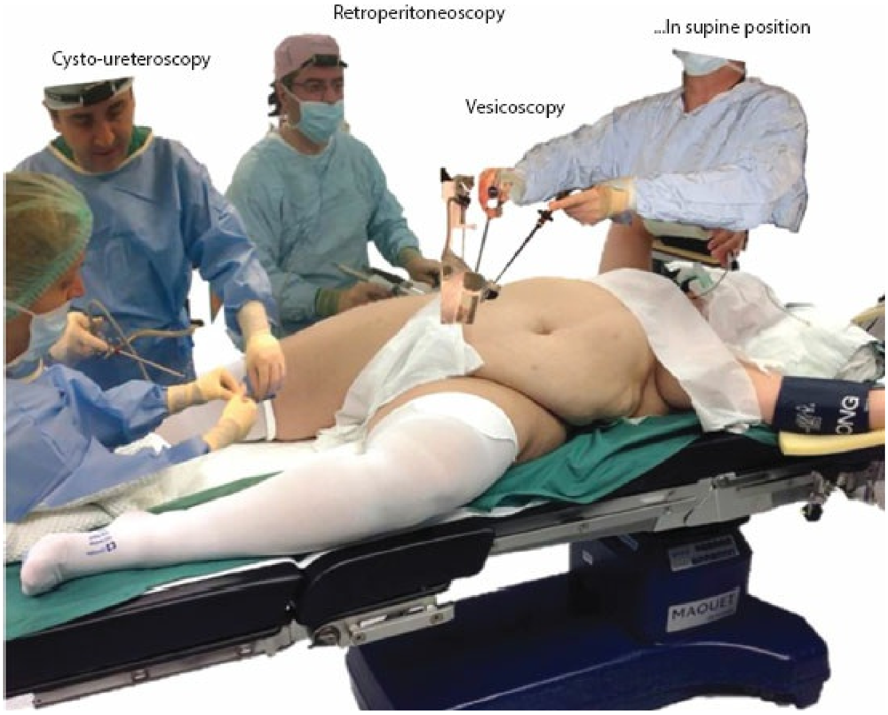

Figure 104.3 Patient’s position and choreography for endoscopy, retroperitoneoscopy, and vesicoscopy.

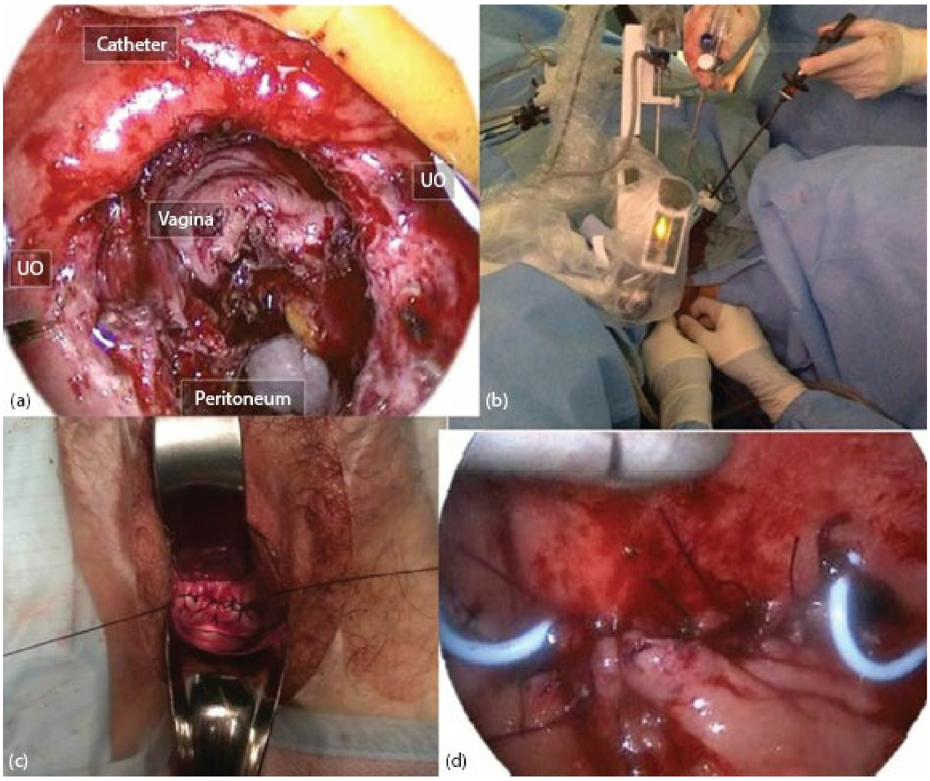

Figure 104.4 Vaginal and vesicoscopic closure of a large fistula defect after wide excision. (a) Vesicoscopic view of large fistula in bladder base, (b) external view of instrumentation, (c) vaginal view of vaginal closure, (d) vesicoscopic view of bladder closure with illuminated stents in ureters.

Ectopic Ureter in Duplex System

One teenage patient had been suffering from day and night incontinence for 17 years since she was born. She unfortunately had a long history including surgical treatments for stress urinary incontinence with a colposuspension and injection of bulking agents. She was eventually referred to our urogynecology unit and was diagnosed with an ectopic ureter in a left duplex system. She underwent a successful vesicoscopic reimplantation. A double-barrel extravesical ureteroneocystostomy was performed purely through the transvesical route. She was dry on the same evening. At follow-up, the left system was not obstructed. As expected from the choice of technique, the left lower ureter shows grade I reflux, which we do not intend to treat (Figure 104.5a).

Distal Ureteric Stricture

Two adult patients in their 60s presented with distal ureteric strictures. One was following radiation therapy. The second morbidly obese patient had a distal right stricture after the endoscopic treatment of a low-grade distal transitional cell carcinoma (TCC). Both underwent a distal resection and proximal replantation in the form of a ureteroneocystostomy using the vesicoscopic route. At follow-up, both patients presented with satisfactory results: a nonobstructed normally functioning kidney. At 40 months ureteroscopic follow-up, no TCC recurrence was demonstrated [2].

Reflux: Simple Antireflux System

Four adult patients with recurrent infections and pain in the context of grade III reflux were treated with a vesicoscopic antireflux procedure. One patient underwent a bilateral procedure (Cohen submucosal advancement) in two separate operations. The other three patients underwent unilateral replantation, one with the Cohen [3] submucosal advancement technique and two with the Leadbetter and Politano proximal ureteroneocystostomy technique, reimplanting the ureteric orifice at its original site [4]. All cases were successful with no complications at follow-up (Figure 104.5b).

Bilateral Reflux: Combined Vesicoscopy and Supine Nephroureterectomy

One further patient presented with severe bilateral grade V reflux with a nonfunctioning kidney on the right side and grade III on the left side. She underwent a combined vesicoscopic left antireflux procedure using the Leadbetter–Politano reimplantation technique. Two ports only were used for the instruments, while the vision was provided by a high-definition (HD) distal chip flexible cystoscope inserted transurethrally. At the same time, the right ureter was disconnected from the bladder, dissected transvesically in a retrograde manner up to the obliterated ligament. When the former ureteric orifice defect was closed, the lower ureter was buried into the extravesical space. Finally, a right nephroureterectomy was completed using the supine retroperitoneoscopic technique described in our video presentation [5]. The supine retroperitoneoscopy allows straightforward antegrade dissection of the ureter down to the obliterated ligament, which is the upper limit of the vesicoscopic approach: making both approaches complementary. In this patient with low BMI, two 5 mm ports and one 11 mm port were used for the supine nephroureterectomy. The kidney was retrieved after morcellation, leaving her with only a 15 mm visible scar in addition to two 5 mm scars and two other suprapubic 5 mm scars.

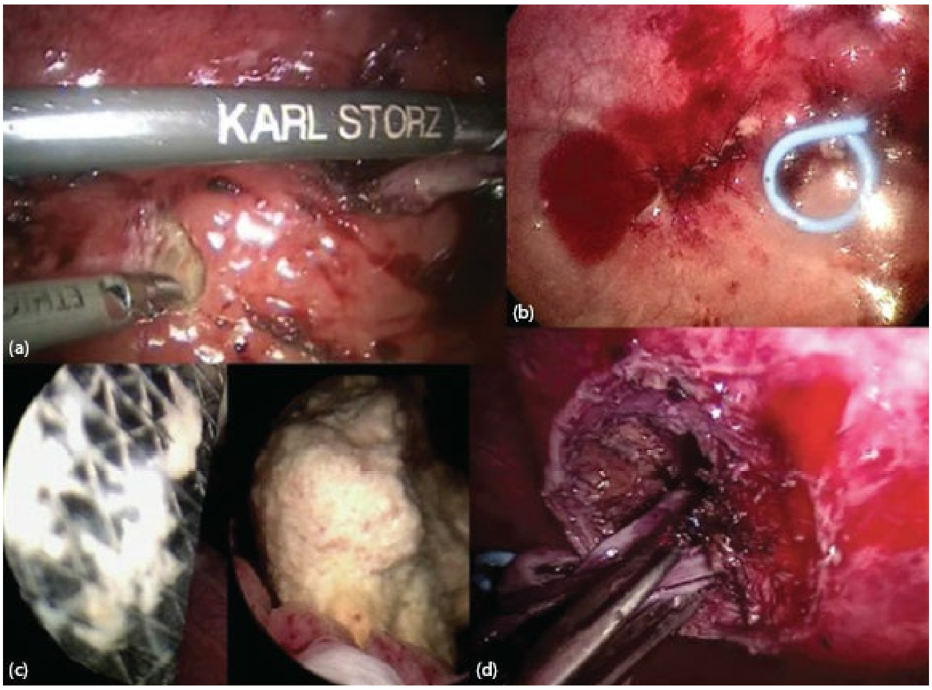

Figure 104.5 (a) Ureteroneocystostomy, (b) left Cohen procedure, (c) encrusted nail file, and (d) bladder diverticulum.

Reflux: Ureteric Remnant Postnephrectomy

Chronic ureteric reflux was also the cause in the symptoms of another patient with a high BMI who presented with infection and pain related to a ureteric remnant left after simple laparoscopic nephrectomy for a poorly functioning chronically infected kidney. She underwent a combined vesicoscopy and retroperitoneoscopy in the supine position. The latter with the help of a semirigid ureteroscope allowed identification in the fibrotic scar tissue, the safe mobilization of the iliac vessels, and the antegrade dissection of the ureter down to the obliterated ligament. The former enabled the disconnection of the ureteric orifice, retrograde dissection of the ureteric stump up to the obliterated ligament, and antegrade extraction of the whole remaining specimen prior to closing the defect of the ureteric orifice (Figure 104.6).

Congenital Pelvic Nephroureteric Remnant

A third patient underwent a combined supine retroperitoneoscopy and vesicoscopy. This 13-year-old teenager was found to have a congenital ureterocele and retrovesical right pelvic mass. No functioning kidney was present on that side. The vesicoscopy allowed the transvesical excision of the ureterocele and the retrograde dissection of a short megaureter. It was unclear from that route where the upper part of the mass was actually ending. The addition of a supine retroperitoneoscopic step allowed the safe identification and final dissection of the pelvic nephric remnant, which was then easily retrieved. The bladder defect was closed transvesically.

Bladder Diverticulectomy

Vesicoscopy has gained popularity in adult urology for bladder diverticulectomy, a condition that is frequently associated to bladder neck obstruction in men. We have carried out a bladder diverticulectomy on two female patients presenting with voiding dysfunction, infection, and a large urinary residual. The technique in women does not differ from its counterpart in men. Insertion of a double J stent is recommended due to expected proximity between the pelvic ureter and diverticulum. Both cases were uneventful and successful from an anatomical and functional point of view (Figure 104.5d).

Bladder Endometriosis

A nodule of endometriosis located on the ureteric bar between the ureteric orifices was excised, and the bladder sutured. Follow-up at 4 years was unremarkable. We are not aware of similar case reported in the literature using that route (Figure 104.7a).

Foreign Bodies

One 29-year-old patient presented with an encrusted nail file protruding from the bladder into the vagina. Vesicoscopy facilitated easy removal of the foreign body, which could not be removed transvaginally because of a large calculus round the nail file. We subsequently repaired her fistula vaginally, but she died from the progression of a rapidly spreading metastatic cancer unknown at the time of her first presentation (Figure 104.5c).

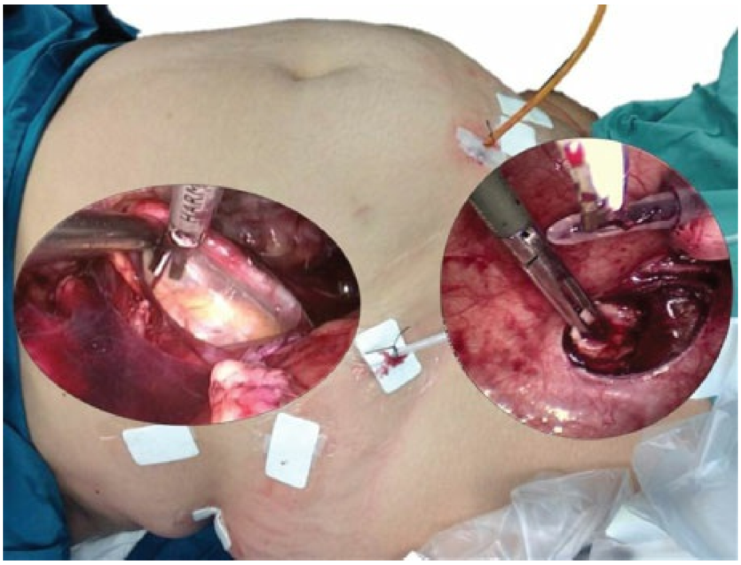

Figure 104.6 In supine position, antegrade retroperitoneoscopic (ureteroscope lifting the ureter) and retrograde vesicoscopic dissection of a ureteric remnant.

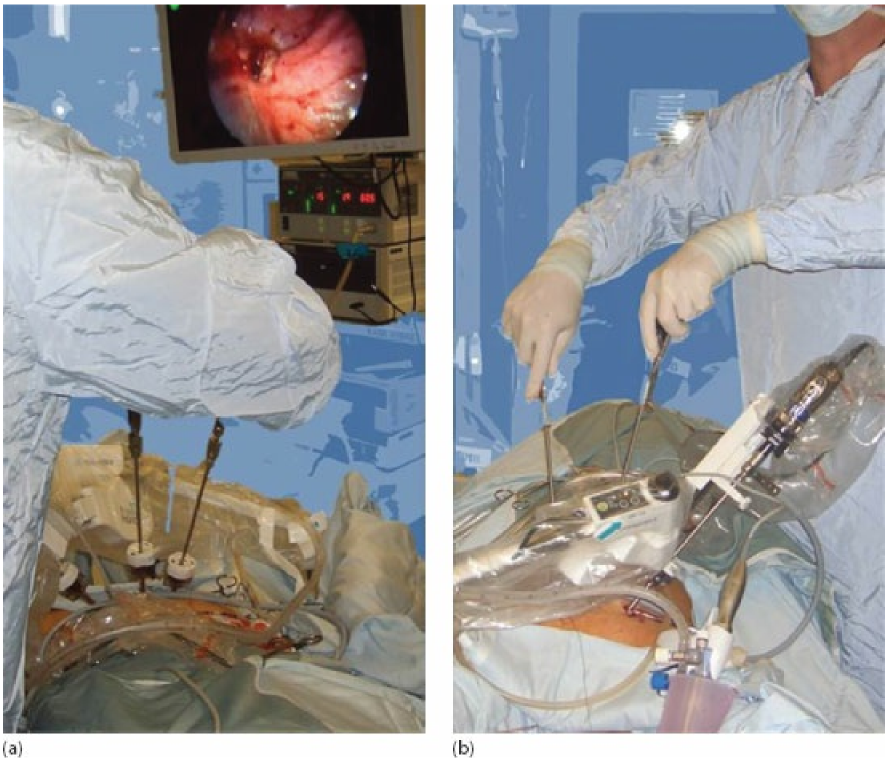

Figure 104.7 Excision of bladder endometriosis (a) operator in standing “toreador” position (b).

Three other patients were treated for complications related to various types of tapes inserted for stress urinary incontinence that had totally or partly transected the urethra or bladder neck. All three patients were tertiary referrals with a long history of endoscopic, vaginal, and open reinterventions. One tape that was infected was totally removed through the vesicoscopic route. Two others were partly resected. One patient suffered increasing dysuria afterwards; the bladder urothelium was normal, but the mesh was still exposed into the urethra. She underwent a second vesicoscopic procedure, allowing the complete removal of the tape purely through the vesicoscopic route with minimal damage to the posterior wall of the urethra and bladder neck (Figure 104.8).

Postoperative Events

Despite the “minimally invasive” branding, postoperative pain must not be underestimated. The vast majority of the patients irrespective of the indication or technique were in need of a strong proactive pain management for 48 hours or longer. No adverse events or complications were recorded using the Clavien–Dindo classification. One patient having a fistula repair had an intraoperative peritoneal gas leak that was managed with an umbilical drain for the duration of the procedure. We report one delayed dysuria after partial resection of an eroded tape that needed a reintervention at 6 months and one failed attempt to repair a VVF in a woman with a BMI of 60 who had a history of cesarean section for placenta percreta. She suffered a massive hemorrhage requiring an emergency hysterectomy and partial cystectomy. She received a total of 100 units of blood and blood products and underwent embolization, following which she lost three toes on her left foot and part of her left buttock. She is dry with a suprapubic catheter in situ, which has considerably improved her quality of life. All other procedures were successful, although one young woman died 18 months after her procedure from metastatic lung cancer.

DISCUSSION

Bladder Distension: Gas vs. Liquid?

One could ask if there is any specific reason to prefer gas or liquid for bladder distension and why it should differ between transluminal and endoluminal surgery. Typically, gas is used in vesicoscopy (a sensible choice for a technique inspired by laparoscopy), and liquid is used in cystoscopy (also a sensible option to fill an organ meant for storing urine). However, the literature suggests that a wider use of gas is a long missed opportunity: Bristow demonstrated experimentally in 1893 the benefits of using gas over liquid to dilate the bladder in suprapubic cystostomy [6]. Faulds reported in 1904 the advantages of using gas for cystoscopy with improved vision for the surgeon and comfort for the patient [7]. Further evidence came in the twentieth century [8,9]. Bridging the gap between evidence and evidence-based practice is not the purpose of this chapter, although a less scientific, but important, advantage of the gas is what keeps our socks dry.

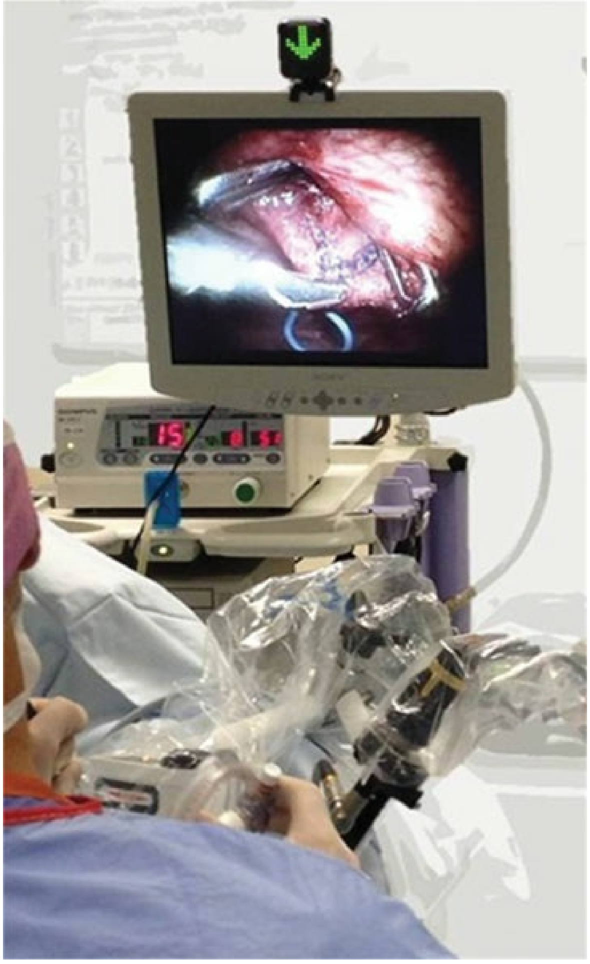

Figure 104.8 An exposed urethral tape is dissected using a transurethral laparoscopic grasper as a retractor.

Port Access: To See or Not to See?

Percutaneous access to the bladder has been mastered by generations of surgeons who have inserted suprapubic catheters for centuries in acute or chronic circumstances of urinary bladder distension; the vesicoscopic access used here does not deviate much from this routine task, and one could be tempted to blindly insert the primary port. Instead, we prefer the visible insertion of nonsharp ports for these reasons: knowing that blind insertion carries the same morbidity and mortality as major pelvic operations [10], we cannot find any good reason at teaching institutions to prefer blind over visible and sharp over blunt tip insertion. The use of a Step-port^{TM} under cystoscopic control is an option; we prefer the nonsharp tip of a translucent port [11].

Bladder Suspension: Stitch or Balloon-Tip Port?

We do not consider balloon-tip trocars as an alternative to 5 mm trocars and a suspension stitch. Needles or energy devices may just pop the balloon of the ports [12]. To suspend the bladder wall, rather than driving a straight needle–mounted suture, we prefer to use a dedicated device. This avoids straining on the fulcrum point of the needle driver, which could stretch the bladder point of entry resulting in gas leakage developing in the cave of Retzius and a reduction in the working space in the bladder.

Why Place Ports So Close to Each Other?

The position of our ports inevitably leads to some clashes as most ports have disproportionately large heads without any technological need. This limits the triangulation of our instruments (Figure 104.1). In a series of four fistula repairs, a wider and higher port position has been described, which certainly reduces instrument clashes and allows more triangulation; however, this increases the risk of an injury to the peritoneum, leading to intraoperative pneumoperitoneum and postoperative peritoneal urine leak as shown with the reported 50% Clavien–Dindo IIb complications [13]. We have in our series only one case of intraoperative gas leak and no case of postoperative urine leakage. Should an intraperitoneal gas leak happen, we recommend exploring it systematically and placing a 14-gauge soft silicone drain through a 5 mm port at the umbilical site, which allows flattening of the abdomen at the cost of an acceptable leak of gas at a rate of 3 L/minute, which is easily compensated by modern insufflators.

Which Port Site for Camera?

It has always been our choice in any pelvic surgery to breach the "triangulation rule" and place the camera into the right side port. Although a side view requires some mental adaptation, this is a small price to pay compared with the benefit of an ergonomic setting. It allows working seated reducing fatigue, which eventually benefits the patient and addresses some ergonomic issues [14]. In support to our claim, we argue that no pilot would be allowed to fly over the sea for 6 hours or more in a standing laparoscopic surgeon position. However, not everybody would agree as shown by one of the experienced surgeons we have trained in this technique (Figure 104.7a). The "toreador" position carries its own risk of surgeon neck and arm injury. The limited triangulation between ports is an issue only to anthropomorphic minds, figuring that the camera head should stay between the shoulders. Picasso has demonstrated a long time ago that there are perfectly workable alternatives.

Why Camera Holding Device When We Have Numerous Assistants Keen to Help?

Beyond declared conflict of interest, the reason we prefer a motorized camera holder to its human counterpart is that it gives a perfectly stable picture and reduces the stress related to misunderstanding or tension between the surgeon and assistant. The assistant is often not needed anymore or at least not in that unrewarding role. It is also worth exploring the concept of solo surgery.

Semantics

Percutaneous cystoscopic surgery has been reported over two decades in different situations. It came first in male urology before finding its application in female urology. In 1990, Badlani et al. reported "a percutaneous cystolithotripsy" and predicted a growing role for "percutaneous bladder surgery" [15]. In 1995, the percutaneous approach made a major breakthrough with the publication in the *Lancet* of "percutaneous cystoscopy" in fetal surgery for posterior urethral valves [16]. An experimental video-assisted "percutaneous cystoscopy" was applied to laser prostatectomy in a dog [17]; it is under a "technique of suprapubic percutaneous telescopy" in that bladder control during laparoscopic gynecological surgery was reported in 1997 [18]. Gill et al. [19] published in 2001 a preliminary series of "percutaneous Cohen antireflux". In 2008, Valla et al. reported their 5-year experience of "transvesicoscopic" Cohen antireflux technique [20]. Nerli and Reddy [13] have reported a "transvesicoscopic" Latzko-type repair in four cases of VVF and further complex fistula repair through the transperitoneal transvesical laparoscopic route. The use of "intravesical laparoscopy" or "transvesical laparoscopy" in the literature is confusing; it can cover transperitoneal transvesical laparoscopic procedures like the four cases of mesh erosion presented at the ICS–IUGA meeting [21] or purely vesicoscopic procedures such as bladder diverticulectomy [22], singleport prostatic benign adenomectomy [23], single-port robotically assisted radical prostatectomy [24], and foreign body [25] and urethrorectal fistulae [26]. We like the word vesicoscopy because it is short and fits the purpose.

Supine Retroperitoneoscopy

There have been previous reports of supine position in retroperitoneoscopic vascular surgery [27], extraperitoneal lymph node dissection [28], and hand-assisted laparoscopic bilateral nephrectomy [29]. To our best knowledge at the 2013 American Urological Association meeting, we gave the first video presentation of a retroperitoneoscopic nephrectomy in the supine position on a frail patient unsuitable for other upper tract interventions; we have found since that the supine position approach is particularly good for chasing a difficult pelvic ureter in previously multioperated large patients, for instance, in the repair of a severed ureter after unrecognized initial injury during pelvic surgery. Furthermore, the combination of vesicoscopy and retroperitoneoscopy makes it easily feasible to approach a benign pelvic ureter in a single supine setting without having to reposition the patient, and we find that there is no longer any excuse for leaving in situ a refluxing ureteric stump after laparoscopic or open nephrectomy in an obese patient. In a patient with low BMI, should the peritoneal cavity be free, we would however still prefer a transperitoneal nephroureterectomy.

About Fistula Repair: From Below vs. from Above?

This is a very old discussion [30] to which we have a clear answer: the vaginal approach was, is, and will remain our first choice. It is quick to perform, has excellent results, and is postoperatively uneventful. We won’t replace the Latzko technique or other vaginal repairs by its vesicoscopic equivalent [13,31]. We reserve vesicoscopy for the most challenging and complex cases. We are conscious that we report here a limited series; however, we think that vesicoscopy is of importance as it has entirely replaced in our departments the open approach for the repair of those difficult VVFs. Its principles rely on closing the bladder defect from its lumen under vesicoscopic view, the vaginal defect from its own lumen via the perineal approach, and in one case, the peritoneum from its own cavity via a standard laparoscopic route. In that particular case, the need occurred for an additional transperitoneal laparoscopic step in order to mobilize and close a gigantic peritoneal defect due to a previous open surgical resection of the pouch of Douglas for ovarian cancer. It is also in that case, after chemotherapy, that an omentum interposition would have been much needed and that it had been removed for cancer treatment. Should the need occur again, we would not hesitate to combine vesicoscopic and transperitoneal route in order to mobilize and interpose the omentum. Even if a transperitoneal step is considered, the primary vesicoscopic route remains justified for the bladder appears surprisingly easier to close from the vesicoscopic side than from the peritoneal cavity as shown in our video [32]. Furthermore, in patients with previous multiple abdominal operations, the peritoneal access and dissection may be difficult, dangerous, and time-consuming due to dense adhesions. Should eventually a vaginal access be extremely poor and comprise the closure from its own lumen, vesicoscopy would still allow a decent vaginal closure without claiming the perfection obtained from below.

Should an interposition of the omentum be needed, which has been recently subjected to debate [33], it would then be feasible laparoscopically and compatible with our technique [34]. Finally, vesicoscopy has avoided a urinary diversion in two of our patients, who were given that reasonable option at other centers of excellence of international reputation.

Antireflux Techniques: Open, Endoscopic, or Vesicoscopic?

One could wonder what are antireflux techniques doing in a textbook of urogynecology; the answer is clear—gynecological diseases and techniques flirt dangerously with the ureter, and the experience acquired with antireflux techniques will free the mind of urogynecologists when the time comes to displace or reimplant a ureter. Open antireflux techniques have a high success rate; on the other hand, the endoscopic submucosal injection of foreign material is less invasive, hence its adoption despite a high rate of long-term failure, incremental cost of repeated procedures, and uncertainty regarding the long-term tolerance of foreign particles migrating from their implantation site. Will vesicoscopy, a small technique squeezed between two powerful giants—conservatism and industry—make the difference and those two redundant? In their initial report of three cases, Gill et al. [19] have described a transurethral cystoscopic vision with laparoscopic instrumentation inserted percutaneously into the bladder in the treatment of symptomatic unilateral ureteric reflux. It has since gained popularity; however, its reproducibility by other teams was made difficult by the use of the transurethral cystoscopic visualization, which causes difficulties during the usage of the working instruments because their movement will be “mirror-imaged” on the screen. Yeung et al. [11] used three 5 mm suprapubic ports, allowing percutaneous vision, avoiding this “mirror-image” effect, and reported a series of 23 reimplanted ureters in 16 children with one conversion to open surgery due to a port displacement and a success rate of 96%, which is comparable to conventional techniques. In a comparative to open approach study, Canon et al. reported that in 52 children vesicoscopy was less painful [35]. A recently updated series of 103 children reported a feasibility rate of 98%, and success rate for resolution of the reflux was 94%. Vesicoscopy seems to be an elegant alternative to both open and endoscopic techniques.

Is Fishing Manufactured Foreign Material in Murky Water Still Justified?

On continence and anatomical restoration grounds, a growing number of female pelvic organs are tacked, stapled, taped, and meshed. No one will dispute the fact that as a result a proportionate number of erosions, infections, rejections, incrustations, and migrations do occur. This carefully chosen vocabulary suggests that those manufactured foreign bodies have acquired an unpredictable capacity of misbehaving despite a perfect initial tension-free, atraumatic, meticulous, elegant, and of course clean implantation. When the time comes for the urologist to look after this type of complications, a conservative endoscopic approach eventually prolongs the complication itself, while the bladder becomes increasingly obstructed, overactive, hypertonic, infected, and incrusted. Like a subaquatic cyclops whose single eye is extended with an appendix—claw, loop, or antenna—we, urologists, tear apart, bury, resect, burn, or melt between the bone and bladder just a few millimeter of tape or mesh. We understand that patients and surgeons are reluctant to undergo an open retrieval of the responsible foreign material.

We suggest that vesicoscopy has an earlier role to play, if after a reasonable attempt of conservative management the problem persists. Aiming at completely removing the foreign material is a sound concept that resonates with well-established open surgical principles. Removing transvaginally what can be done from below, following with vesicoscopy for what can be done inside the bladder—which is obviously more than the routine endoscopy—pursuing with laparoscopic extraperitoneal exposure of the cave of Retzius, intraperitoneal laparoscopy, and finally, if needed, open surgery is a logical sequence that we are not hesitant to follow. Vesicoscopy can bridge the gap between repeated cystoscopic maneuvers and open surgery.

Transperitoneal Transvesical Laparoscopy or Vesicoscopy

It does not matter which of the extra- or transperitoneal laparoscopic technique is used; vesicoscopy, which removes the need to open and close a bladder access, is the winner.

Learning Curve

For the advanced laparoscopic surgeon able to suture like an open surgeon, the technique is within easy grasp and will need only minor adjustments. Working in a fairly limited space requires an economy of movements similar to single-site techniques. In and out motions replace the usual lateral motions. For laparoscopic surgeons with lesser suturing practice, this is indubitably a limiting factor that we acknowledge. The extracorporeal Mignot–Grange knot, which is an upside-down version of the fly-fishing knot, easily overcomes the difficulty of intracorporeal knot–tying skills acquisition [36]. Intracorporeal needle handling and intracorporeal suturing skills remain challenging to develop; however, the answer could come from novel methods of mental simulation training, which speeds up and enhances the acquisition of any skill, as demonstrated at our simulation center [37].

CONCLUSION

We suggest using the word vesicoscopy, which is short and convenient. Beyond the encouraging results from our rather small series, we believe vesicoscopy has potentially much more to offer. The few tips presented could be of help to newcomers to the technique. We acknowledge that our results rely on a long laparoscopic and pediatric vesicoscopic experience acquired in France prior to this adult series. We are confident that vesicoscopic skills can be developed successfully with the blended model of simulation training we have designed. We believe that anticipated technological developments should make vesicoscopy even more accessible. A reusable 5 mm port with a noninflatable distal tip stabilization system, narrow head, and translucent pencil-tip trocar is the ideal product we expect to be developed. We have recently used in a vesicoscopic antireflux a 3 mm pre–series kit that is actually stronger than most tools in the commercially available 5 mm range. The digital treatment of the image captured by the HD flexible cystoscope will allow flipping it into an intuitively workable display. This feature available with the last generation of integrated theaters will, for some cases, remove the need for a camera port. However, the soft flexible sheet of the flexiscope should be reinforced to resist the risk of needle puncture or thermal damage from energy devices. There are excellent motorized needle holders available in the 10 mm range. A 5 mm version is anticipated and would make vesicoscopic suturing accessible to all with minimal access training. The ultimate improvement would be a package consisting of a 5 mm motorized stereoscopic videoendoscope, dominant handheld 5 mm motorized needle holder, and 3 mm nondominant handheld instrumentation. That would offer to institutions and countries that cannot consider larger capital investments a decent platform coming at a fraction of the cost, footprint, and skin incisions of those implied with the larger robotic systems. Under the latter perspective, the next generation of multiarm robotic systems follows a size reduction pathway, which is also excellent news for the future of vesicoscopy.

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Cost-Effectiveness in Laparoscopic and Robotic Surgery in Urogynecology

Karen Ward

INTRODUCTION

Over the last two decades, laparoscopic and robotic-assisted surgeries have been used for a number of applications in urogynecology, including colposuspension, paravaginal repair, sacrocolpopexy, and sacrohysteropexy. The majority of the evidence comparing standard, laparoscopic, and robotic approaches relates to sacrocolpopexy. The minimally invasive approach is considered to have advantages, which include a shorter hospital stay, faster recovery, and return to normal activity.

Prolapse is one of the most common indications for surgery in women, with over 200,000 procedures per year for the condition in the United States [1]. The cost associated with prolapse surgery was conservatively estimated as $1.01 billion per year in 1997 [1]. In Europe in 2005, the number of admissions for prolapse surgery was 36,854 in Germany, 36,679 in France, and 28,959 in the United Kingdom. The estimated costs associated with these admissions were €144 million, €83 million, and €81 million in the three countries, respectively [2]. With an aging and active population, the demand for services related to female pelvic floor dysfunction is likely to continue to rise, with an increasing burden on health-care budgets.

The last two decades have seen significant changes in the pattern of prolapse surgery worldwide, with a move toward more minimally invasive treatments. The minimally invasive approach is considered to be advantageous as it is associated with reduced pain, bleeding, hospitalization, and recovery time, with improved cosmetic results.

Sacrocolpopexy, first described via the abdominal route in 1957, is considered to be one of the most effective and durable operations for apical vaginal prolapse [3] with reported long-term success rates of 78%–100% [4]. Despite the advantages of sacrocolpopexy, vaginal vault surgery is more often performed because it is faster, is less painful, allows a rapid recovery, and is cheaper.

Laparoscopic sacrocolpopexy, first described in 1994 [5], has been adopted by pelvic floor surgeons to address concerns about morbidity and to shorten postoperative recovery. Success rates for the open and laparoscopic routes have been shown to be comparable [6] with reduced blood loss and a similar operating time. However, the laparoscopic route requires high levels of laparoscopic skills as it involves extensive dissection and suturing. Laparoscopic instruments have a limited range of movement in the abdominal cavity. Manipulation of the instruments for suturing and knot tying in the pelvis is technically challenging. Adoption has therefore been limited despite the clinical advantages of the laparoscopic route.

Robotic technology has made laparoscopic sacrocolpopexy a more feasible operation for many surgeons as it offers enhanced visualization, an increased range of movement of instruments and improved ergonomics for the surgeon. Some argue that it more closely approximates to the open technique and is therefore easier for the surgeons who do not have advanced laparoscopic skills to learn, with a shorter learning curve. The da Vinci Surgical System (Intuitive Surgical Inc., Sunnyvale, CA) is the only robotic surgery platform currently available.

There has been a rapid adoption of robot-assisted surgery across surgical specialties, particularly in the United States. The number of robotic procedures performed worldwide almost tripled between 2007 and 2010, from approximately 80,0 to 205,000 [7]. By 2014, over 3000 robots had been installed worldwide and over half a million procedures performed (http://www.intuitivesurgical.com/company/profile.html). Uptake has been greatest in urology and gynecology and these specialties perform the majority of robotic surgeries [8].

Enthusiasm for technological innovation by both surgeons and patients often leads to rapid adoption before efficacy and safety is established relative to existing procedures. Rapid increases in cost are often seen with such technology. This may be due to a higher cost of the new procedure or that its introduction results in more patients being treated overall. This is particularly pertinent when the procedure is relatively easy to learn and applicable to a large number of patients. While uptake of laparoscopic sacrocolpopexy has been relatively slow, due to the technical difficulty involved in learning the procedure, robotic surgery is perceived as easier to learn, and uptake of robotic sacrocolpopexy has been rapid in countries with access to the technology.

Concern has been raised regarding the increased financial costs associated with robotic surgery, particularly with regard to acquisition of the system, annual maintenance costs, and disposable robotic instruments. Robotic surgical systems are expensive with prices ranging from $1 million to $2.3 million. The system requires costly maintenance ($100,000–$170,000 per year) and robotic consumables ($700–$3200 per procedure) (http://www.intuitivesurgical.com/company/profile.html). Across all surgical specialties, it is estimated that the additional cost of using a robot-assisted procedure is approximately $1600, about 6% of the cost of the procedure or $3200 when the cost of the robot is included [7]. For many procedures, it is yet to be established whether the increased cost of the technology is offset by improvement in surgical outcomes.

ECONOMIC ANALYSES IN HEALTH CARE

The terms economic evaluation or economic appraisal cover a range of techniques to assess the evidence on expected costs of different procedures or treatments [9]. It involves the systematic identification, measurement, and valuation of all relevant costs and consequences of the options under review.

Effectiveness is a crucial factor in economic evaluation because of the finite nature of resources. With unlimited resources, the most effective treatment would always be selected. Where there is a limited budget, it is important to assess whether the additional costs of adopting a more expensive treatment option are counterbalanced by improved outcomes for patients. Cost-effectiveness is a method of assessing whether the new treatment is good “value for money.” Economic analysis examines the trade-off between a less costly approach and a less-effective approach. Effectiveness is measured in terms of outcomes, e.g., survival, or as utilities such as health-related quality of life.

If there is a reason to believe that the outcomes of procedures under consideration are the same, cost-minimization analysis may be undertaken.

Ideally, economic evaluation should be undertaken alongside a randomized clinical trial, as it is important to include cost comparisons in the evaluation of new treatments. There is an inherent risk of undertaking economic analysis too early in the development of a new technique in that the treatment may not be applied in the most economical fashion when it is first tested. A seemingly high-cost treatment may become less expensive with further refinement. The treatment could also become more cost effective if the refinement also improves efficacy. Thus, the cost-effectiveness of a new procedure is likely to change with time. Studies comparing an existing and a new procedure are also problematic with regard to ensuring that surgeons are sufficiently experienced in both procedures at the beginning of the study.

Perspective of Cost Comparison

The perspective of the cost analysis is key to the understanding of the study. It is possible to view the costs from the point of view of the patient or payer (in health-care systems with direct patient contribution, such as the United States), the hospital, and society as a whole. In health-care systems with universal coverage, such as the United Kingdom, all costs are born by society.

Most analysis is performed from the hospital perspective, and this would appear to be appropriate for surgical procedures such as prolapse surgery as the majority of the costs are associated with hospitalization. This approach is less relevant for conditions managed on a predominantly outpatient basis, such as diabetes. Hospital costs include all of the resources involved in the surgical treatment and inpatient care. There are direct costs, which include equipment, medication, and bed or “hotel” costs and staffing, as well as indirect costs such as hospital administration. The cost of capital equipment can play a significant role in determining cost-effectiveness. In most health-care systems, the hospital does not get additional payment for a robot-assisted procedure but has to pay for the robotic system and its maintenance. These costs may be passed on to patients or payers in other ways by hospitals, to offset the costs of the robot.

The patient perspective will vary according to the type of health-care system due to factors such as employment status, health insurance, and access to health care.

The cost to society should also take account of loss of work productivity of patients and carers during surgery and recovery, together with future morbidity relating to the condition or treatment, e.g., the need for further surgery for recurrent prolapse or incontinence. These costs are difficult to measure but contribute to national productivity. Factors influencing the ergonomics of the procedure and risk of injury to the surgeon, with consequent loss of productivity, may also impact on cost to society.

Costs

Direct Costs

Direct costs of treatment include all inpatient and outpatient costs related to the treatment.

Direct costs may include the following:

- Theater/operating room costs
- Bed or "hotel" cost
- Equipment
- Consumables, e.g., mesh
- Pharmacy
- Anesthesia
- Laboratory tests
- Radiology
- Outpatient or day-case visits

Future costs include the cost of readmission and postoperative resource use. It may also include the cost of repeat surgery or surgery for conditions resulting from treatment, such as urinary stress incontinence. These differences ideally should be identified and accounted for in comparative long-term studies. This will only be relevant for analysis from the patient or society perspective rather than the hospital perspective.

The three biggest contributors toward direct costs for laparoscopic and robotic surgery are operating times, length of stay (LOS), and equipment [10,11]

- Operating room costs, which include staffing, and overheads, such as electricity and heating, are directly related to operating time. When a new procedure is introduced, the operating time will typically be prolonged as the surgeon commences on their learning curve. This initially results in higher costs. In addition, there may be additional steps, such as docking the robot, which contribute to additional theater time in comparison to open or laparoscopic surgery.
- The main financial advantage of laparoscopic surgery is reduced length of postoperative hospital stay. Not only does this result in lower "hotel" costs but a rapid recovery will also incur fewer costs compared with a prolonged recovery such as IV fluids, monitoring, and medication. A reduction in costs associated with hospital stay for minimally invasive surgery can offset the additional equipment costs of the procedure [12].
- The cost of surgical equipment plays a significant role in cost-effectiveness of laparoscopic and robotic procedures. Costs for surgical equipment include capital costs such as the cost of monitors, cameras, laparoscopes, and insufflators as well as consumable costs, which may include mesh as well as disposable laparoscopic or robotic equipment. Equipment that is used for existing procedures, such as that used in laparoscopic surgery, incurs very little additional cost per case. Conversely, the cost associated with acquisition and maintenance of a surgical robot is significant and can add an average of $1600 per case [7]. Since there is currently only one robotic system on the market, there is no price competition and it is unlikely that costs will fall significantly. Consumable costs for robotic surgery may also be significant as instruments have a limited 10 procedure life-span. Cost of capital equipment will also vary according to its utilization. If the cost of the robot is distributed over a large number of patients, the cost per case will be lower. The cost of the robot must be viewed in relation to the institution budget rather than that of a department such as the operating theater suite. The price of surgical equipment can

also vary according to local sales contracts, which are usually related to the volume of equipment purchased.

Interpretation of economic evaluations may be problematic, and the conclusions of a study may not be readily generalizable outside of the context in which the study was undertaken. There are a number of factors to consider:

- The majority of economic analyses of laparoscopic and robotic sacrocolpopexy have been undertaken in the United States and may not be generalizable to practice elsewhere in the world. For example, there may be differences in LOS in Europe where there is a different health-care funding model.
- Costs may not only vary between institutions and different health-care systems but also between different countries.
- Studies undertaken from the hospital perspective often utilize charging data from the hospital billing system, rather than measuring costs directly. While these data are easier to obtain accurately, the charge not only includes direct and indirect costs but also includes a profit margin. The cost to charge ratio needs to be established to establish the underlying cost. This may vary between hospitals as well as within different departments in a single institution.

Indirect Costs

Indirect costs of surgery are difficult to establish but may have a significant effect on the cost to society. If patients recover more rapidly and return to work earlier following laparoscopic rather than open surgery, there may be significant benefits to the economy. It has been estimated that a 15-day difference in return to work has a value to society of just over $2000 (2001 prices), which would reduce or negate the additional cost of robotic or laparoscopic surgery [13].

The physical challenges of performing laparoscopic surgery are well recognized with over 85% of laparoscopic surgeons reporting physical discomfort, which is persistent in up to 50% [14,15]. The potential effects of work-related injury on the surgeon’s productivity and career longevity are difficult to quantify. Surgeons who perform minimal access surgery are reported to be two to three times more likely to become unfit for work compared to medical doctors not performing such surgery [16]. Neck, back, and shoulder pain are rarely reported in surgeons performing robotic surgery but occur commonly in laparoscopic surgeons [17]. A correlation has been observed between raised patient BMI and risk of strain symptoms in surgeons performing laparoscopic but not robotic surgery. Given the global obesity crisis, surgeon ergonomics are more likely to become a consideration in the choice of operative modality in the future [14].

LAPAROSCOPIC AND ROBOTIC SACROCOLPOPEXY

Outcomes

A number of cohort studies have been published with short- to medium-term outcomes of laparoscopic and robotic-assisted sacrocolpopexy. Long-term series are lacking and there have been few randomized studies.

Freeman et al. [6] compared abdominal sacrocolpopexy with laparoscopic sacrocolpopexy in a multicenter randomized trial with follow-up at 1 year. Based on objective and subjective outcomes, they found the procedures to be equivalent, with reduced blood loss and shorter LOS in the laparoscopic group. Operation times were not significantly different.

In a randomized trial comparing robotic and laparoscopic sacrocolpopexy, Paraiso et al. found no differences in vaginal support and functional outcomes between the two procedures at 1 year [18]. Operating time was significantly longer in the robotic group and participants in this group also had greater postoperative pain. Anger et al. [19] reported similar findings in their randomized trial of laparoscopic and robotic sacrocolpopexy designed to compare costs and outcomes. They found the procedures to have equivalent short-term outcomes and complication rates. They also found higher postoperative pain following robotic surgery, together with longer operating time. Data from cohort studies of laparoscopic and robotic surgery support these findings [20–22]. Despite the relative lack of data on long-term outcomes, complications and need for reoperation of both procedures have similar outcomes in terms of subjective and objective measures.

Cost Comparisons

A number of U.S. studies have attempted to quantify costs associated with laparoscopic and robotic surgery. There have been no full cost-effectiveness studies comparing sacrocolpopexy route, and the majority of studies are cost-minimization studies, which assume no difference in outcome between the procedures.

Open versus Robotic Sacrocolpopexy

Elliott et al. [23] undertook a cost-minimization analysis in a retrospective cohort of patients comparing costs for 40 robotic and 19 open sacrocolpopexies between 2006 and 2010. An estimate of the cost of robot purchase and maintenance per case was included in the analysis. They found operation times to be similar between the groups with a shorter LOS in the robotic group. They demonstrated cost savings of the robotic procedure over open sacrocolpopexy. Further analysis of their data suggested that the biggest factor in the cost of the robotic procedure is the number of cases performed at the institution. Other significant drivers of cost were cost per day of hospital stay, LOS, operating room time, and disposable equipment costs.

A retrospective review of 73 robotic and 91 open sacrocolpopexies also found the robotic procedure to be less costly than open [24]. The authors of this study considered themselves to be past the learning curve for both procedures, with the senior author having performed more than 300 open and 100 robotic procedures prior to starting the study. They found operative times to be longer by 30–45 minutes in the robotic group but LOS was shorter. They also factored in robot purchase and maintenance and found the total direct hospital costs to be $1136 cheaper for the robotic approach.

Li et al. [25] analyzed data from the 2009 to the 2010 U.S. Nationwide Inpatient Sample database. They reported trends in utilization and outcomes of both robot-assisted sacrocolpopexy and “open” vaginal vault surgery. These were identified using ICD-9 codes and do not distinguish between vaginal or abdominal approaches to vaginal vault suspension. They identified 2,381 robotic procedures and 11,080 “open” procedures. An increase in the proportion of robotic procedures was seen over the time period, from 14.1% in the first quarter of 2010 to 21.8% in the fourth quarter. Blood transfusion and prolonged hospital stay were less likely following robotic surgery, and although intraoperative complications were higher, there was no difference in postoperative complications. Hospital charges were significantly lower in the open surgery population compared with robotic surgery patients.

Robotic versus Laparoscopic Sacrocolpopexy

Two randomized trials, and a retrospective cohort study comparing clinical outcomes and costs of robotic and laparoscopic sacrocolpopexy, have found robotic surgery costs to be higher than those of laparoscopic surgery [18,19,26].

Paraiso et al. reported a prospective randomized study with 38 laparoscopic and 40 robotic procedures. They found no significant differences in complications, clinical outcomes at 1 year and LOS. Operating time was longer by 67 minutes, 14 minutes of which was robot docking time, in the robotic group. The differences in the two procedures, such as intracorporeal knot tying in the robotic group and extracorporeal in the laparoscopic group, may also have contributed to longer robotic operating time. Postoperative pain was greater at 3–5 weeks in the robotic group. It was postulated that differences in pain might be due to the greater number and size of ports in the robotic arm. Robotic surgery was more expensive than laparoscopic by a mean of $1936 (95% CI $417–$3454). This is a conservative estimate as robot acquisition and maintenance costs were not included in the analysis. The difference in costs was accounted for by the operating room costs since costs associated with hospital stay and postoperative care were similar.

The other randomized trial of robotic and laparoscopic sacrocolpopexy reported surgical costs and costs associated with rehospitalization up to 6 weeks, as well as outcomes at 6 months [19]. Costs were derived from applying a cost-to-charge ratio to the hospital charges rather than from accounting for individual costs of items used. In this multicenter study, no difference was demonstrated in LOS, blood loss, and complications. Operating time was longer in the robotic group and short-term pain was greater in this group. It was felt that the increase in pain might be related to the operating time and the increased tension on the robotic ports due to a lack of tactile feedback from robotic surgery; i.e., the surgeon is unable to sense the pressure on the ports. Over 6 weeks, costs were higher for robotic surgery

($19,616 versus $11,573) but when purchase and maintenance costs were excluded, the cost difference decreased to only $1,000. They concluded that the higher costs were as a result of the robot purchase and maintenance, rather than surgical costs.

Both of these studies stipulated that surgeons should have performed at least 10 of procedures of each type prior to starting the study. It is possible that the surgeons, who were experienced laparoscopists, were still at the start of the learning curve of robotic surgery after 10 cases. Surgeons with greater robotic experience may have obtained different results.

In the retrospective cohort study of 104 subjects, Tan-Kim also found that costs were higher for robotic surgery. The increase in costs was attributed to increased surgical time [26]. Differences in surgical technique between the procedures may have contributed to this. Titanium tacks were used to fix the mesh to the sacrum in the laparoscopic group whereas suturing with intracorporeal knot tying was the method in the robotic group. Robot docking time accounted for only 9 of the 72 minutes difference in operating times. They also acknowledge that the study covered a period when some of their surgeons were at the start of their learning curve for the procedures.

Cost Comparisons of Open, Laparoscopic, and Robotic Sacrocolpopexy

A cost-minimization analysis by Judd [27] concluded that robotic was more expensive than laparoscopic or open sacrocolpopexy under baseline assumptions. They derived parameter estimates from a review of the literature and applied a decision-analysis model to compare costs (US $2008). They used two models; one based on current hospital ownership of a robotic system and one including the purchase and maintenance costs. Sensitivity analyses were performed to assess the effect of varying the parameters. They found robotic sacrocolpopexy to be the most expensive, with an incremental cost of $1155 over laparoscopic and $2716 over open sacrocolpopexy. Robotic and laparoscopic surgery costs only became equivalent when robotic operating time is reduced to 149 minutes, robotic disposable costs reduced to $2132, or laparoscopic disposable costs increased to $3413. The additional costs associated with the robot purchase model were between $581 and $1724 per procedure, depending on robotic throughput. The cost differences reflect higher disposable equipment costs and longer operating time. Despite these findings, the authors suggest that continued robotic innovation might lead to future cost savings in terms of reduced operating time and cheaper equipment.

Patel et al. [11] retrospectively looked at hospital records for five open, five laparoscopic, and five robotic sacrocolpopexy procedures and performed a cost-minimization analysis, assuming that outcomes were equivalent. Operation times in this study were significantly greater than other referenced studies (418 minutes for open, 510 for laparoscopic, and 358 for robotic procedures). The estimated direct costs were higher for robotic surgery than open but not significantly different for robotic and laparoscopic approaches. The differences in costs were attributed to operating room time and equipment. It is not clear whether costs associated with robot purchase and maintenance are included in this analysis.

Learning Curve of Laparoscopic and Robotic Sacrocolpopexy

The learning process of laparoscopic sacrocolpopexy presents a challenge to most urogynecologists. Many of them have little experience of advanced laparoscopic surgery and are traditionally trained as predominantly vaginal surgeons. To become proficient in a new surgical technique, surgeons need a sufficient individual caseload. Even though vaginal prolapse is a common indication for surgery, vault prolapse is relatively uncommon. In England in 2005, only 10.3% of prolapse operations involved a vault support procedure [2].

In order to assess the learning process, it is necessary to define an endpoint at which a surgeon is judged to be proficient. Assessment of the learning curve should include measures of quality and efficiency. Quality of surgery can be assessed by functional outcomes or by complication rates. Efficiency is usually assessed by measuring duration of surgery but may also include conversion to open surgery.

A number of studies have attempted to quantify the learning curve of laparoscopic sacrocolpopexy. They focus on the number of cases required to reduce the operating time, largely due to low rates of reported complications associated with the procedure in the studies [28–30]. Mustapha et al. found that duration of surgery reduced after 15 cases but suggested that 30–40 cases are necessary to master the technique [30]. Operating time declined rapidly during the first 30 cases in the study reported by

Claerhout et al. reaching a steady state after 90 cases [29]. Complications were unchanged throughout this series. The same group further analyzed the learning curve in a subsequent study [31]. They divided the procedure into 5 steps and examined the learning curve for each. Dissection of the vault was the most time-consuming step; times comparable with the teacher (the control) were achieved after 31 cases. Duration of suturing fell within the range of the teacher after only 10 cases, but it should be noted that the participants had attended a 15 hour laparoscopic skills lab prior to commencement of the study. There was no learning curve associated with dissection and fixation to the sacral promontory.

The learning curve for robotic sacrocolpopexy has not been extensively studied. Two studies have found operative times to drop significantly after just 10 cases [32,33]. Germain et al. [33] suggest that the short-learning curve may be due to their extensive previous experience with robotic surgery. The learning curve of robotic hysterectomy has found to be significantly longer than these small series suggest. In a study of 325 cases, performed over 3 years, Woelk et al. used cumulative summation analysis to show that proficiency is achieved after approximately 91 cases [34]. This is similar to the number suggested by Claerhout et al. for laparoscopic sacrocolpopexy. This study also found no decrease in complications with experience. The extent to which this study can be extrapolated to robotic sacrocolpopexy is debatable and further studies of the learning process are required for this procedure.

Yohannes et al. [35] evaluated the time taken to perform suturing and dexterity skills on a pelvic model using either laparoscopy or robot assistance. They demonstrated that the robot allowed suturing and dexterity skills to be performed more quickly than with laparoscopic assistance after only five trials. The study is limited by the small number of participants, the lack of standardized dexterity tasks, and the number of times each participant performed the task. It would have been useful to increase the number of trials to determine how many are required for participants to reach their plateau.

From the available evidence, it would appear that proficiency in laparoscopic sacrocolpopexy, based on duration of surgery, is achieved after 30–90 cases. The corresponding figure for the robotic procedure is yet to be determined. There is some evidence to suggest that some of the necessary skills for minimally invasive sacrocolpopexy are acquired more quickly using robot assistance.

CONCLUSIONS

Financial considerations play a major role in health-care systems worldwide. The high cost of robotic surgery needs to be evaluated carefully in terms of evidence-based outcomes. The following conclusions are made from the limited data available:

1. Similar short-term outcomes have been reported for open, laparoscopic, and robotic sacrocolpopexy. Formal cost-effectiveness analysis has not been undertaken for different surgical approaches to sacrocolpopexy; the majority of studies use cost-minimization analysis to estimate costs from the hospital perspective. Longer-term studies, including data on quality of life, long-term outcomes, complications, and the need for further surgery, would allow the cost to society of such surgery to be evaluated. Interpretation of the literature with regard to cost is problematic, and the results of studies comparing robotic surgery costs to other routes are conflicting. Conclusions vary considerably depending on the model used, the assumptions made, and the method of analysis.
2. Operating time is one of the main drivers of cost in robotic surgery. Large variation in operating time is reported and there is a lack of clarity in many studies as to how operating time is defined. Other factors that need to be taken into consideration when assessing operating time in studies include
    a. Surgeon experience when the study was undertaken (learning curve)
    b. The inclusion or exclusion of concomitant procedures from the analysis
    c. Differences in surgical technique between the comparator procedures, e.g., knot-tying method (intra- or extracorporeal), the use of barbed sutures to fix the mesh to the vagina, and method of sacral fixation of mesh (sutured or tacked)
3. LOS is an important cost contributor especially for open sacrocolpopexy. The cost per day of hospital stay may vary considerably between institutions.
4. Equipment costs account for a large part of the difference between open versus laparoscopic or robotic costs. There are differences in the extent to which all possible items are accounted for in different studies as well as the time period over which the study is undertaken. Some studies

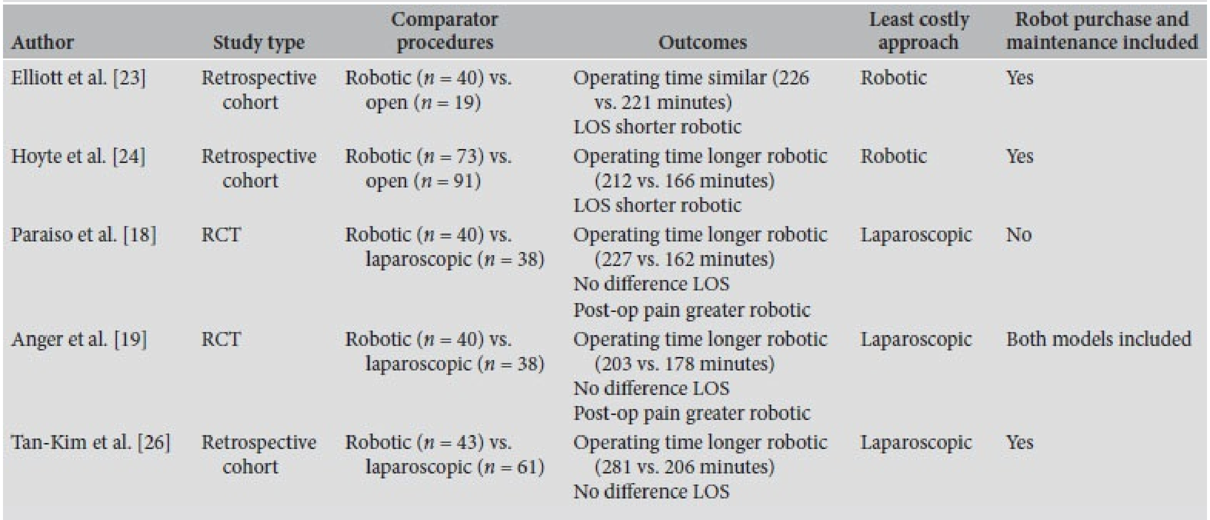
only include inpatient costs, whereas others itemize costs up to 6 weeks postoperatively.

Surgeons outside the United States may struggle to interpret the cost data from existing literature and the extent to which it can be extrapolated to their own health-care systems. There have been no studies of costs associated with robotic sacrocolpopexy in settings outside of the United States.

Robotic technology will continue to develop and is likely to become cheaper as new manufacturers enter the market. There is currently a lack of competition to the da Vinci system, which may, in part, stem from patented technologies as well as acquisition of a competitor by Intuitive Surgical in 2003. Whenever there is minimal or no competition in a market, companies are able to command high premiums for their product and operating margins can be higher compared with other companies within that industry [36]. Until competitors enter the market, the only other option to enable more centers to utilize this technology is the emerging availability of cheaper, preowned systems.

Despite the heterogeneous nature of the cost comparison studies, they appear to demonstrate that robotic sacrocolpopexy is associated with greater direct costs than the laparoscopic approach (Table 105.1). While improvements in the technique and technology, together with future market competition, may drive down costs, robotic sacrocolpopexy does not yet appear to be cost effective compared with the open and laparoscopic approaches.

Table 105.1 Cost Comparison Studies of Open or Laparoscopic Sacrocolpopexy versus Robotic Sacrocolpopexy



Author	Study type	Comparator procedures	Outcomes	Least costly approach	Robot purchase and maintenance included
Elliott et al. [23]	Retrospective cohort	Robotic ($n = 40$) vs. open ($n = 19$)	Operating time similar (226 vs. 221 minutes) LOS shorter robotic	Robotic	Yes
Hoyte et al. [24]	Retrospective cohort	Robotic ($n = 73$) vs. open ($n = 91$)	Operating time longer robotic (212 vs. 166 minutes) LOS shorter robotic	Robotic	Yes
Paraiso et al. [18]	RCT	Robotic ($n = 40$) vs. laparoscopic ($n = 38$)	Operating time longer robotic (227 vs. 162 minutes) No difference LOS Post-op pain greater robotic	Laparoscopic	No
Anger et al. [19]	RCT	Robotic ($n = 40$) vs. laparoscopic ($n = 38$)	Operating time longer robotic (203 vs. 178 minutes) No difference LOS Post-op pain greater robotic	Laparoscopic	Both models included
Tan-Kim et al. [26]	Retrospective cohort	Robotic ($n = 43$) vs. laparoscopic ($n = 61$)	Operating time longer robotic (281 vs. 206 minutes) No difference LOS	Laparoscopic	Yes

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Section X

Complex Problems

106 Diagnosis of Urogenital Fistula

Ekene A. Enemchukwu and Benjamin M. Brucker

INTRODUCTION

Urogenital fistulas are abnormal connections between an organ of the urinary tract and an adjacent organ of the female genital tract. They can occur in a number of anatomical locations along the urinary tract and the female reproductive system (Table 106.1). The majority of urogenital fistulas worldwide occur in the developing world [1]. Over 90% of these are obstetrical in nature, caused by obstructed labor and poor access to medical care [2]. In contrast, the majority (90%) of urogenital fistulas in the developed world are iatrogenic, occurring after pelvic surgery [3–5].

There are an estimated 500,000 women with untreated urogenital fistulas worldwide [6]. The actual worldwide incidence is unknown. Many women in developing countries never present for treatment due to poor access to care and lack of financial resources. In one study, women who sought treatment presented an average of 5 years after the development of symptoms. Worldwide estimates have largely been collected from hospital data. The incidence of urogenital fistula in the developing world has been estimated to be 30,000–130,000 per year [1]. Garely and Mann evaluated the U.S. 2007 hospital discharge data and found that approximately 5,000 urogenital fistula repairs were performed in the United States each year [7,8]. However, these data are limited by the inability to differentiate between primary repairs, reoperations, and erroneous medical coding. Furthermore, this figure does not account for fistulas that were managed on an outpatient basis or managed conservatively without surgical intervention.

Urogenital fistulas are often devastating. The social isolation, depression, and physical discomfort that can occur as a result of constant urinary leakage can cause significant damage to the woman's physical and psychosocial well-being [9]. Furthermore, it can negatively impact her quality of life. The medicolegal implications and financial impact on the healthcare system are also important considerations [10]. In order to minimize the negative impact of urogenital fistula, accurate and timely diagnosis is critical. Effective management requires accurate diagnosis and avoidance of unnecessary tests and therapies. Finally, the clinician must be certain that any concomitant injuries to the urogenital tract have been ruled out or adequately addressed. This chapter will focus on the epidemiology, etiology, presentation, and diagnosis of female urogenital fistula.

ETIOLOGY AND PATHOPHYSIOLOGY

Common causes of urogenital fistulas include obstetrical trauma, iatrogenic injury during pelvic surgery, infection, pelvic radiation, inflammation, pelvic trauma, foreign bodies, pelvic neoplasms, and complications of pelvic surgery (i.e., postoperative hematoma, leading to breakdown of suture lines) (Table 106.2). Poor nutrition, diabetes, atherosclerosis, steroid use, tobacco use [38], and ischemic states further increase the risk of fistula development in these patients [6].

Obstetrical injury due to obstructed labor is the leading cause of urogenital fistula in the developing world. Arrowsmith et al. characterized the *obstructed labor complex*, which describes the potential multiorgan effect of prolonged labor. These include vesicovaginal fistula (VVF), urethral loss, stress urinary incontinence (SUI), rectovaginal fistula, ureteral obstruction with subsequent hydroureteronephrosis and renal failure, fecal incontinence secondary to anal sphincter incompetence, cervical and vaginal scarring, amenorrhea, secondary infertility, osteitis pubis, and/or foot drop [11]. The exact cause of foot drop is unknown, but it is thought to occur as a result of sacral nerve injury during fetal descent or peroneal nerve injury from prolonged squatting during obstructed labor [1]. The level of injury to the pelvic viscera is determined by the level at which fetal descent stops [12]. Therefore, any combination of urogenital fistulas, including vesicovaginal, urethrovaginal, ureterovaginal, vesicouterine, ureterouterine, and vesicocervical fistula, can develop as a result [9]. Rectovaginal fistulas can also occur after obstructed labor; however, they will not be discussed as they are beyond the scope of this chapter.

Iatrogenic injury during pelvic surgery is the most common of cause of urogenital fistula in the developed world. Ninety percent of urogenital fistula are estimated to occur as a result of inadvertent injury during pelvic surgery [4,5,13–22]. Symmonds reviewed 800 cases in the United States and found that 75% of these injuries occurred during hysterectomy, while only 5% were caused by obstetrical injury [23]. Approximately 600,000 women undergo hysterectomy annually in the United States, and approximately 60% of these are performed for benign disease, including uterine leiomyoma and endometriosis [24]. Studies indicate that the rate of bladder injury during hysterectomy ranges from 1% to 5%, while the rate of ureteral injury ranges from 0.2% to 2.5% [25–27]. Some injuries are identified and repaired intraoperatively [28]. However, a majority of postoperative fistulas are thought to occur as a result of an unrecognized injury [29].

The risk of injury is increased by anatomical distortions caused by intraoperative bleeding, previous pelvic surgery, adhesions, endometriosis, fibroids, ovarian masses, radiation, and malignancy [5,6,19,26,30–33,40]. In 2012, Hilton et al. evaluated the rate of urogenital fistulas after hysterectomy in the British National Health System. They found that the risk of fistula development was the greatest among women who had an abdominal hysterectomy performed for cervical cancer (1.2%) and lowest for those women who had a vaginal hysterectomy for pelvic organ prolapse (0.03%) [34]. Women undergoing total abdominal hysterectomy for benign diseases had a urogenital fistula rate of 0.2%.

Table 106.1 Types of Urogenital Fistulas

I. Ureteral
    a. Ureterovesical
    b. Ureterouterine
    c. Ureterofallopian
II. Vesical
    a. Vesicovaginal
    b. Vesicouterine
    c. Vesicocervical
III. Urethral
    a. Urethrovaginal
IV. Combination

Source: Andreoni C et al., *J Urol*, 170(6), 2330, 2003.

Table 106.2 Etiology of Urogenital Fistulas

I. Foreign body [54,56]
    a. Retained pessary
    b. Chronic indwelling Foley catheter
II. Radiation
    a. External beam
    b. Brachytherapy
III. Infection
    a. Pelvic inflammatory disease
    b. Tuberculosis [61]
IV. Inflammation
    a. Endometriosis
V. Iatrogenic
    a. Postsurgical
        1. Hysterectomy
        2. Mesh kits
        3. Anti-incontinence surgery
        4. Prolapse repair
        5. Urethral diverticulectomy
        6. Endoscopic procedures
        7. Vaginal laser procedures [84]
        8. Colorectal, urologic, vascular procedures
VI. Neoplasm
VII. Obstetric

- a. Cesarean section
    - b. Obstructed labor
    - c. Forceps delivery
    - d. Vacuum assisted delivery
    - e. Manual placental extraction
- VIII. Trauma
    - a. Sexual trauma
    - b. Pelvic fracture
- IX. Congenital (rare) [85]

Sources: Margolis T and Mercer LJ, *Obstet Gynecol Surv*, 49(12), 840, 1994; Volkmer BG et al., *Ultrasound Med Biol*, 26(5), 771, 2000; Yu NC et al., *RadioGraphics*, 24(5), 1331, 2004.

Another important cause of urogenital fistula is the pelvic irradiation. Approximately 4%–10% of urogenital fistulas are thought to develop due to pelvic radiation therapy [14,19,23,29]. Previously irradiated tissue undergoes progressive changes secondary to obliterative endarteritis, which can cause fibrosis, necrosis, and subsequent fistula formation [5,35]. The cumulative dose and proportion of external beam or brachytherapy delivered to the genitourinary organ have been shown to be associated with higher rates of fistula formation in some studies [36,37]. Smoking has also been implicated as an added risk factor in patients undergoing pelvic radiation therapy. In one study, current smokers undergoing radiation treatment were more likely to develop VVFs than nonsmokers (73% vs. 23%) [38].

Spontaneous fistulas can develop in patients with a history of malignancy or pelvic irradiation weeks to decades after treatment with a median of 8.7 months [35,38]. Thus, secondary malignancies and oncological recurrences should be ruled out in patients with a history of pelvic malignancy [39]. Examination under anesthesia should be strongly considered in these patients in order to obtain biopsies and evaluate for concomitant pelvic masses prior to planned surgical repair.

UROGENITAL FISTULA TYPES

Urogenital fistulas can occur between a number of structures. A high index of suspicion is needed to ensure that all fistulous communications are identified, including those that communicate with nonurogenital organs or structures. In the next section, we will discuss the most common urogenital fistulas.

Vesicovaginal Fistulas

VVFs are the most common type of urogenital fistula, comprising over half of all urogenital fistulas [31,40–42]. In developing countries, over 90% of VVFs are caused by obstetrical trauma from prolonged labor [2]. This occurs secondary to inadequate emergency obstetrical care during obstructed labor. The consequent prolonged contact between the fetus and a large area of pelvic soft tissue and visceral organs causes an ischemic pressure necrosis [11,15]. Widespread vaginal scarring and fibrosis ensues [6,43]. The level of injury to the lower urinary tract is determined by the level at which fetal descent is halted during labor [11,12]. This often occurs distally, involving the bladder trigone, bladder neck, and urethra, causing large VVFs and urethrovaginal fistulas surrounded by poorly vascular tissue [44]. Although rare, obstetrical VVFs do occur in the developed world [23]. However, these fistulas typically occur in the setting of operative deliveries requiring forceps or vacuum assistance.

Over 75% of VVFs in the developed world occur as a result of unrecognized injury during hysterectomy [19,45]. With an estimated incidence of 0.2%–2%, iatrogenic VVFs often occur as a result of inadvertent bladder injury from aggressive blunt dissection, sharp dissection, electrocautery, or crush injury from a retractor or clamp during pelvic surgery [5,19,23,26,31,32]. A urinoma can form and subsequently drain urine through the vaginal cuff forming an epithelialized tract with subsequent fistula formation. Another potential cause of posthysterectomy urogenital fistula is inadvertent suture incorporation of the posterior bladder wall during the vaginal cuff closure. The ensuing posterior bladder wall ischemia can lead to tissue necrosis and subsequent fistula formation. These injuries are typically supratrigonal and medial to the ureteral orifices [6,19]. The vaginal vault is the most common site of postabdominal hysterectomy VVF. In one series, over 60% of vaginal vault fistulas occurred after total abdominal hysterectomy [3]. It is estimated that only about half (51%) of all bladder injuries are identified and repaired intraoperatively [28].

Radiation is another important cause of VVF. One study found that 0.6%–2% of women irradiated for cervical cancer will eventually develop a VVF [46]. In a 2007 study, the authors observed a 47.8% fistula rate in 23 women who had concurrent chemotherapy and radiation for stage 4 cervical cancer [38]. The risk of fistula development was even higher in smokers. Finally, pelvic organ prolapse surgery and synthetic midurethral slings have also been implicated as causes of VVFs [47,48]. A 2008 meta-analysis noted a 1.3% bladder injury rate during anterior prolapse repair with nonabsorbable mesh, half of which were associated with mesh introducer kits [49]. The percentage of injuries ultimately leading to VVF development was not reported. Unfortunately, the true incidence of urogenital fistula after peer-reviewed data is sparse, largely comprised of case reports.

Ureterovaginal Fistulas

Ureterovaginal fistulas are rare complications that are often caused by unrecognized injury to the ureter during pelvic surgery. Considered one of the most serious complications in pelvic surgery, consequences include paralytic ileus, sepsis, renal failure, and renal loss [13,16]. Although the ureter can be injured during any pelvic surgery, injury occurs most commonly during gynecological operative procedures. Approximately 60%–75% of ureterovaginal fistulas developed as a result of ureteral injuries during abdominal hysterectomy [50,51]. In the literature, the incidence of ureteral injury during hysterectomy ranges from 0.2% to 2.5%, with only one third of injuries recognized at the time of surgery [4,5,11,25]. The incidence of concomitant vesicovaginal and ureterovaginal fistula has been reported to be as high as 12%–25% [6,52,53]. Ureterovaginal fistulas are less common in the developing world but have been described in the *obstructed labor complex* [11].

The ureter is at greatest risk of iatrogenic injury in the distal third centimeters. It is most commonly injured during its course over the pelvic brim, through the cardinal ligament, near the uterosacral ligament, and at the level of the vaginal fornix prior to insertion into the bladder [4]. In anatomical studies, the ureter has been noted to pass an average of 1.5–2.5 cm lateral to cervical os at the level of the cardinal ligament [4,54]. The left ureter is at greatest risk of injury due to its course in the pelvis, which places it closer to the cervix than the right ureter [31,55]. However, right-sided injuries are still common and have been reported to occur more frequently in another small series [26]. Ureterovaginal fistulas can occur as a result of partial versus complete ureteral transection, electrocautery, or ischemic injury caused by suture ligation, clamp trauma, or damage to the delicate periureteral blood supply [6,16].

The complex fistulous connections that can develop are often difficult to define due to their tortuosity and proximity to the ureterovesical junction [51]. A missed ureteral injury can be disastrous and should always be ruled out during the diagnostic evaluation of any patient with suspected urogenital fistula. Other rare causes of ureterovaginal fistulas include retained vaginal foreign bodies (i.e., pessaries), which can also present with concomitant VVFs [56–58].

Urethrovaginal Fistulas

Similar to VVF, urethrovaginal fistulas are most commonly iatrogenic in the developed world. Over 70% are associated with anti-incontinence surgery, anterior colporrhaphy, and urethral diverticulectomy [11,12,14,59]. Inadvertent urethral injury during paraurethral dissection and/or trocar passage of urethral slings may cause erosion, tissue loss, and subsequent urethrovaginal fistula [14]. Iatrogenic urethrovaginal fistulas have become more common since the adoption of synthetic midurethral slings and mesh kits [32,60–66]. Pushkar et al. reported their 34-year experience with urethrovaginal fistulas in Russia and found that approximately 30% of urethrovaginal fistulas were associated with anti-incontinence procedures, including autologous slings, periurethral bulking agents, and synthetic slings [59]. Almost 40% were associated with pelvic organ prolapse repair and urethral diverticulectomy. Another 26% were associated with obstetric injury. Concomitant iatrogenic bladder injury can occur. Lee et al. reported and reviewed their 15-year experience and found that 19% of patients presenting with urogenital fistulas had concomitant urethrovaginal and VVFs [5].

In developing countries, much like VVFs, urethrovaginal fistulas are most commonly associated with obstructed labor. These patients often present with concomitant VVFs. Ureterovaginal fistulas can also coexist, so the clinician should make sure to rule out all possible fistulous connections. Other less common but important causes include malignancy, pelvic trauma, pelvic radiation, and chronic indwelling urethral catheters [45,59]. Any patient with a history of malignancy or pelvic irradiation should undergo biopsy to rule out malignancy.

Vesicouterine Fistulas

Vesicouterine fistulas are one of the least common urogenital fistulas, representing 1%–9% of all urogenital fistulas [30,33,41]. They are most commonly associated with lower uterine segment cesarean section [5,19,31–33,40]. Vaginal birth after cesarean, manual extraction of the placenta, induced abortion, misplaced intrauterine device (IUD), brachytherapy, dilation and curettage, pelvic tuberculosis, and congenital anomalies are other known causes [6,19,40,67,68]. Women with vesicouterine fistulas often present with a constellation of symptoms referred to as *Youssef's syndrome*, characterized by cyclical hematuria (menouria), amenorrhea (absence of vaginal bleeding), first trimester spontaneous abortions, and absence of urinary incontinence [33,69]. Vaginal urinary incontinence can also be present and is most likely caused by retrograde filling of the uterus with urine from the bladder and subsequent leakage from a patent, incompetent cervical os [40]. However, concomitant fistulas, such as VVF, urethrovaginal, and ureterovaginal fistulas, should be ruled out, as these are more common causes of continuous urinary incontinence in patients with suspected fistula. Amenorrhea and menouria (cyclical hematuria) may develop as a result of the fistulous communication between the bladder and uterus. The mixture of menstrual blood from the uterus with urine in the bladder manifests as gross hematuria (menouria) that only occurs during the menstrual cycle. As many as 20%–25% of patients with bladder endometriosis involving the bladder mucosa present with cyclical hematuria [70]. Thus, the clinician must rule out other potential causes of cyclical hematuria, including endometriosis and congenital anomalies [68,69]. Ureterouterine fistulas and vesicoure-terovaginal fistulas are also rare. Similar to vesicouterine fistulas, they have been described in patients after cesarean section [71,72], underscoring the importance of ruling out concomitant fistulas.

Ureterofallopian Fistulas

Ureterofallopian fistulas are exceedingly rare urogenital fistulas [18]. Only six have ever been described in the literature, all of which were iatrogenic, attributed to pelvic gynecological surgery for endometriosis [13,15–17], malignancy [73], and urological endoscopic treatment of ureteral stones [5,20,21].

EVALUATION AND DIAGNOSIS

Diagnosis of urogenital fistula requires a high index of suspicion. The evaluation must begin with basic diagnostic principles of a thorough history and physical examination. This may confirm the clinician's suspicion, but additional testing is most often required to confirm the diagnosis, understand the fistula anatomy, and rule out concomitant injuries (Figure 106.1). The information gained is critical to staging appropriate corrective interventions, which will be discussed in the next chapter. In this section, we will discuss the presentation and diagnostic tools that are available to the clinician for the workup of a patient with suspected urogenital fistula.

History

In any patient with a suspected urogenital fistula, the evaluation should begin with a detailed medical, surgical, obstetrical, gynecological, oncological, and social history. Most women will present with complaints of urinary incontinence. The clinician must characterize the urinary leakage and differentiate it from other potential causes of urinary incontinence. The patient should be asked to describe the fluid character, color, volume, onset of leakage, and the position during which leakage typically occurs. Other conditions of the lower urinary tract, including urgency incontinence, stress incontinence, mixed urinary incontinence, vaginal voiding, and overflow incontinence, can mimic the classic presenting symptoms of urogenital fistulas. Also important, some of these conditions can coexist with urogenital fistulas. However, if a fistula is suspected based on the presence of patient risk factors, it must be ruled out.

The patient's past surgical history should be reviewed, including prior pelvic trauma or radiation. In cases of prior abdominal and pelvic surgery, the surgeon's operative notes should be obtained. This can help guide further evaluation and operative planning. The obstetrical history, including number of pregnancies, deliveries, and mode of deliveries (vaginal, vacuum assisted, forceps, cesarean) should be reviewed. The gynecological history including history of endometriosis, abnormal uterine bleeding, IUDs, pelvic inflammatory disease, abnormal pap smears, pessary use, or chronic indwelling urethral catheters should be documented. Any history of gynecological, urological, or colorectal malignancies and subsequent treatments should also be noted. Pathology reports and surgical and/or radiation treatment reports should be obtained. Smoking cessation should be strongly encouraged in order to improve the chances of surgical success.

As the clinician completes this detailed history, the differential diagnosis for continuous vaginal fluid drainage should be kept in mind. This includes VVF, urethrovaginal fistula, ureterovaginal fistula, vesicouterine fistula, vesicocervical fistula [74], ureterouterine, ureterofallopian fistulas [15], vaginal infection/discharge, lymphatic fistula [43], pelvic abscess, leakage of peritoneal fluid from the vaginal cuff [6], vaginal voiding, overflow urinary incontinence, SUI, urgency urinary incontinence, mixed urinary incontinence, and a combination of these conditions (Table 106.3 and Figure 106.2). A careful history will help differentiate some of these conditions; however, additional diagnostic tools should be used when appropriate, to rule out concomitant anatomical causes of urinary leakage (Table 106.4).

Symptoms

The timing, pattern, and severity of the patient’s presenting symptoms can provide useful diagnostic information. This information coupled with the patient’s past medical, surgical, obstetrical, gynecological, and oncological histories can help the clinician determine the potential mechanisms of tissue injury, identify the pelvic organs at greatest risk of involvement, and determine which tests will be needed to rule out concomitant conditions.

The most common presenting symptom of a urogenital fistula is continuous urinary leakage from the vagina [4,14]. This classic presentation includes urinary leakage both day and night, which may notably be present during sleep. However, the pattern of urinary incontinence can be continuous, intermittent, or positional. Gross hematuria, irritative voiding symptoms (i.e., frequency, urgency, dysuria) and recurrent urinary tract infections are also early signs of urogenital fistula [29]. Patients with urinary incontinence from urogenital fistulas will often complain of urine odor, skin irritation, perineal candida infections, and vaginal infections.

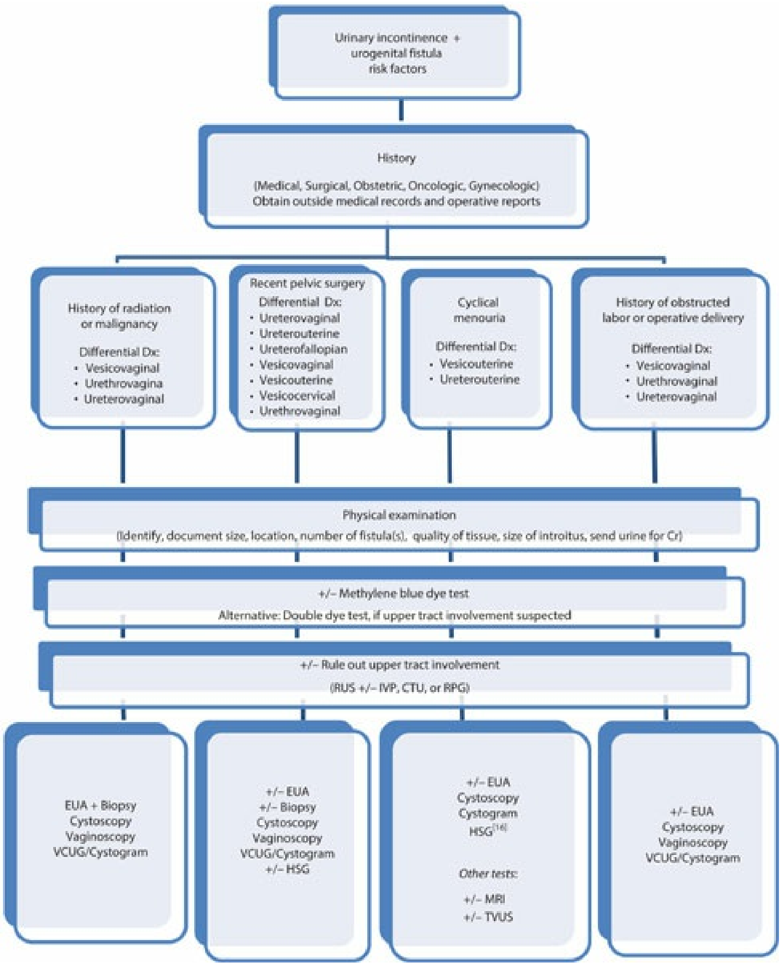

Figure 106.1 Diagnostic algorithm: computed tomography urogram, examination under anesthesia, hysterosalpingogram, intravenous pyelogram, magnetic resonance imaging, transvaginal ultrasound, retrograde pyelogram, renal ultrasound, voiding cystourethrogram.

Presenting symptoms can vary, depending on the etiology, size, location, and presence of coexisting urogenital fistulas. VVFs typically present with the classic continuous urinary incontinence. Vesicouterine fistulas can present with amenorrhea and cyclical gross hematuria (menouria) with or without urinary incontinence. The presenting symptoms for urethrovaginal fistulas are dependent upon the fistula location and its relation to the external urinary sphincter. The symptoms can range from continuous urinary incontinence to postvoid dribbling [40]. If the fistula is distal to the external sphincter, the patient may be spared of continuous leakage. Ureterovaginal and ureterofallopian fistulas may present with paralytic ileus, abdominal distension, pelvic pain, fever, nausea, and flank pain. Urogenital fistulas can coexist and they can also present with any combination of these nonspecific symptoms; thus, the clinician must rule out all potential fistulas.

Table 106.3 Differential Diagnosis
Vesicovaginal fistula
Urethrovaginal fistula
Ureterovaginal fistula
Vesicouterine fistula
Vesicocervical fistula
Ureterouterine fistula [62]
Ureterofallopian fistula [15]
Vaginal infection
Vaginal discharge

Pelvic abscess
Leakage of peritoneal fluid from the vaginal cuff
Urgency urinary incontinence
Stress urinary incontinence
Mixed urinary incontinence
Vaginal voiding
Overflow urinary incontinence

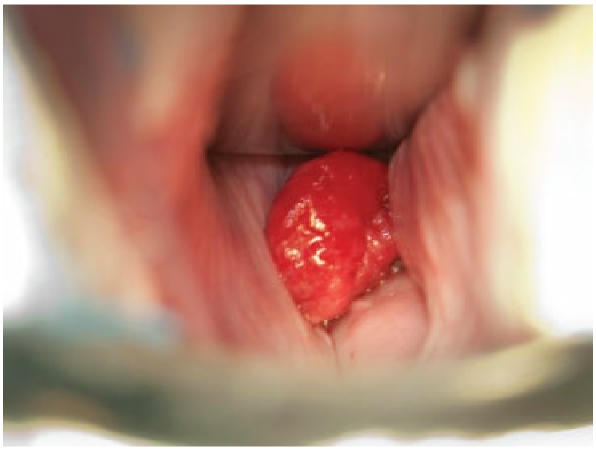

Figure 106.2 Vaginal leakage can be from numerous sources. Here, a fallopian tube prolapse after hysterectomy created a conduit for peritoneal leakage of fluid. (From Ingber M, Vasavada S, Rackley R, Urogenital fistula, in *Textbook of Urology and Urogynecology*, 3rd edn, London: 2010, pp. 951–953, with permission.)

Timing

The onset of symptoms and its relation to a potentially inciting event can provide valuable information. Immediate urinary leakage is suggestive of an unrecognized injury or failed repair of a recognized injury. Electrocautery-related injuries and ischemic trauma caused by clamps, sutures, or ureteral devascularization often have delayed presentations, typically 7–10 days after surgery [14]. Patients undergoing pelvic surgery in previously irradiated field can present weeks to years after their surgery [35,38]. Patients with ureterovaginal fistulas may not experience any urinary incontinence for 7–14 days after surgery, at which point a mucosa lined tract has had the opportunity to develop between the ureter and vagina [51]. These patients may, however, initially present with nonspecific symptoms such as low-grade fever, nausea, paralytic ileus, and flank pain, due to the developing urinoma and obstruction [5]. Although some vesicouterine fistulas present with both cyclical hematuria and vaginal urinary incontinence, other patients without urinary incontinence may not have any symptoms until they develop gross hematuria (menouria) during their menstrual cycle rather than the expected vaginal bleeding [40].

Table 106.4 Diagnostic Tests

Fistula type	Tests	Comments
Vesicovaginal	*Blue dye test* ±EUA Cystoscopy Vaginoscopy VCUG/cystogram Upper tract imaging[a] (IVP, CTU, or RPG)	Biopsy any suspicious lesions in patients with risk factors for malignancy.
Ureterovaginal	*Double-dye test* Upper tract imaging (IVP, CTU, or RPG)	EUA recommended to allow for stent placement, if needed.

	EUA + cystoscopy + vaginoscopy	
Urethrovaginal	*Blue dye test* Cystoscopy VCUG/cystogram ±Upper tract imaging (IVP, CTU, or RPG)	Obtain cystogram to rule out concomitant vesicovaginal fistula.
Vesicouterine Ureterouterine	Cystoscopy HSG Upper tract imaging (IVP, CTU, or RPG)	Methylene blue dye test can be instilled in the bladder and the cervical os observed for blue fluid [78].
Ureterofallopian	HSG Upper tract imaging (IVP, CTU, or RPG)	

Abbreviations:CTU, CT urogram; EUA, examination under anesthesia; HSG, hysterosalpingogram; IVP, IV pyelogram; RPG, retrograde pyelogram; VCUG, voiding cystourethrogram.

[a] Rule out upper tract involvement.

Physical Examination

A thorough physical examination should be performed to evaluate for any signs or sequela of urogenital fistula. Prior to pelvic examination, a careful abdominal examination should be performed to evaluate for abdominal distension, tenderness, and flank pain. In all postsurgical patients, abdominal incisions should be inspected for signs of infection, drainage, or dehiscence. For a variety of reasons, patients often fail to provide accurate surgical histories. The physical examination is an excellent opportunity to review the abdominal and pelvic surgical history.

Inspection of the perineum may reveal signs of skin irritation. The pelvic examination should assess for fluid in the vaginal canal, which can be collected and sent for creatinine levels [29]. The patient can also be asked to provide tampons or pads for creatinine evaluation. A urine specimen should be sent for urinalysis and culture to allow treatment of urinary tract infections prior to surgical repair. A careful speculum examination with appropriate lighting is needed to help identify and determine the size, character, number, and location of the fistula(s) (Figure 106.3). Special attention should be given to the vaginal cuff, anterior vaginal wall, and the cervical os. Irradiated patients may have friable lesions that present months and even years after their treatment. These lesions should be documented and subsequently biopsied to rule out the recurrence of malignancy [35,75].

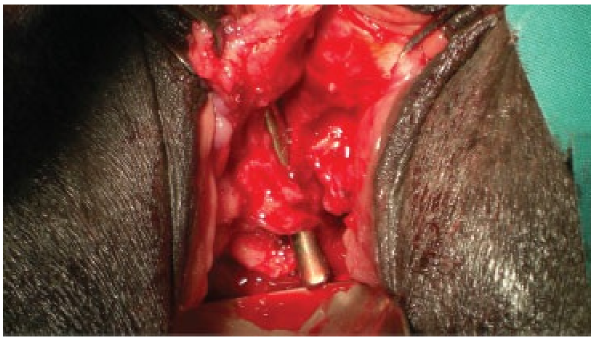

Figure 106.3 The examiner must always evaluate the patient for the presence of multiple fistulas. This patient had both a urethrovaginal and vesicovaginal fistula. (From Ingber M, Vasavada S, Rackley R, Urogenital fistula, in *Textbook of Urology and Urogynecology*, 3rd edn, London: 2010, pp. 951–953, with permission.)

Some urogenital fistulas may be difficult to identify due to the location of the fistula, patient discomfort, and vaginal stenosis. Larger fistulas are usually visible and can often be palpated [59]. However, smaller fistulas can be difficult to identify on physical exam and often require further investigation with examination under anesthesia, endoscopic evaluation, and imaging. If vaginal atrophy is present on exam, it should be treated preoperatively with topical vaginal estrogen to improve the quality of the vaginal epithelium to aid in surgical repair. Finally, the patient’s body habitus, genital anatomy, vaginal tissue quality, and the extent of tissue loss should be documented to aid in presurgical planning. A narrow introitus may warrant relaxing incisions at the time of repair to provide adequate access to the fistula [6].

Dye Test

The *dye test* is a valuable office-based diagnostic test. Although the dye test is considered a routine diagnostic test for urogenital fistula, there are no large series to our knowledge that report the sensitivity or specificity of this test. In one small series, all 12 (100%) patients with VVFs had positive methylene blue dye tests [76].

The dye test is performed by filling the bladder with dilute methylene blue [77] or indigo carmine [39] solution (up to 300 mL). A vaginal exam can be performed at the time of instillation. Often, the fistula is easily identified. If the fistula is not seen, a tampon can be placed into the vagina, and the patient is asked to ambulate, and the vaginal packing is evaluated. If blue staining is noted, the pattern of staining can provide useful information about the possible location of the fistula. Blue staining toward the distal end of the packing or tampon suggests the presence of SUI or urethrovaginal fistula, whereas apical staining suggests the presence of a VVF [45]. The blue dye test has been used in the literature to diagnose vesicouterine fistulas. Setubal et al. instilled methylene blue into the bladder using a Foley catheter and observed leakage of blue fluid from the cervical os [78].

A *modified double-dye test* can be performed if coexisting VVF and ureterovaginal fistulas are suspected [79]. The patient is given Pyridium (phenazopyridine) 200 mg orally. Once the urine is noted to be orange, the bladder is emptied and filled with 300 mL of blue dye diluted in normal saline solution. A tampon or vaginal packing is placed and after ambulation, the packing is evaluated. Orange apical staining is suggestive of ureterovesical fistula. Blue staining is suggestive of a concomitant vesicovaginal and/or urethrovaginal fistula. Upper tract imaging should always be used to confirm ureteral involvement.

Endoscopic Evaluation

Cystoscopy is a valuable diagnostic tool and should be performed in any patient presenting with suspected urogenital fistulas. Cystoscopy has been shown to be a sensitive test identifying 92%–93% of genitourinary fistulas in two small series [42,76]. Mature fistula tracts typically have smooth, epithelialized margins and are often easier to identify [44] (Figure 106.4). Smaller, less-mature fistula tracts can be more difficult to identify. A guidewire or a 5 French open-ended ureteral catheter can be passed through the working port of the cystoscope and used to probe any suspicious appearing erythematous patches, areas of bullous edema, or granulation tissue. Cannulation of the fistulous tract can help the clinician determine the course of the urogenital fistulas. Fistula involvement of the bladder neck, external sphincter, and bladder trigone should be documented. Proximity to these vital structures may warrant concomitant bladder neck reconstruction, autologous pubovaginal sling, or ureteral reimplant, respectively. Cystoscopy under anesthesia should be performed when obstruction is present on ultrasound and upper tract involvement is suspected [23]. This allows the clinician to perform retrograde urography and place a ureteral stent in the same setting, if needed (see in the following text).

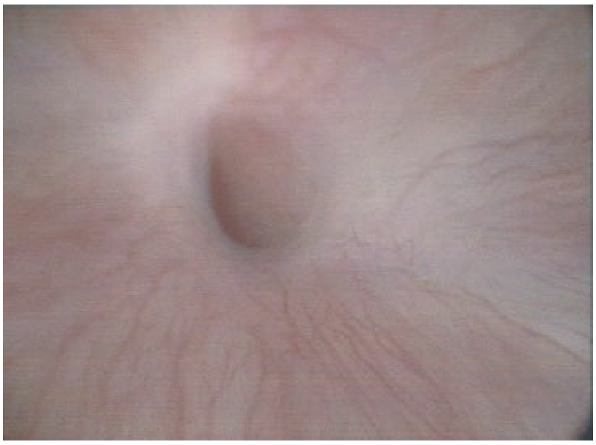

Figure 106.4 Cystoscopic evaluation often will demonstrate the fistula. If vaginal inspection does not demonstrate an obvious connection, placement of a guidewire through the cystoscope port through the fistula can identify the tract. (From Ingber M, Vasavada S, Rackley R, Urogenital fistula, in *Textbook of Urology and Urogynecology*, 3rd edn, London: 2010, pp. 951–953, with permission.)

Vaginoscopy can be used to visualize the vaginal apex and identify the vaginal side of any suspected fistulous tract(s). Patients with a history of gynecological malignancy or pelvic irradiation should have biopsies of the fistula tract taken prior to repair to rule out recurrences and secondary malignancies [35]. If mesh is noted during endoscopic evaluation, operative notes should be reviewed to provide further information regarding the size and course of the mesh. The simultaneous use of vaginoscopy and cystoscopy has been described in the literature as a method for identifying difficult fistulous tracts [80]. We find this practice using a flexible cystoscopy extremely useful for a complete preoperative assessment of the fistula. In cases of small fistula tracts, dye can be used to fill the bladder (ureter or uterus) while simultaneously performing vaginoscopy to look for dye-stained egress of fluid.

Imaging

Imaging can be used to determine the number and location of the fistulous tracts. Imaging is also helpful when the clinician needs to confirm the diagnosis when it is in doubt. Cystography may be a helpful imaging modality for suspected VVFs; however, it is not mandatory if the fistula is clearly documented on physical exam and/or endoscopy (Figure 106.5). Voiding phase images can be added to evaluate for concomitant urethrovaginal fistulas.

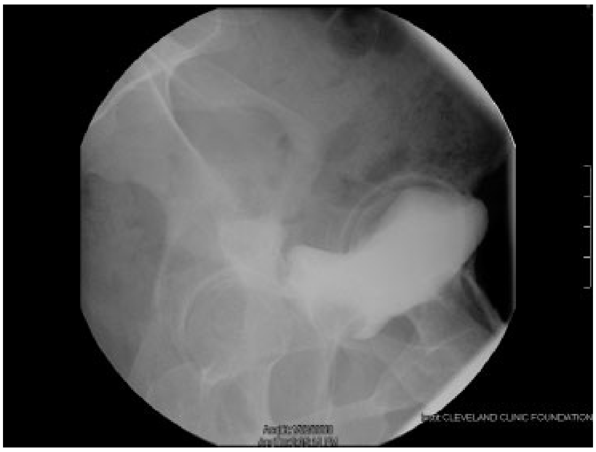

Figure 106.5 Cystogram showing contrast extravasation posteriorly into the vagina. (From Ingber M, Vasavada S, Rackley R, Urogenital fistula, in *Textbook of Urology and Urogynecology*, 3rd edn, London: 2010, pp. 951–953, with permission.)

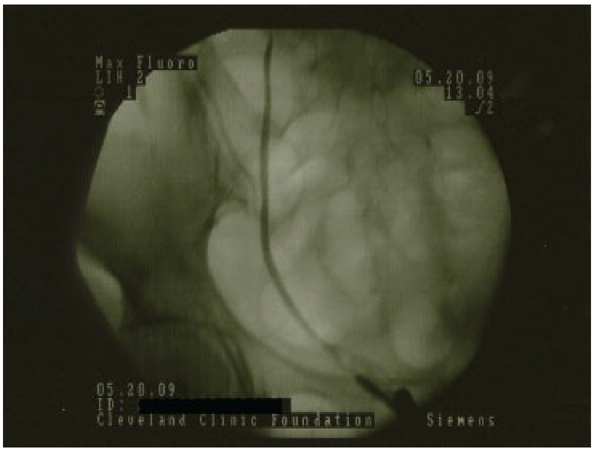

Figure 106.6 Retrograde pyelogram showing a small wisp of contrast tracking medial and posterior into the

vagina. Ureterovaginal fistulas can be present in up to 12% of patients presenting with vesicovaginal fistulas. (From Ingber M, Vasavada S, Rackley R, Urogenital fistula, in *Textbook of Urology and Urogynecology*, 3rd edn, London: 2010, pp. 951–953, with permission.)

Upper tract imaging is also important. Ultrasound can be used to rule out hydronephrosis and signs of obstruction. However, excretory urogram in the form of an intravenous pyelogram (IVP), retrograde pyelogram, or computed tomography urogram (CTU) should always be done to rule out upper tract involvement (Figure 106.6). Normal upper tract imaging essentially rules out ureteral injury, although there have been reports of false negatives with IVP. In one study, only 76 of 84 (90%) patients with ureterovaginal fistulas demonstrated an abnormality on I VP [81]. Partial ureteral obstruction in a patient with a suspected fistula is suggestive of an ureterovaginal fistula until proven otherwise [77]. If the IVP and/or CTU findings are unclear, retrograde pyelography should be performed in the operating room. If examination under anesthesia is planned or if obstruction is noted on initial imaging, intraoperative retrograde pyelography can be performed instead of IVP or CTU. This allows the clinician to place a ureteral stent in the same setting. If ureteral stents cannot be passed beyond the site of obstruction, a percutaneous nephrostomy tube should be placed to maximally drain the urinary system prior to operative repair. An antegrade nephrostogram can be performed to evaluate the remaining upper tract for other injuries, malignancy, and congenital anomalies.

For a patient who presents with cyclical hematuria and amenorrhea, symptoms concerning for vesicouterine fistula, a hysterogram with a short-tipped cannula can be performed [40] if the diagnosis cannot be made with other imaging techniques such as a CT cystogram. As described by Tancer, the uterus is filled with dye, and cystoscopy is performed to evaluate for the presence of dye and identify the fistulous tract, if present [3]. Hysterography and cystography have been used successfully to identify vesicoureterine fistulas [40]. In one series, hysterography was 100% sensitive in patients with suspected vesicouterine fistulas [81]. Upper tract imaging should also be performed in conjunction with these imaging tests to rule out concomitant ureteral involvement (i.e., ureterouterine, ureterovaginal, and ureterofallopian fistulas) [40,71,72]. In the literature, the use of magnetic resonance imaging, transvaginal Doppler ultrasound, and hysterosalpingography for vesicouterine and vesicofallopian fistulas have been described [76,82]. These imaging modalities provide additional useful information in select patients; however, these tests are not usually necessary [83].

Urodynamics

Urodynamics is not considered a routine test in the urogenital fistula workup. However, videourodynamics (VUD) may be considered in any patient with confirmed or suspected urogenital fistula and concomitant lower urinary tract symptoms. Video images can help differentiate lower urinary tract symptoms, such as urgency incontinence, SUI, and mixed urinary incontinence from other causes of incontinence, including vaginal voiding, urethral diverticula, and fistulas.

Preoperative VUD testing can help establish baseline bladder dysfunction and evaluate urethral function for preoperative counseling and planning. Lower urinary tract symptoms, such as urinary frequency and urgency can coexist with urogenital fistulas. Urodynamics can identify the presence of detrusor overactivity and/or concomitant intrinsic sphincter deficiency. Similarly, bladder outlet obstruction can coexist with urethrovaginal fistulas due to scarring, stricture formation, bladder neck disruption, and/or the presence of foreign material (i.e., mesh, urethral bulking agents, stones). If obstruction is suspected, this can be evaluated with a postvoid residual (PVR) and cystoscopy. However, if these tests are unclear, VUD can be used to evaluate for other causes of elevated PVR, including detrusor underactivity.

Approximately 10%–15% of patients with urogenital fistula have concomitant SUI [84]. Coexisting SUI may necessitate concomitant anti-incontinence surgery. Up to 52% of patients develop SUI after successful urethrovaginal fistula repair [59]. The clinician may choose to offer concomitant antiincontinence procedures (i.e., autologous sling) to patients at high risk for postoperative SUI or as an extra layer in patients at high risk of failure due to a history of radiation.

Urodynamics can also identify small capacity or poorly compliant bladders in patients with a history of pelvic irradiation and other risk factors for poor compliance [85], thereby identifying patients that may require a concomitant augmentation cystoplasty procedure [75] or alternatively require a urinary diversion [63,86]. Bladder capacity should be established in any patient who may require ureteral reimplantation, in the event a psoas hitch is needed [44]. Furthermore, VUD can potentially help distinguish urogenital fistulas from other causes of insensible urinary loss, especially when the fistula has yet to be identified [85].

Performing urodynamics in a patient with a large fistula can be challenging. There are a variety of strategies that can be employed to allow adequate bladder filling during the test. First, vaginal packing can be placed at the beginning of the study, during catheter placement to slow the leakage of fluid per vagina. Second, the patient can be placed in the supine position, rather than sitting or standing. If these maneuvers fail, the clinician can attempt to place an 8 French Foley catheter through the large fistula tract. If the fistula is distal, the urodynamics catheter can be placed alongside a small urethrally placed Foley catheter. The Foley balloon will, in some cases, sufficiently obstruct the fistulous tract to allow bladder filling.

CONCLUSION

Urogenital fistulas can be devastating, taking a significant emotional toll on the patient and the treating clinicians. Whether iatrogenic or obstetrical in origin, the clinician must maintain a high index of suspicion in any patient with continuous leakage of urine per vagina. A thorough history and physical examination will often identify the location and mechanism of fistula formation. Appropriate imaging and endoscopic evaluation can provide valuable information needed to determine the size, number, and location of the fistulous tract. Upper tract imaging is mandatory. A missed ureteral injury can be disastrous and should always be ruled out. Urodynamics can help establish baseline capacity, compliance, as well as bladder and urethral function if the fistula is small enough to occlude. Careful presurgical planning is critical for successful surgical repair. A high index of suspicion is needed to ensure that all fistulous communications are identified, including those that communicate with nonurogenital organs or structures.

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107 Transvaginal Repair of Urogenital Fistula

Barry G. Hallner, Kristi L. Hebert, and J. Christian Winters

INTRODUCTION

Urogenital fistula is defined as an abnormal communication between the vagina and the bladder, urethra, and/or ureter (vesicovaginal, urethrovaginal, ureterovaginal, respectively). The earliest evidence dates back to 2050 BC in the mummified remains of a female in the court of Mentuhotep II of the Eleventh Dynasty. During the 1935 cadaveric dissection, a large vesicovaginal fistula (VVF) was identified in a significantly contracted pelvis [1]. It is difficult to know the true incidence of urogenital fistula formation; the generally accepted incidence is derived from surgeries to correct these fistulas and approximates 1% or less of all genitourinary operations [2]. In another study, Mattingly et al. reported that urogenital fistulas have an incidence of 0.3%–2% [3]. According to the World Health Organization, it estimates that there are more than 2 million women worldwide affected by obstetric fistula and more than 100,000 new cases of urogenital fistula occurring per year worldwide [4].

CLASSIFICATION

Currently, there is no single accepted standardized method to classify genital tract fistulas. Urogenital fistula may be classified by anatomic communication, size, location, complexity, and extent of involvement (Table 107.1).

ETIOLOGY

A comprehensive list of the various etiologies for urogenital fistulas is shown (Table 107.2). In developed countries, the most common cause of urogenital fistula is hysterectomy [5]. The incidence is 1/1000 with total abdominal hysterectomy, 2.2/1000 with the laparoscopic approach, and 0.2/1000 with vaginal hysterectomies. A database study by Hilton et al. on >350,000 elective hysterectomies performed in England, demonstrated the rate of urogenital fistulas was highest among women who had a hysterectomy for cervical cancer [6]. Mechanisms of fistula development following hysterectomy may include localized ischemia of the bladder by inadvertent dissection into the bladder or thermal injury creating thin and ischemic areas of the bladder prone to subsequent breakdown, unrecognized injury into the bladder with subsequent extravasation or leakage of urine, foreign body (suture) within the bladder, and finally following repair of a recognized bladder injury. If occurring as a result of pelvic operations, the symptoms of the fistula usually appear within 10 days postoperatively. In contrast, radiation-induced fistulas may appear years after radiation therapy.

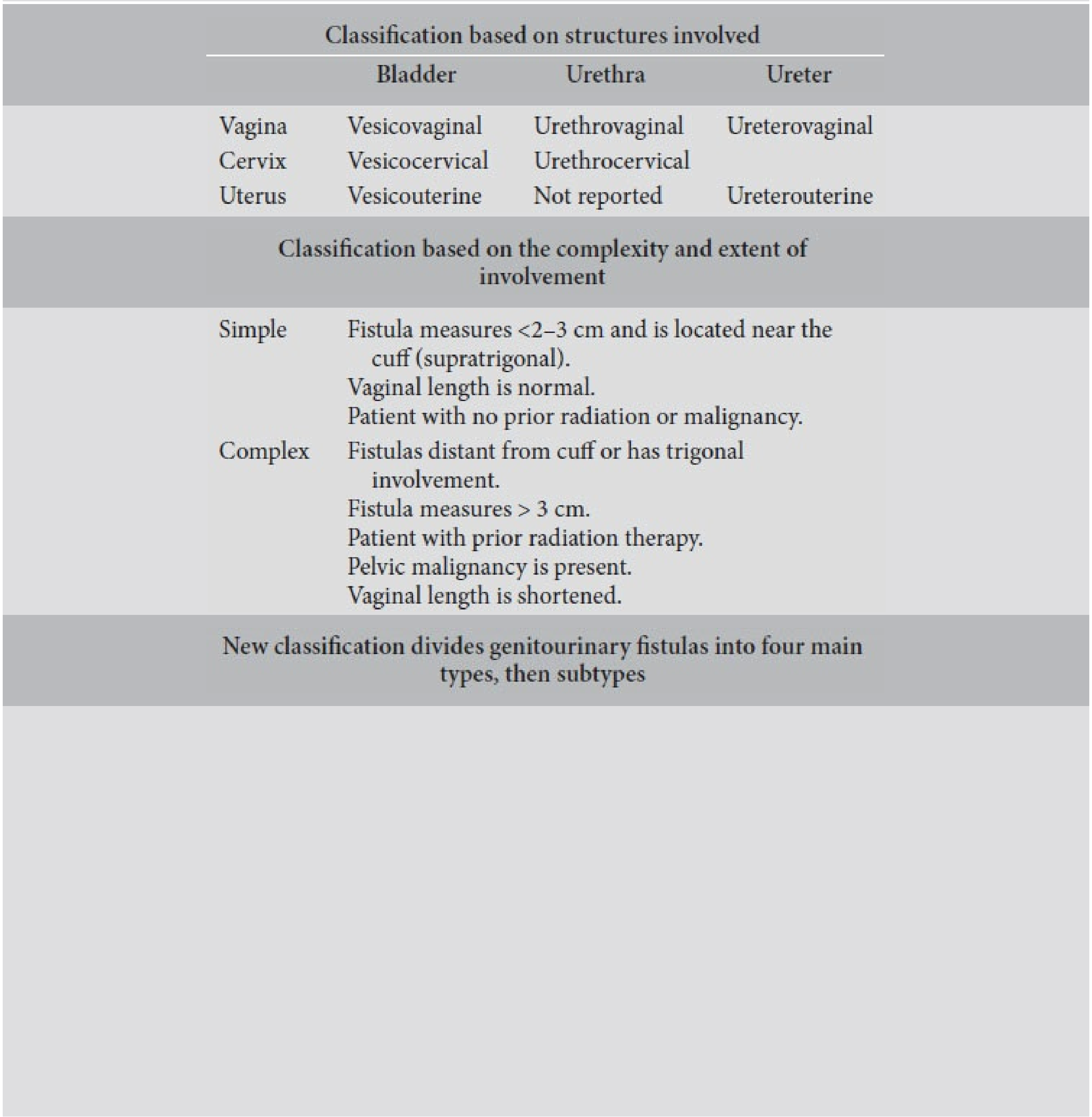
There are several factors that predispose patients to development of urogenital fistulas, including history of cesarean section, pelvic malignancy, cervical conization, radiation therapy, and endometriosis [7]. In a retrospective analysis by Maier et al., of 10,709 patients who underwent radiation for gynecological malignancy, 35 of them subsequently developed urinary fistulas [8]. Angioli and others reported the incidence of developing a VVF after surgery or radiation for gynecological malignancy at 1% [9]. Radiation promotes aggressive endarteritis obliterans that results in the breakdown of mucosal surfaces by disrupting its blood supply [10]. This promotes impaired vascularization of local tissues, which predisposes this tissue to subsequent necrosis/breakdown that may result in fistula formation—even years after the initial treatment.

In developing countries, there is a much higher incidence of fistulas being caused by obstetrical complications. A study done by Singh et al. in India reported 59% of urogenital fistulas were caused by obstructed or protracted labor [11]. In many developing countries, cesarean section is not readily available. Women are likely to be in labor for prolonged periods of time, and engagement of the fetal head within the pelvic outlet for this long of a period predisposes the vagina to pressure necrosis and tissue breakdown. As a result, these fistulas tend to be larger and oftentimes more complex with coincidental urethral destruction. Unfortunately, this is a problem with significant social consequence. These women tend to become “outcasts” within many of their communities and have little resources for care. Fortunately, many have recognized this problem, and there are many heroic efforts to improve the access, quality, and continuity of care for these women.

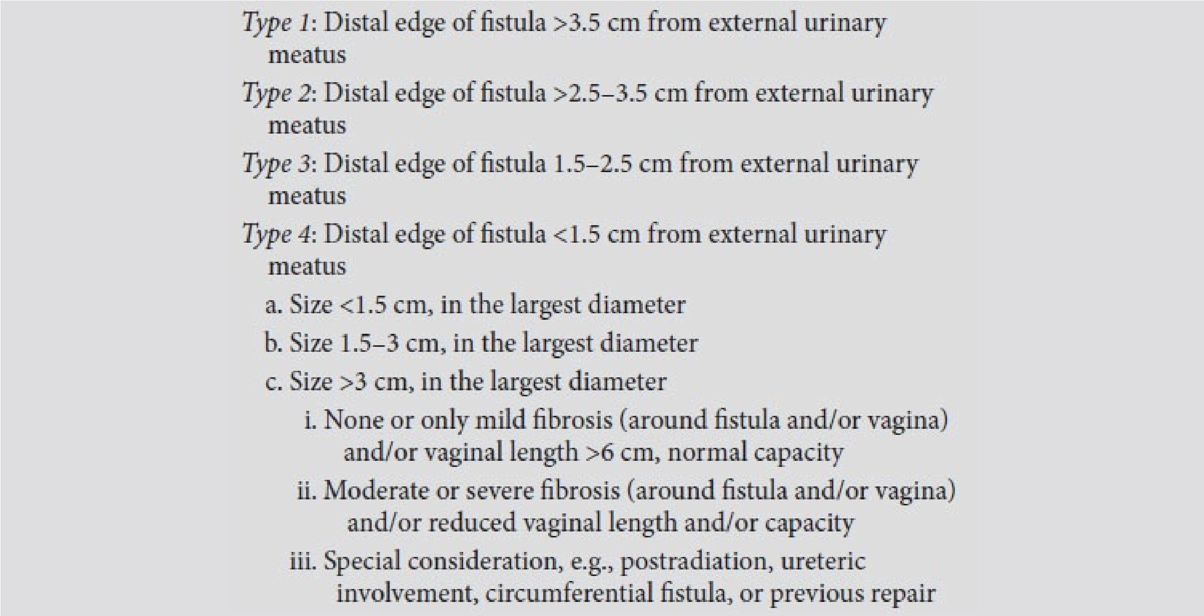
SYMPTOMS

Patients with urogenital fistulas typically present with complaints ranging from vaginal discharge or “drainage” of urinary leakage. If the fistula follows a surgical procedure, the onset of leakage occurring 5–10 days after surgery is most common. Depending on the location of the fistula, this may range from occasional small leakage between normal urethral voids and positional change to total insensate urinary incontinence without normal voids. Some women may present with recurrent incontinence following an antiincontinence procedure. Patients may also experience gross hematuria, recurrent cystitis or pyelonephritis, fever, flank, vaginal, suprapubic pain, and a strong ammonia odor. Patient may also complain of irritation to the vulvar and perineal area from the constant wetness. Essentially, the presentation of fistulas may be quite variable, and it is essential to suspect a fistula in order to achieve the diagnosis in some cases.

Table 107.1 Genitourinary Fistula Classification



	Classification based on structures involved		
	Bladder	Urethra	Ureter
Vagina	Vesicovaginal	Urethrovaginal	Ureterovaginal
Cervix	Vesicocervical	Urethrocervical	
Uterus	Vesicouterine	Not reported	Ureterouterine
Classification based on the complexity and extent of involvement			
Simple	Fistula measures <2–3 cm and is located near the cuff (supratrigonal). Vaginal length is normal. Patient with no prior radiation or malignancy.		
Complex	Fistulas distant from cuff or has trigonal involvement. Fistula measures > 3 cm. Patient with prior radiation therapy. Pelvic malignancy is present. Vaginal length is shortened.		
New classification divides genitourinary fistulas into four main types, then subtypes			



Type 1: Distal edge of fistula >3.5 cm from external urinary meatus

Type 2: Distal edge of fistula >2.5–3.5 cm from external urinary meatus

Type 3: Distal edge of fistula 1.5–2.5 cm from external urinary meatus

Type 4: Distal edge of fistula <1.5 cm from external urinary meatus

- a. Size <1.5 cm, in the largest diameter
- b. Size 1.5–3 cm, in the largest diameter
- c. Size >3 cm, in the largest diameter
  - i. None or only mild fibrosis (around fistula and/or vagina) and/or vaginal length >6 cm, normal capacity
  - ii. Moderate or severe fibrosis (around fistula and/or vagina) and/or reduced vaginal length and/or capacity
  - iii. Special consideration, e.g., postradiation, ureteric involvement, circumferential fistula, or previous repair

Source: Goh JT, *Aust N Z J Obstet Gynaecol*, 44, 502, 2004.

PHYSICAL EXAMINATION

speculum vaginal exam should be performed in all patients with suspicion of urogenital fistula. The fistula may appear as an epithelialized luminal tract of various sizes (ranging from small pinpoint hole to large defect) or localized “dimpling,” scarring, or granulation of the vaginal wall. Following anti-incontinence surgery, foreign body materials (suture or graft) may be adjacent to or involving the fistulous tract. The quality of the surrounding vaginal and labial tissue should be noted as well. Areas of infection, suture reaction, or granulation may need to be addressed before repair can be contemplated. Biopsies should be considered in any areas of suspicious tissue and of the fistulous tract in patients with history of malignancy. The size, location, and number of the fistula(s) should be documented (Figure 107.1). The vaginal depth, diameter, and mobility should be noted as these factors can help determine the appropriate method of surgical repair. The bladder may be filled with methylene blue during the vaginal exam to help identify the location of the fistula. If there is still a question of urogenital fistula despite a negative examination, the fluid leaking per vagina may be sent for creatinine. If the fluid is indeed urine, the result will be severalfold times the serum creatinine level.

Table 107.2 Causes of Urogenital Fistula

- I. Congenital
- II. Acquired
  - a. Iatrogenic
    - i. Postoperative
      - 1. Hysterectomy
        - a. Abdominal
        - b. Transvaginal
        - c. Laparoscopic
      - 2. Incontinence procedures
        - a. Transvaginal slings
        - b. Retropubic
        - c. Laparoscopic
      - 3. Prolapse procedures
        - a. Anterior colporrhaphy
        - b. Mesh kits
        - c. Sacrospinous/uterosacral fixation
      - 4. Urethral diverticulectomy
      - 5. Endoscopic procedures
      - 6. Bowel and vascular surgeries
    - ii. Radiation injury
  - b. Noniatrogenic
    - i. Pelvic malignancy
    - ii. Obstructed labor
    - iii. Trauma
    - iv. Sexual injury
    - v. Infection
    - vi. Foreign body

DIAGNOSTIC TESTING

A full description of diagnostic procedures including dye tests, endoscopy, and imaging can be found in Chapter 106. If a urogenital fistula is not readily identified or the precise location is not clear from the physical and endoscopic examinations, a “double dye” test may be performed. In this, phenazopyridine is given PO if no leakage is seen on the pad; the bladder is retrofilled with methylene blue; blue dye is then seen staining the most distal part of the pad, indicating leakage from the urethra, whether as a result of bladder overactivity or of intrinsic sphincter deficiency (ISD). With an ureterovaginal fistula, the most proximal pad stains yellow/orange; no blue staining is noted. With a vesicovaginal or urethrovaginal fistula, the pad stains blue in the middle to proximal area of the pad. Reflux of the blue dye to the proximal pad in an ureterovaginal fistula makes true diagnosis difficult [12].

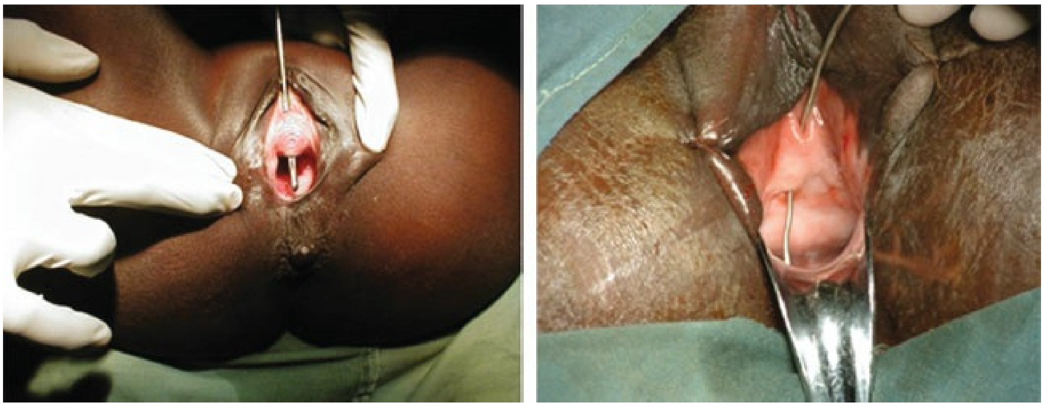


Figure 107.1 Exam performed under anesthesia. Note the probe passed through the fistulous tract. In both cases, a single urethrovaginal fistula was noted.

We believe that cystoscopy should be performed in all patients with suspicion of urogenital fistula (Figure 107.2). The goal of cystoscopy is to identify the location of the fistula, the size of the fistula, and the number of fistulas and to determine the location of the fistula(s) relative to the ureteral orifices. In the absence of an obvious fistulous tract, a fistula may be suspected in an area of dimpling, scarring, or localized edema within the bladder wall. The integrity of the bladder tissues should also be carefully assessed to assist in determining the timing of repair. If there is a history of malignancy, a biopsy of the fistulous tract must be performed. Vaginoscopy can also be performed after cystoscopy, to confirm the location of the fistula within the vagina and assist in assessing the quality of the vaginal tissues for repair. A retrograde pyelogram should be performed at the time of cystoscopy if upper tract imaging has not been performed or if there is high suspicion of ureteral involvement (see Chapter 106). Coexisting ureteral pathology (obstruction/hydronephrosis/fistula) has been reported in approximately 10% of cases of VVF [5]. Partial or complete ureteral obstruction on retrograde pyelography should raise suspicion for the presence of ureterovaginal fistula [13]. CT urogram is our preferred imaging modality for preoperative upper tract imaging. Not only can the ureters be visualized on excretory and delayed phases, but also urinary tract reconstruction images can provide precise anatomical detail preoperatively. Voiding cystourethrography or plain cystograms may be used for diagnosis of VVF; however, they may be suboptimal for identifying exact location of a fistulous tract (see Chapter 106). According to Narayanan et al., MR should be considered when evaluating for urogenital fistula in patients with a history of pelvic malignancy. MR evaluates for fistula as well as recurrence of pelvic malignancy [10]. On T2-weighted images, the fistula will appear as a high-intensity fluid-filled connection. Transvaginal ultrasound is rarely performed as <30% of fistulas are identified sonographically [14].

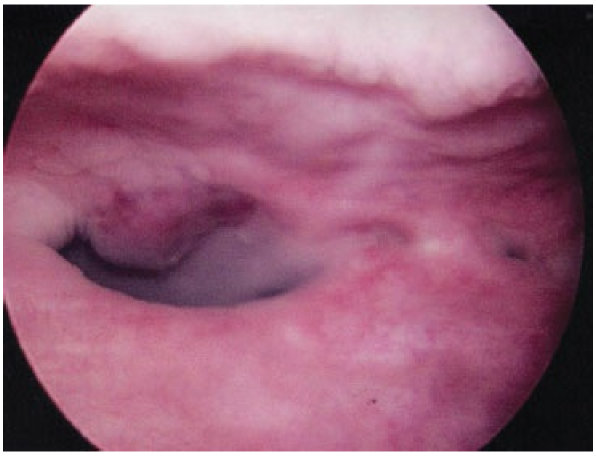


Figure 107.2 Cystoscopic evaluation often will demonstrate the fistula. In this figure, note the abnormal appearing tissue at the edge of the fistula indicated by black arrow. Biopsy noted a recurrence of vaginal squamous cell carcinoma.

MANAGEMENT

Conservative Management and Minimally Invasive Techniques

The psychological and physical distress caused by a VVF can be overwhelming to patients due to the constant wetness, odor, and potential infections. Ideally, the goal of treatment of a VVF is the closure of the fistula and resolution of urinary leakage as quickly as possible. The most conservative treatment option of a VVF is simple continuous bladder drainage. Davitas and Miranda described four patients who underwent successful postoperative VVF closure by simple bladder drainage [15]. Although outcomes have not necessarily been proven and constant, 12%–80% of fistulas that are small (<1 cm) and diagnosed early may spontaneously resolve within 4 weeks with continuous bladder drainage [16]. If, after several weeks of continuous bladder drainage, the fistula persists, alternative therapeutic treatments such as fibrin glue and electrocautery can be considered instead of surgery.

If the fistula is small (<5 mm), fibrin glue may be attempted as a sealant. Fibrin glue, also called as fibrin sealant, can be produced from pooled blood sources or from a single blood donor. The single-donor blood can be allogenic or autologous. The use of pooled blood products such as Tisseel^{TM} (Baxter, Inc., Deerfield, IL) and Beriplast^{TM} (CSL Behring, Inc., King of Prussia, PA) has been more commonly used in VVF treatment in Europe. A primary component of the synthetic fibrin sealant is highly concentrated human fibrinogen [17]. A common mode of application is the double-barreled syringe apparatus, which enables simultaneous application of equal amounts of the fibrinogen and thrombin solutions through a blunt-tipped needle. Bijan and Stoller [17] note a number of studies using fibrin glue to treat VVF with a success rate of approximately 66%–100%. It must be considered that reports of fibrin glue usage in VVF treatment are limited to case reports and small case series only. These reports have not been replicated on a large-scale basis. Although results have been satisfactory, it appears that applying fibrin sealant for fistula closure should be individualized [17]. Fibrin sealant has been used successfully in combination with and without bovine collagen as an additional "plug" [18,19]. Additionally, small VVF may be repaired with electrocoagulation or laser ablation of the fistulous tract [20]. Falk in 1957 and Stovsky in 1994 successfully treated patients with electrocoagulation that had VVF <3.5 mm in diameter, followed by catheter drainage for 10–14 days [21,22]. The fistulous tract is electrocoagulated by endoscopically inserting a Bugbee electrode inside the fistulous tract as far as possible. The electrode is slowly withdrawn from the track with the electrode on coagulation, till the edges of the fistula tract blanch [22]. Care is taken not to overcoagulate as this can cause widespread tissue necrosis, sloughing, and enlargement of the fistula [23]. It is important to mention that in patients with a thin vesicovaginal septum, large VVF, nonoblique fistula tract, or significant inflammation around the fistulous tract, there is an increased risk of failure and the possibility of enlarging the size of the fistula [24]. All patients who choose these options (cautery/fibrin glue) of fistula management must be warned that these procedures may change the adjacent tissue integrity for a subsequent repair, if needed.

In the case of an ureterovaginal fistula, the initial management is ureteral stenting [25]. Stenting tends to be more successful when performed sooner rather than later. In one study, 82% of attempts of ureteral stenting in patients whose fistulas were <1 month old were successful compared with only 33% of attempts with older fistulas (>1 month) [26]. Once a stent has been successfully placed, it should be left in place for 6–8 weeks. Once the stent is removed, sequential follow-up over time with upper tract imaging should follow to rule out ureteral stricture development. If a stent can't be placed by way of a retrograde approach, options of surgical repair versus a percutaneous nephrostomy must be considered. If a percutaneous nephrostomy tube is placed, attempts at antegrade stent placement should follow. If a stent is successfully placed in the bladder, the patient can be followed as in patients who are successfully stented via a retrograde approach—surgery will likely not be needed. If a percutaneous nephrostomy is not done or if a stent cannot be placed via an antegrade approach, surgery will be necessary to correct the problem. Urethrovaginal fistula should be repaired as soon as they are diagnosed unless that tissue is inflamed or infected [27].

SURGICAL REPAIR

When planning for surgical repair, several considerations must be made in order to optimize patient outcomes because the best opportunity to achieve successful repair of the fistula is within the initial operation [28,29]. As the number of attempts increase so does the amount of scar tissue, anatomical distortion, and a decrease in potential reconstructive flaps. Unfortunately, there is no single "best" approach to all patients with VVF, and each case should be individualized based on the fistula characteristics and the surgeons' experience.

TIMING OF REPAIR

In most cases of iatrogenic fistulas identified early, they may be repaired immediately. Early repair of the fistula spares the patient the devastating physical, psychological, and social impact on their quality of life [30]. The emerging consensus is that uncomplicated fistulas may be repaired early, as soon as the tissue quality is deemed suitable for repair. This is unlike radiated, infected, or indurated tissue, where a waiting period of several months is recommended to allow tissue sloughing, necrosis, and inflammation to resolve prior to attempting surgical repair. Typically, a 3–6 month waiting period is recommended in these settings. During this waiting period, vaginal examinations should be done every 3–4 weeks to monitor tissue quality and evaluate for resolution of inflammation and/or infection. Even in complex fistulas, many can be closed in a more timely fashion without a 6-month waiting period, if sequential examinations reveal tissues amenable to repair [16].

PREOPERATIVE CONSIDERATIONS

When the decision to proceed with surgical closure of the fistula is made, it is important that the patient be medically optimized and capable of tolerating the planned surgery. Nutritional status should be optimized to aid healing. Vaginal, oral, or transdermal estrogen should be considered in cases of vaginal atrophy to help improve the vaginal epithelium. We prefer the use of vaginal estrogen due to the lack of systemic effects. In the case of excessive urinary leakage, the use of vaginal estrogen may not be possible. Short-term use of oral or transdermal estrogen therapy may be used even with a history of breast or gynecological cancer [31,32]. Zinc oxide topical ointment and sitz baths may help control ammonia dermatitis [33]. Preoperative antibiotics are recommended, and several studies have shown that various regimes may be equally effective in successful repair and reducing the need for postoperative antibiotics. The American Urological Association and the American College of Obstetrics and Gynecology have set forth guidelines regarding preoperative antibiotics as well as deep venous thrombosis prevention [34–37].

SURGICAL APPROACH

VVF may be repaired transvaginally or transabdominally. Factors such as size, location, and the need for adjunctive procedures should influence the choice of approach. One of the most important factors is the individual surgeons' experience. Transabdominal repair of VVF is discussed in the following chapter. The majority of VVF can be repaired transvaginally [38]. In 1988, Lee et al. reported that 80% of 303 patients were repaired transvaginally, regardless of fistula size, number, or history of previous repairs [39]. There are several advantages to the transvaginal approach when compared to a transabdominal approach such as shorter operating time, shorter hospital stay, less postoperative pain, and less blood loss [40]. Relative disadvantages include vaginal shortening and difficult exposure involving VVF that are high near the vaginal cuff, especially in deep, narrow vaginas or in cases without any apical prolapse [24].

TRANSVAGINAL APPROACH OF VESICOVAGINAL FISTULA

Transvaginal repair of VVF usually includes one of two strategies. One may excise the vaginal epithelium and perform a partial colpocleisis procedure (Latzko repair) or utilize a multilayer flap closure with or without tissue interposition (Figure 107.3).

Latzko Procedure of Vaginal Cuff Fistulas

The Latzko procedure is a partial colpocleisis without excision of the fistula tract [41,42]. It is indicated for VVF at the vaginal apex that area <3 cm [43]. This technique avoids widening of the fistula tract that can be associated with excising it, excessive bleeding, tissue necrosis caused by cautery, and injury to the ureters if close to the repair site. Success rates between 93% and 100% for primary and repeat repairs without significant vaginal shortening have been reported [44].

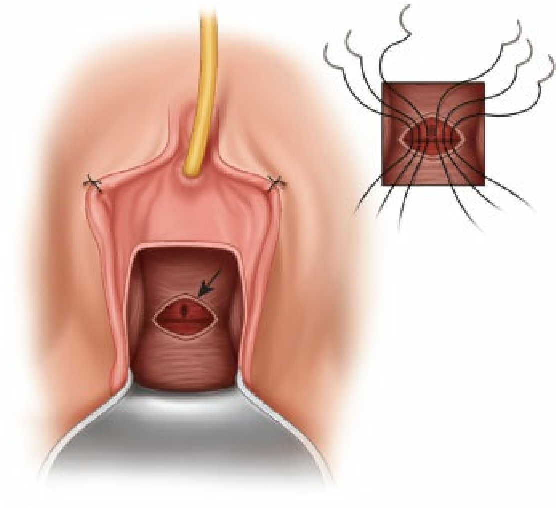


Figure 107.3 The Latzko procedure. The vaginal epithelium is sharply dissected from the anterior and posterior vagina approximately 2–3 cm from the fistula. The fistula tract is not excised. The underlying fibromuscularis is closed in at least two layers with absorbable suture. The vaginal epithelium is then closed with absorbable suture.

Technique of Latzko VVF Repair

The patient should be placed in a high dorsal lithotomy position. Choice of stirrups should be surgeon preference. A self-retaining ring retractor will facilitate exposure. The patient is examined under anesthesia. In the case of a narrow introitus, a midline episiotomy or medial lateral episiotomy may aid in exposure. The ureters should be catheterized at this time if the fistula opening is close to the ureteral orifices [45]. Several techniques may be used in order to pull the fistula toward the introitus for better access. In one method, a pediatric Foley catheter or Fogarty catheter can be placed through the fistulous tract and placed on traction after the balloon is inflated. If the fistula is too small to accommodate the pediatric Foley, the fistula tract can be gently dilated to allow insertion of the catheter. Another method is to place stay sutures at least 2 cm away from the fistula margin. This helps keep orientation and aids in traction. We prefer to use the self-retaining ring retractor with the sharp hooks to pull the tissue around the fistula toward the introitus. Next, starting a point at least 2 cm extending from the fistula is marked with a surgical marking pen circumferentially around the fistula. The dissection area may be developed by hydrodissection with either injectable saline or a dilute solution of a vasoconstrictive agent or simply sharp dissection. In either situation, a 2 cm margin of vaginal epithelium is sharply dissected from the underlying fibromuscularis circumferentially. Once the vaginal epithelium has been sharply removed, the fibromuscular layer can be imbricated in an anterior to posterior fashion using a # 3-0 delayed absorbable suture in an interrupted fashion. A second-layer closure should be performed to ensure a watertight seal. The bladder can be tested for watertightness either at this point or once the vaginal epithelium is closed. Test for watertightness by retrofilling the bladder with either sterile milk or methylene blue. Cystoscopy is performed to confirm ureteral patency. The remaining vaginal epithelium is closed with # 2-0 delayed absorbable sutures in either a running or interrupted fashion. A transurethral Foley or a suprapubic tube is placed to continuously drain the bladder for 10–14 days.

The Latzko procedure is optimal for cuff or very proximal fistulas near the cuff. In the case of more distal or complex VVF, urethrovaginal fistula, or urethrovesicovaginal fistula, the Latzko procedure is more likely to result in increased loss of vaginal length and a multilayer flap closure with or without tissue interposition is indicated [33].

Transvaginal Multilayer Flap Repair

A transvaginal multiple layer flap repair is among the most common surgical approaches to repair VVF. The advantages include lack of an abdominal incision, elimination of cystotomy, easy incorporation of interposition material, and the ability to repair fistulas at any location in the vagina. The essential components of procedure include creation of full-thickness well-vascularized vaginal flaps, excision of the fistula tract, closure of the fistula defect, multilayer closure, avoidance of overlapping suture lines, and adequate drainage. Tissue interposition may be incorporated as needed. Success rates of 72%–90% have been reported, and most authors advocate early repair of VVF using some modification of this approach.

Technique of Transvaginal Multilayer Flap Repair

To begin, the patient is placed in a high dorsal lithotomy position. A self-retaining ring retractor may be used to facilitate exposure. Stay sutures may be placed to help expose the fistula. The layered technique involves circumscribing the vaginal epithelium around the fistula (Figure 107.4). Hydrodissection can be used to help develop the plane or simply sharp dissecting the vaginal epithelium from the fibromuscularis. Depending on the size, shape, or location of the fistula, the initial vaginal epithelium incision can be a U-shaped, inverted-U, J-shaped, or oval incision. These incisions can be incorporated into the incisions made to circumscribe the fistula. These incisions should be created in order to facilitate an advancement flap over the fistula closure at the time of vaginal closure. After incision, sufficient vaginal epithelium is separated from the underlying fibromuscularis to permit a tension-free closure of the tissue. Usually, this requires a significant amount of tissue mobilization surrounding the fistula. Unlike the Latzko procedure, the fistula tract is excised in the classical approach. Care must be taken not to overexcise the fistula edges, which can enlarge the defect, increase the risk of bleeding from the fistula edge, and decrease bladder volume by removing bladder tissue. If the fistula is large and a tension-free closure is difficult, regular circumferential vaginal relaxing incisions are made at a distance from the fistula and may facilitate mobilization and tension-free closure [45]. Once the tract is excised, a layered closure is performed. The first layer is closed with interrupted # 4-0 delayed absorbable sutures. Ideally, a second layer of the pubocervical fascia is closed over the fistula. Alternating horizontal and vertical suture lines prevent the suture layers from lying directly over one another. The bladder may be tested for watertightness by retrofilling the bladder with sterile milk or methylene blue or by giving indigo carmine via IV. The remaining vaginal epithelium is then advanced over the closure site and closed with # 2-0 delayed absorbable sutures in an interrupted or running fashion. A vaginal pack may be inserted. A transurethral Foley catheter is used to continuously drain the bladder for 2–3 weeks. Alternatively, a suprapubic tube may be used solely or in conjunction with a transurethral Foley catheter.

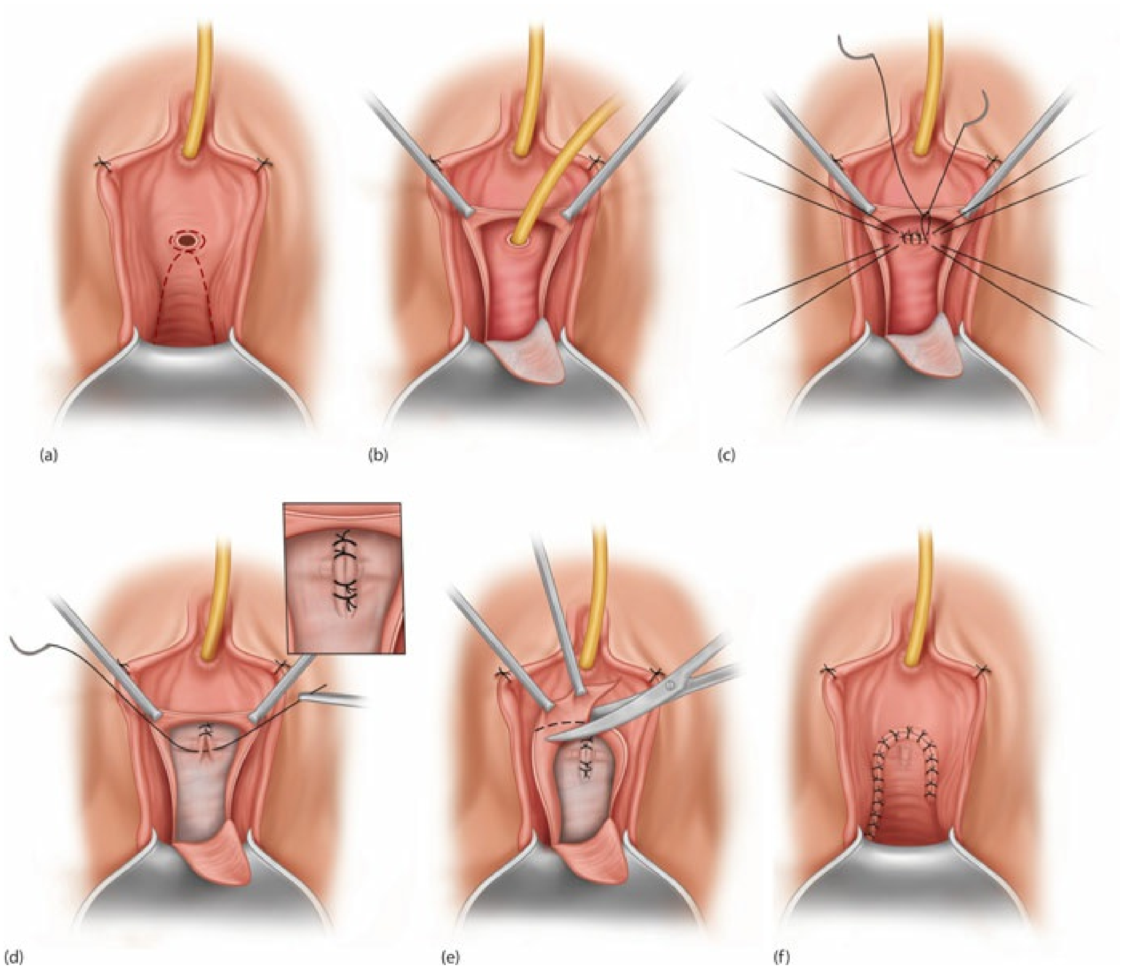


Figure 107.4 Steps in transvaginal vesicovaginal fistula repair. A Foley catheter may be inserted into the fistula for retraction purposes. Incisions should be planned to provide adequate flap mobilization and vaginal closure over the fistula repair, such as an inverted-U (a). A small Foley may be placed within the tract for exposure. The vaginal epithelium is dissected off of the fistula site, until healthy tissue is obtained (b). The fistula is closed with absorbable suture (c). If possible, a second layer of overlying fascia is closed in a perpendicular fashion (d). Excess vaginal mucosa may be trimmed (e). Finally, the vaginal flap is closed after advancing the repair (f).

If the fistula is recurrent, large, or at the surgeon's discretion, tissue interposition flaps may be used as an additional layer and provide a blood supply to the repair [45]. Local vaginal flaps include Martius graft, gluteal skin flaps, gracilis muscle flaps, peritoneal flaps (Figure 107.5), rectus abdominal flaps, labial myocutaneous flaps [24], collagen xenografts, and oxidized cellulose [27]. The most commonly used vaginal flap is the Martius graft, a transposition of a labial fat pad with or without the bulbocavernosus muscle. It was first described in 1928 [46]. It has a high reported success rate in complex fistula repair [47]. Success of the Martius graft is 70%–100% [27]. It is a long band of adipose tissue from the labia majora and has excellent strength and vascularity. The superior and anterior blood supplies come from the external pudendal artery. The lateral border is supplied by the obturator branch, and the inferior aspect of the graft is supplied by the inferior labial artery [45]. Typically, the graft is mobilized on each side and left intact at either the superior or inferior end. The vaginal epithelium is mobilized and a long curved clamp is passed through the vaginal incision to the mobilized fat pad. This will create a tunnel in which the graft will pass through. Grasping the free end of the graft, it is passed medially under the labia minora and attached with delayed absorbable suture to cover the fistula repair. The vaginal and labial incisions are closed without tension. Alternatively, for proximal fistula near the cuff, a peritoneal graft can be utilized by advancing the posterior peritoneum including the preperitoneal fat after mobilization by sharp dissection. The flap is advanced to cover this fistula closure and secured utilizing small absorbable sutures. Following this, the vaginal advancement flap is closed thus completing the repair.

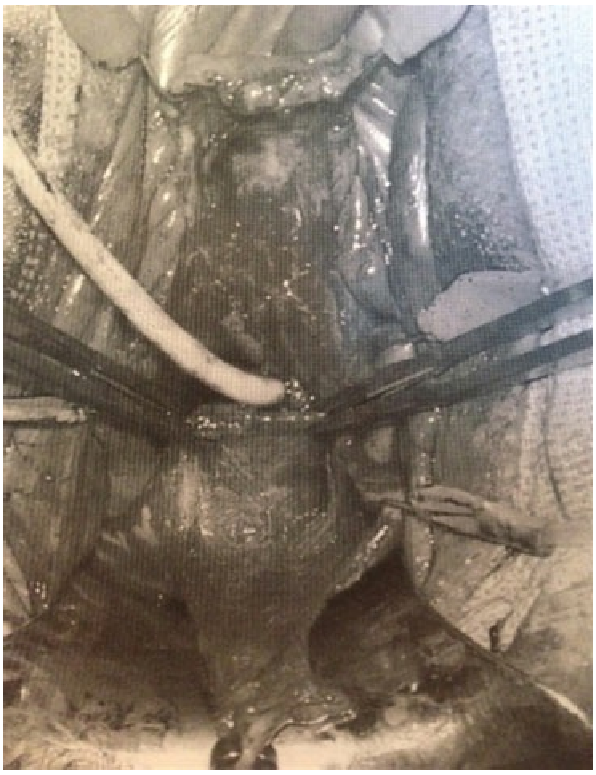


Figure 107.5 A flap of peritoneum is developed and used to buttress the fistula repair. (From Mattingly RF, Harkki-Siren P, Petri E, et al. in: Vasavada SP, ed. *Female Urogynecology, and Voiding Dysfunction*. New York: Marcel Dekker, 2005. 761–764. Print. With permission.)

COMPLICATIONS

As with any surgical case, complications can be divided into early and late complications. Early complications include hemorrhage, bladder spasms, bladder infections, vaginal infections, and intra-abdominal infections. Treatment of these early complications should be initiated as soon as complications present to prevent fistula recurrence. Antimuscarinic agents can be used for bladder spasms. Postoperative antibiotics may be used in the cases of bladder, vaginal, and intraabdominal infections. Delayed complications include fistula recurrence, urinary incontinence, vaginal shortening, vaginal stenosis, and ureteral injury from the repair. It is not uncommon for patients to complain of dyspareunia from vaginal stenosis and/or from the Martius graft site [45]. In patients who have undergone a repair of a VVF, elective cesarean delivery is recommended for all subsequent births in females contemplating future fertility. Patients must have a realistic expectation of possible complications and outcomes related to fistula repair. It is equally important to counsel patients that urinary incontinence after successful repair can be as high as 12%. Waaldijk reported occurrence of urinary incontinence after repair of fistulas in 1% of cases without sphincter involvement, 13% with sphincter involvement with no additional tissue loss, and 16% with both sphincter and tissue loss [48].

CONCLUSION

In developing countries, urogenital fistulas are extensively related to obstructed labor due to limited access to obstetrical care. In developed countries, urogenital fistulas are typically a result of a gynecological procedure, most commonly a hysterectomy. The literature on urogenital fistulas is mainly based on small case series and expert opinion. The tenants of fistula surgery are well established and include adequate exposure and visualization of the fistula tract, careful dissection of the surrounding tissues to allow a tension-free watertight closure, and use of well-vascularized flaps, nonoverlapping suture lines, and appropriate bladder drainage. Timing of repair remains controversial. Prevention is key and good surgical technique is mandatory in any surgical procedure but especially when operating deep in the pelvis. Even when injuries to the bladder do occur during a surgical procedure and are properly and promptly repaired, a fistula may still occur. Proper patient counseling is vitally important and may help mitigate medicolegal action. Success in management is dependent upon multiple factors including the individual patient, the fistula characteristics, and the surgeons' experience. VVF is a devastating outcome physically and emotionally to patients. Each patient should undergo individualized management using the principles outlined throughout this chapter. Patients must undergo extensive counseling regarding what happened, the rationale in identifying the problem, and the appropriate steps to fix the problem as soon as technically feasible. In the vast majority of cases, early intervention via vaginal repair is associated with outstanding success rates. These patients should be reassured at frequent intervals throughout the process, and meticulous follow-up after surgery insuring adequate drainage and absence of other complications is critical to achieving surgical success.

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Transabdominal Vesicovaginal and Vesicouterine Fistula Repair

Howard Goldman and Christopher Tenggardjaja

Genitourinary (GU) fistula is a devastating condition that leads to decreased quality of life due to incontinence. The surgeon who can cure someone of their leakage caused by vesicovaginal/uterine fistula can truly make a difference in the patient's life. The best opportunity for success lies in the initial diagnosing and treating surgeon's hands. GU fistulas are composed of any nonanatomic communication between the urinary tract (ureters, bladder, and urethra) and vagina, cervix, or uterus. While fistula repair can be approached in myriad ways, the most effective way of closure lies with the approach with which the surgeon is most comfortable. In this chapter, the indications and techniques for transabdominal surgical management of vesicovaginal and vesicouterine fistula (VVF, VUF) will be discussed. The reader is directed to other chapters to further learn diagnosis/evaluation and transvaginal techniques for management of GU fistulas.

TRANSABDOMINAL VESICOVAGINAL FISTULA

Open Repair

The traditional reasons for a transabdominal approach to VVF include surgeon's technical expertise, high location of the VVF, need for concomitant abdominal procedures such as augmentation cystoplasty/ureteral reconstruction, and hostile vaginal environment such as scarring from radiation or narrowed introitus due to nulliparity [1,2]. Again, the best approach for the treatment of VVF will be the approach that the surgeon has the most experience with. If there are any concerns about multiple abdominal adhesions due to prior surgeries or radiation, preoperative planning with colorectal surgery may be prudent.

The patient is placed in the low lithotomy position with stirrups. Perioperative antibiotics are administered within 30 minutes to 1 hour of incision time and are chosen to appropriately cover the skin and vaginal flora. If possible, the patient is positioned above the break in the bed to allow for exposure of the pelvis. Pneumatic compression devices are placed on the legs and per our protocol, subcutaneous heparin is administered prior to all our pelvic surgery cases. If there is concern for fistula proximity to the ureters, a cystoscopy can be performed prior to the procedure and ureteral stents placed for localization. During this time, the fistula tract can be cannulated to help with manipulation during the surgery. Cystoscopy can be deferred if a transvesical approach is planned and open-ended catheters or feeding tubes can be placed through the cystotomy under direct visualization of the ureteral orifices.

Transabdominal VVF repair has been described from an intraperitoneal or extraperitoneal approach. The main benefit of an extraperitoneal approach is the avoidance of entering the peritoneum. Depending on the etiology of fistula, the intraperitoneal approach could be less desirable due to multiple adhesions. The drawback of an extraperitoneal approach is the inability to utilize different types of flaps, such as omentum, that are only available intraperitoneally. After a catheter has been inserted into the bladder, a Pfannenstiel or infraumbilical midline incision is made. The dissection is carried into the space of Retzius. The bladder is then entered through a cystotomy. If there is any difficulty locating the bladder due to prior surgical interventions in the retropubic space, the urethral catheter can be backfilled. The classic transvesical approach first described by O'Conor describes bivalving the bladder widely down to the VVF [3]. Furthermore, the bladder should be dissected free from the VVF proximally and distally for a tension-free closure. Proper dissection and mobilization of the surrounding tissue allows for the placement of an interposition flap such as omentum or peritoneum. The benefit of bivalving the bladder is the ability to catheterize the ureteral orifices intraoperatively and increased exposure [4]. The drawback is the possible morbidity associated with a large bladder incision. The alternative to minimize the potential complications of a large cystotomy is a transvesical approach [5]. In this setting, a limited anterior cystotomy is made. The posterior bladder at the area of the fistula is exposed. The fistula tract is circumscribed and can be excised. Another option is to leave the fistula tract in situ and incorporate it into the repair. The vaginal muscularis is dissected free and closed. The bladder detrusor and mucosa are then closed separately using absorbable suture.

An intraperitoneal approach can also be utilized. Once the peritoneal cavity is entered, the bowels are packed cephalad with moist lap sponges and a self-retaining retractor is placed. Slight Trendelenburg can be useful to keep the bowel out of the field. If minimal adhesions are encountered and the VVF is away from the trigone, a dissection plane can be carried between the vagina and the bladder without the need for an O’Conor approach. The bladder and vagina are mobilized apart from each other for several centimeters beyond the fistula tract to enable a tension-free closure. The vaginal muscularis is closed using absorbable suture. If possible, the bladder is closed in two layers. At the surgeon’s discretion and given the patient’s anatomy, an interposition flap can be harvested and may be placed between the bladder and the vagina to keep the suture lines apart (Figures 108.1 through 108.3). A traditional O’Conor approach with wide bladder exposure can be useful in many cases and may be preferred by many. An intraperitoneal approach can be useful for easy mobilization of an omental interposition flap. Also, numerous other flaps have been described including peritoneum, bladder mucosa autograft, urachus, perisigmoid fat, and epiploica. An abdominus rectus myofascial flap has also been described [6–8]. The intraperitoneal approach also allows for concomitant procedures such as ureteral reconstruction and augmentation cystoplasty. After the cystotomy and fistula are closed, the repair is evaluated by low-pressure retrograde filling of the bladder. Postsurgical drainage is achieved with large-bore urethral catheterization with the addition of a suprapubic cystotomy being an option. It is our preference to leave a urethral and suprapubic catheter and remove the urethral catheter within a few days once the urine has cleared. Cystotomy closure is achieved using a two-layer closure with absorbable sutures. A drain is left postoperatively and discontinued when the output is low. Postoperative care is similar to any abdominal case with appropriate pain control, early ambulation, and advancing diet when the patient is tolerating clears. Anticholinergic medication during recovery is also an integral part of the postoperative regimen.

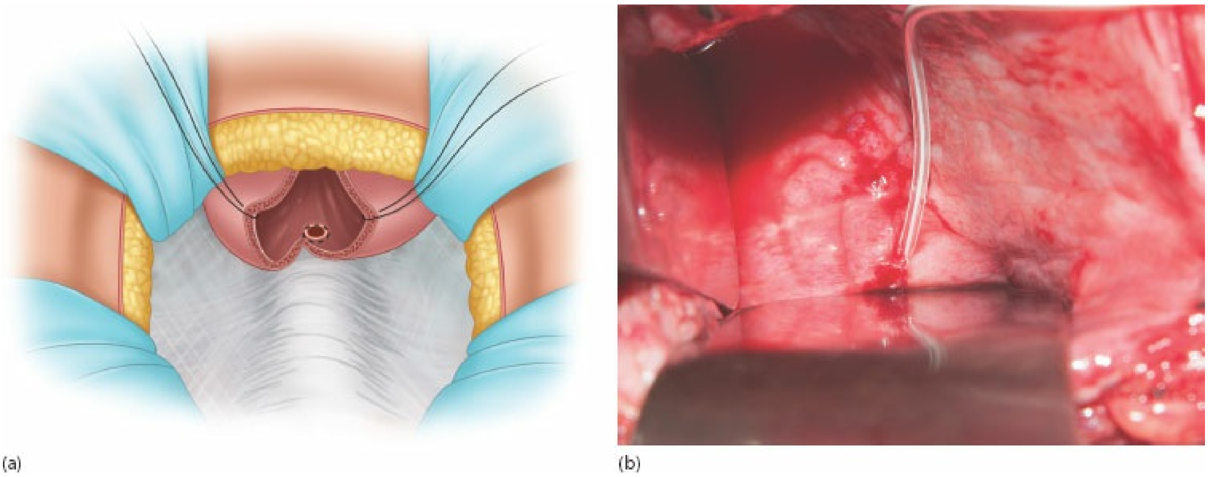

Figure 108.1 Transabdominal vesicovaginal fistula repair. (a) Intraperitoneal approach with cystotomy shown with bladder edges retracted by stay sutures and the fistula tract marked. (b) Intraoperative picture demonstrating cannulization of the fistula tract with a feeding tube. (Courtesy of Cleveland Clinic, Cleveland, OH.)

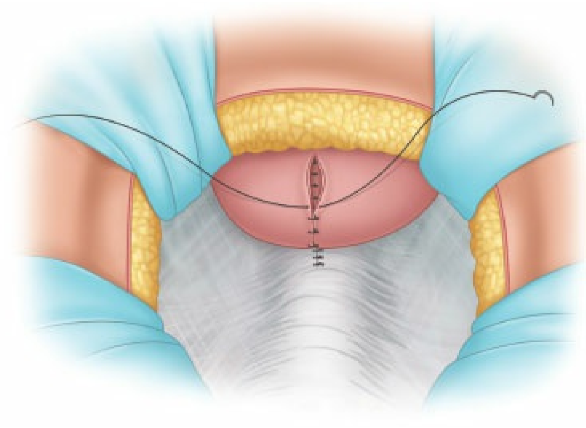

Figure 108.2 Transabdominal vesicovaginal fistula repair. Two-layer, watertight closure of the bladder using absorbable sutures. The fistula tract on the vaginal side is closed using absorbable suture with or without excision of the fistula tract. (Courtesy of Cleveland Clinic, Cleveland, OH.)

Minimally Invasive Transabdominal Approaches

Conventional Laparoscopy

Transabdominal VVF repair is subject to the morbidity associated with a laparotomy incision, bowel manipulation, and an open abdomen. Laparoscopy affords the convenience of a transabdominal approach with improved visualization in the pelvis while being minimally invasive. The main drawback of laparoscopy is the steep learning curve associated with its adoption [9]. Since the first description of laparoscopic VVF repair in 1994, multiple large series have described good results with conventional laparoscopic VVF repair [10]. Most series describe ureteral and fistula catheterization with cystoscopic assistance at the start of the case. Access to the peritoneum is performed with a Veress needle and trocar placement with a visual obturator or with an open Hassan technique. Laparoscopic ports are placed in a standard configuration utilizing a midline infraumbilical 10–12 mm port for the laparoscope, an additional 10 mm port on the left side in the midclavicular line midway between the umbilicus and the anterior superior iliac spine, an additional port at the right midclavicular line mirroring the left side, and 5 mm ports as needed. Dissection has been described with either a transvesical or an extravesical approach. Pneumoperitoneum is sustained by inserting a Vaseline soaked gauze pack in the vagina and a clamped catheter in the bladder. Principles regarding VVF repair remain the same with wide mobilization of the area around the fistula tract, closure of the vaginal muscularis and bladder with separate suture lines utilizing absorbable suture, and placement of an interposition flap when available. Again, placement of a drain at the end of the case and prolonged catheter drainage post-op are mainstays of VVF repair.

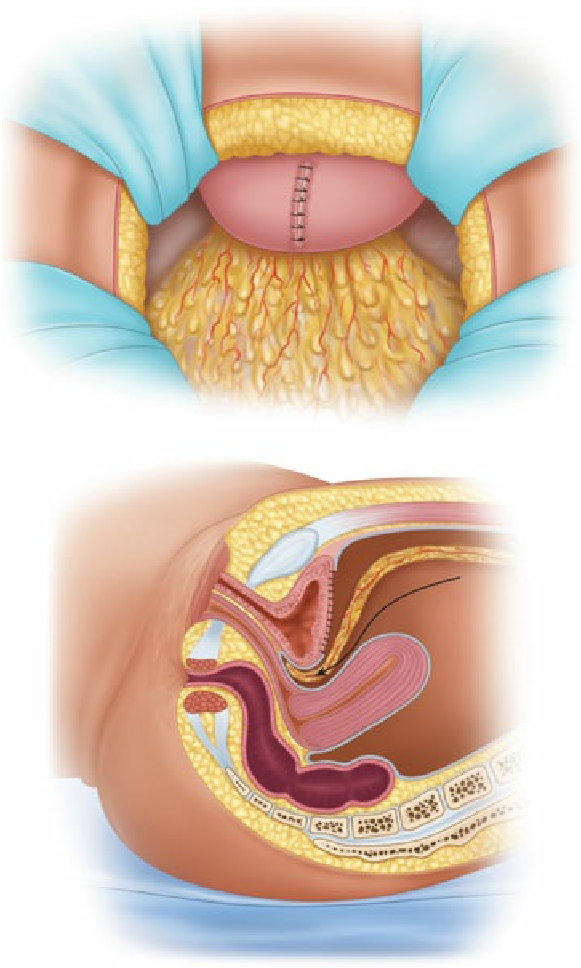

Figure 108.3 Transabdominal vesicovaginal fistula repair. Interposition omental flap placed between the bladder and the vaginal closure, which can also be used in vesicouterine fistula repair. (Courtesy of Cleveland Clinic, Cleveland, OH.)

Robot-Assisted Laparoscopic Repair

The advantage of robot-assisted laparoscopy in the repair of VVF is the ability to perform a minimally invasive procedure without the learning curve associated with conventional laparoscopy. This advantage must be weighed against longer operative times involved with docking the robot in addition to the added expense compared to conventional laparoscopy [11]. Robot-assisted laparoscopy has been described with port placement similar to that of a standard “W” configuration with a 10–12 mm port placed periumbilically, 8 mm robotic arm ports placed at least 9 cm apart to prevent external collisions, and an assistant port on the patient’s right lateral side (Figure 108.4). A parallel or side docking of the robotic arms is helpful to allow for access to the vagina. Instruments typically utilized include monopolar shears, bipolar grasping forceps, and needle drivers. Dissection then proceeds in an extravesical or transvesical manner in the same way described for conventional laparoscopy.

VESICOUTERINE FISTULA REPAIR

Open Repair

Given the high location of VUF, most case series discuss a transabdominal approach although transvaginal repair has been successfully reported [12]. The decision to perform a hysterectomy at the time of VUF repair depends on the patient. If the patient has had multiple children or does not desire any more pregnancies, then concomitant hysterectomy can be performed at the time of VUF repair. If the patient is of childbearing age, uterine sparing would be the more logical approach if technically feasible [13]. For subsequent pregnancies, the patient and their obstetrician should discuss the risks and benefits of delivery by elective cesarean versus vaginal delivery.

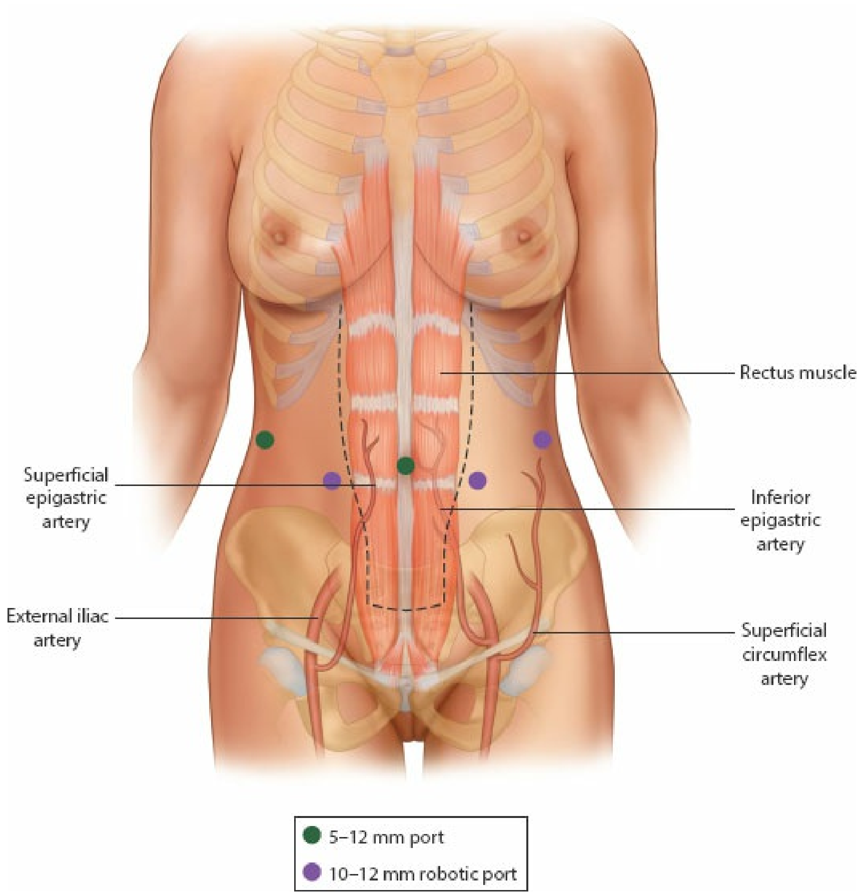
Rectus muscle
Superficial epigastric artery
Inferior epigastric artery
External iliac artery
Superficial circumflex artery
● 5–12 mm port
● 10–12 mm robotic port

Figure 108.4 Minimally invasive vesicovaginal fistula/vesicouterine fistula repair. Port placement for robot-assisted laparoscopic fistula repair. (Courtesy of Cleveland Clinic, Cleveland, OH.)

The transabdominal approach for VUF repair begins much as that for a VVF. Placement of ureteral stents is based on the preference of the surgeon and the location of the fistula. The patient is placed in a low lithotomy position and either the previous Pfannenstiel incision or an infraumbilical midline incision is made. While an extraperitoneal transvesical approach can be utilized, a transabdominal intraperitoneal approach is straightforward and may often be necessary. The bladder is opened to the site of the fistula at which time the bladder is separated from the uterus. The uterus is then closed that usually just requires a few sutures on the outer surface, and the bladder is closed in a multilayer fashion. Typically, an omental or peritoneal flap is placed between the uterus and the bladder, utilizing a long-acting absorbable suture to parachute the flap past the repair to prevent overlapping suture lines.

If a hysterectomy is to be performed instead of a uterine-sparing procedure, the usual method of transabdominal hysterectomy is performed. We typically perform cystoscopy with evaluation for bilateral ureteral efflux after the hysterectomy prior to closure of the fistula. After the closure of the bladder and vaginal cuff, an interposition flap can be placed to decrease the chance of a VVF. Finally, the postoperative course and recovery are similar to that of a VVF repair.

Minimally Invasive Transabdominal Approaches

Both conventional laparoscopy and robot-assisted laparoscopic techniques have been described for VUF repair. Both are limited to case series in the literature with both transvesical and extravesical techniques being described. For conventional laparoscopy, a traditional five-port approach is used. A laparoendoscopic single-site (LESS) approach has also been described but is hampered by the difficulty of suturing and may necessitate the placement of additional 5 mm ports [14].

After pneumoperitoneum is achieved with a Veress or Hassan technique and all ports are placed, dissection is carried down to the vesicouterine plane. The bladder can be entered above the fistula tract and a limited cystotomy is performed down to the previously cannulated fistula tract. Cautery is used minimally in this area to avoid tissue necrosis/devascularization. If an extravesical approach is utilized, the dissection is continued between the uterus and the bladder until the cannulated fistula tract is reached. This dissection can be more arduous if the plane is densely adherent/fibrotic. The tract can be excised or incorporated into the repair and the uterus and bladder are repaired using absorbable suture. An interposition flap can then be mobilized and placed between the repaired areas.

Given the technical skill needed for intracorporeal knot tying with conventional laparoscopy and the reliance on a familiar assistant, robot-assisted laparoscopic surgery has become more popular. Multiple case series have also described VUF repair via a robot-assisted laparoscopic approach. Docking of the robot proceeds as mentioned previously for VVF repair. The fistula tract is cannulated prior to cystoscopy and if there is any concern regarding proximity to the ureters, they are stented. Dissection can then be performed transvesically or extravesically and continues much like that during conventional laparoscopy. Specific to VUF repair, if a hysterectomy is anticipated, then the assistant port can be utilized for either application of a hemostatic clip applier or vessel-sealing device. After completion of the hysterectomy, the uterus can be delivered through the vaginal cuff or if small enough through the camera port with the help of a laparoscopic specimen bag.

OUTCOMES

Vesicovaginal Fistula

Regardless of the approach for VVF repair, the highest possibility of success lies with the technique the surgeon is more familiar with. Series with transabdominal VVF repair report success rates of 80%–90%. The postoperative continence rate is known to be discordant with closure rate due to the complex nature of incontinence after both obstetric and postsurgical fistula repair including de novo urgency or stress incontinence [15,16]. In a retrospective series on postobstetric fistulas, success of repair has been linked to other characteristics such as primary versus secondary attempt at closure, amount of fibrosis, fistula size, location, and patient parity [16]. While there is a theoretical risk of increased bladder dysfunction with a transvesical repair, no prospective study has been performed to actually document postoperative functional changes utilizing urodynamics.

In regards to minimally invasive techniques for GU fistula repair, most series demonstrate a success rate of 86%–100% [17–21]. Morbidity is limited to those inherent to minimally invasive procedures including conversion to open surgery and enterotomy. All minimally invasive studies are limited to small case series with no prospective trials to analyze outcomes compared to transvaginal or transabdominal approaches. In a retrospective case-matched fashion, robot-assisted laparoscopic cases have been compared to open transabdominal cases with outcomes for minimally invasive cases being significantly shorter in regards to length of hospital stay [22]. Lengths of hospital stay and convalescence have been touted as advantages to minimally invasive approaches when compared to any type of open procedure. Adoption with robot-assisted cases though has been hindered by the prohibitive costs associated with console time and equipment when compared with conventional laparoscopy and open techniques.

Vesicouterine Fistula

Given the lower incidence of VUF compared to VVF, most outcomes in regards to VUF repair are limited by rather small numbers and retrospective reviews [12,23]. Due to the increase in cesarean sections, it is believed that the incidence of VUF will rise. Some of the larger series of VUF repairs are reported in conjunction with VVF repair with closure rates approaching that of VVF repair [15]. Success rates in uterine sparing versus concomitant hysterectomy have never been evaluated in a prospective analysis. Thus, hysterectomy during VUF repair is not mandatory. A frank discussion should be with the patient and surgeon regarding a uterine sparing versus non-uterine-sparing repair. If the patient desires future pregnancy, a uterine-sparing procedure should be attempted. Conversely, if the patient is past reproductive age, then a meaningful discussion regarding VUF repair with hysterectomy should occur.

The success rate with minimally invasive surgery has been described as 100%. This is complicated by the rarity of the condition and that all minimally invasive series, whether it be conventional laparoscopy, robot assisted, or LESS, are all case series formats with typically less than five patients [14,24–26]. All series describe successful repair of the fistula without recurrence but suffer from lack of long-term follow-up. Theoretical risks from minimally invasive surgery are those inherent to the procedure including need for conversion to open, enterotomy, and recurrence. Also, the technical demands of conventional laparoscopy/LESS or the prohibitive costs of robotic surgery are potential drawbacks to minimally invasive approaches. No retrospective or prospective studies have been done specifically comparing minimally invasive techniques to open transabdominal surgeries for VUF.

Flap Coverage

One advantage of transabdominal VVF and VUF repair is the availability of multiple flaps. While multiple flaps have been described (bladder, omental, peritoneal, urachal, rectus, perisigmoid fat, epiploica, and porcine small intestine submucosa), the routine use of flap coverage in a nonradiated primary repair has been debated [6,27–30]. Proponents argue that the placement of a healthy flap of tissue helps to oppose suture lines, interpose a vascular tissue flap that enables healing, and also gives an extra layer of coverage. It can be argued though that in a primary repair in the nonradiated patient, an adequate dissection and a tension-free closure without overlapping suture lines should be adequate enough for a successful repair. No prospective study has been undertaken to evaluate routine flap coverage versus not in transabdominal VVF or VUF repair.

Evans et al., in a retrospective study, evaluated their success rate using interposition flaps in transabdominal VVF repair. They demonstrated 100% successful closure rates in the 10 benign VVF cases that used interposition flaps versus a 63% successful closure rate in the other 19 benign VVF repairs. In the malignant VVF group, the successful rate of closure was 67% in patients who did not have an interposition flap. The study though was limited due to the inherent bias of a retrospective study design [30].

Timing

Conventional teaching regarding timing of VVF/VUF repair is to wait at least 3 months. This allows for tissue quality to improve and the fistula tract to mature. Within this 3-month period, the possibility of spontaneous fistula closure with conservative management exists even if the success rate hovers around 12% at best in a multicenter retrospective study of vesicovaginal fistula management [31]. During conservative management with catheter drainage, other minimally invasive approaches are at a surgeon’s disposal. Endoscopic fulguration of the tract or injection of hemostatic agents has been described with limited success [32]. For vesicouterine fistula, hormonal induction of amenorrhea with subsequent spontaneous closure has also been described in the early period. Rates for closure with hormonal induction vary widely though with the literature dominated by case series due to the relative rarity of VUF [23,33–35]. Thought should also be given to the etiology of the fistula. If the VVF/VUF is due to radiotherapy, it is unlikely to heal with conservative management due to the underlying poor tissue quality. The opponents of waiting suggest that the limited gain in success is countered by the detriment to patient’s quality of life, while the fistula tract is open. The data for timing of fistula closure are limited to small case series reported in the literature with no large-scale randomized studies having been performed [36–38]. That being said, patients with a GU fistula should be followed with serial exams and proceed to surgical correction when the tissue is robust.

CONCLUSION

VVF and VUF are detrimental to a patient’s quality of life. Transabdominal repair can be performed through a traditional open approach or minimally invasive conventional or robot-assisted laparoscopy. At select centers, single-site surgery has also been performed successfully. The transabdominal approach is most commonly performed in cases with a high supratrigonal fistula, complex fistula repair, vagina not conducive to transvaginal repair, surgeon’s preference, or concomitant procedures such as hysterectomy or ureteroneocystostomy. Success rates depend on a variety of factors including number of previous repairs, history of radiation, size of the fistula, and degree of scarring. Flap coverage and timing of repair are often debated with many suggesting the use of an interposition flap if readily available and waiting a minimum of 3 months prior to closure. Regardless of approach utilized for repair, the greatest opportunity for success lies in the approach the surgeon is most comfortable with.

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109 Management of Obstetric Urogenital Fistula

Andrew Browning

INTRODUCTION

The last decade and a half has seen great efforts to reduce maternal mortality and morbidity rates across the world. Despite this, many women in the developing world still do not have access to medical attention for the delivery of their child. Maternal mortality is still unacceptably high in these areas, and paralleling this are high rates of maternal morbidity. One of the most feared consequences of a morbid delivery is the obstetric fistula—reducing a woman to a life of shame, isolation, and misery and a life that sometimes ends in suicide or at least the victim wishing she had died during that frightful labor.

ETIOLOGY AND EPIDEMIOLOGY

The etiology of obstetric fistula is ischemic necrosis from a long unrelieved obstructed labor. The impacted presenting part compresses the pelvic tissues against the mothers' bony pelvis. This connection was made 1000 years ago. The early medical text *Al Kanoun* by Avicenna, who died in 1037, gave the warning of labor causing a hole in the bladder—a condition "incurable and remains so until death" [1]. This accounts for the vast number of obstetric vesicovaginal fistula seen throughout the world.

There are also an increasing number of fistulae occurring after cesarean section, up to 24.5% in one series [2]. These may or may not be iatrogenic. Often, the cesarean operations are performed in difficult circumstances with difficult pathology, with little or no lighting, poor equipment, and the surgeon having little or poor training and experience. But the fistula may have been present by the time the patient reached the health facility having labored too long at home before the patient's family decided to get help.

Fistula can also occur after forceps delivery or manipulations and cuttings from poorly trained health attendants. They have been recorded after almost every pelvic surgery. Less common causes include advanced pelvic cancer; sexual trauma, particularly in young undeveloped girls; infections, such as tuberculosis of the bladder; schistosoma; and lymphogranuloma venereum.

There have been numerous epidemiological studies of obstetric fistula patients from various parts of the globe. Typically, the patient is primiparous 43%–62.7% [3,4] but a significant number are multiparous (up to 20%–25% having had four or more deliveries) [3,5], the obstructed labor presumably due to delivering larger children or secondary to malpresentations. Interestingly, a number of studies have shown these women to be short, often less than 150 cm in Nigeria [5], India [6], Ethiopia [7], and Niger [8]. Ampofo showed them to be 7 cm shorter than the general female population [9]. The women are largely uneducated, more than 92% having had no formal education [4,10,11]. A recent study showed that women suffering fistula in Tanzania and Sierra Leone have a much narrower intertuberous space as compared to those women delivering normally and also reconfirmed a short stature among fistula sufferers, but the latter was a weak predictor of fistula formation [12].

Fistula patients are often young. Although it is difficult to get a true estimate of their age, as it is often unknown, it is evident from their appearance that many are in their teens. If their age is asked and the answer relied upon, a 42% are aged less than 20, with 65% being less than 25 years old [4]. Other studies confirm this trend [10,11,13,14]. The majority have had home deliveries with no skilled attendant present and typically more than 50% have been divorced by their husbands due to their offenses [4]. It has been noted in Nigeria that if the woman is childless, she is more likely to be divorced, whereas those women who have live children are more likely to be attending those children and the husband has remained with her [11]. What is unclear is the association of obstetric fistula and female genital mutilation (FGM) or cutting. The opinion of many fistula surgeons is that the obstructed labor occurs against the mothers' bony pelvis and not against the scarred tissues resulting from a circumcision at the outlet. This was confirmed in a study comparing fistula patients with and without circumcision in northern Ethiopia. There was no difference between the presentation, type of injury, and outcomes when comparing 255 obstetric fistula patients with type 1 and 2 circumcision and 237 obstetric fistula patients without circumcision. It was concluded that FGM was not a variable in fistula formation [15]. From further experience in Ethiopia, fistula can indirectly result from type III circumcision or infundibulation. During labor, a traditional health attendant may cut the circumcision open, cutting anteriorly, damaging the urethra, bladder neck, and bladder base.

The other factor that leads to some controversy is early or child marriage. It seems reasonable to assume that because adult height and sexual maturity are reached before the completion of pelvic growth, early marriage and, hence, pregnancy may lead to an increase in obstructed labor and, hence, obstetric fistula [16]. On the other hand, a younger patient may have more flexible ligaments when young, and indeed, in a recent unpublished series of 1000 consecutive fistula patients from Ethiopia in an area with a high prevalence of early marriage, 55% of fistula sufferers received their injury in their second or higher delivery, that is, when they were older. Just less than half received their injury in their first delivery. The ratio of primiparous to multiparous is similar in areas not so renowned for early marriage. The correlation of early marriage and fistula formation has been theorized and probably does contribute slightly to fistula formation, but it certainly would not be a major contributing factor, but this has not been concretely confirmed by studies in the field. Unfortunately, early marriage can result in traumatic fistula, if the husband needs to enlarge the vagina of a young girl to enable intercourse to take place. This is sometimes done, again by a traditional healer cutting open the vaginal tissues anteriorly and sometimes damaging the urethra and/or bladder in the process. This is similar to a “gishiri” cut performed in some areas as a traditional treatment in some areas for a variety of gynecological ills [10].

PREVALENCE

There are no accurate figures for the true prevalence of obstetric fistula. There have been few population-based studies to determine the scope of the problem [17]. A large hospital-based study of over 22,000 patients gave the incidence of obstetric fistula as 0.35% of deliveries [18]. Knowing the majority of women in the developing world deliver in their villages and not in a hospital, the true incidence was thought to be higher. That having been said, the World Health Organization (WHO) often quotes the incidence as 0.3%. Using this figure, there are probably between 50,000 to 100,000 new cases of obstetric fistula occurring across the world each year and about 2 million women suffering from this condition throughout the world [19]. Others have taken further calculations equating the obstetric fistula rate with maternal mortality. Danso, knowing that for every maternal death, there are at least 30 women suffering from morbidity, considered one of which may be an obstetric fistula. This would make about 500,000 new cases of obstetric fistula worldwide each year [3]. Recent studies hint that this might be overestimated, and a meta-analysis done in 2013 suggests that the prevalence is 0.29 per 1000 women of reproductive age and incidence is 0.09 per 1000 recently pregnant women and suggested that there may be 1 million women living with this condition in low- and middle-income countries across the world [20].

SYMPTOMS AND SIGNS

The majority of deliveries are stillborn. The woman is weak and shocked postdelivery and on average, it takes 26.1 days before she is strong enough to be able to walk unaided [4].

The immediate course of the injury is that 3–10 days postdelivery, a necrotic slough is extruded through the vagina, and the vesicovaginal fistula is exposed rendering her completely incontinent of urine, leaking every minute of the day and night (Figure 109.1). Rarely, if the fistula is very small, she can describe symptoms more like stress urinary incontinence, but leaking from the vagina rather than the urethra. If she has sustained similar injuries to the posterior compartment, she is also rendered incontinent of feces and flatus per vagina.

It is easy to think of the obstetric fistula as merely just a hole in the vagina to the bladder and perhaps the rectum. However, unlike iatrogenic surgical fistula that is usually just a discreet injury, the pathology of the obstetric fistula is broader, and the term “field injury” has been coined to refer to the range of injuries. Another term that is used is the “obstructed labor injury complex” [21]. The ischemic process affects not only the tissues of the genitourinary tracts and bowel but also all the other tissues in the mothers' pelvis, that is, nerves, muscles, and bones. This results in primary conditions, those associated with the etiology of obstetric fistula and the ischemic process within the mothers' pelvis over a broad area, and also secondary conditions—conditions delayed, arising later as a result of the incontinence or scarring within the pelvis.

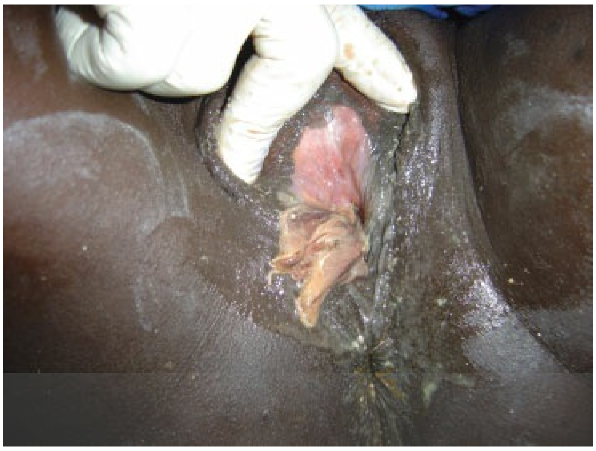

Figure 109.1 Necrotic tissue extruding from the vagina.

Primary Conditions

Vesicovaginal Fistula

The level of impaction during labor determines the site of injury. If the impaction occurs at the pelvic inlet, the vesicovaginal fistula may be juxta- or even intracervical [22] (Figures 109.2 and 109.3). If impaction occurs lower, the urethra may be involved. The urethra is injured in 28% of cases with 5% of patients in Ethiopia having the urethra completely destroyed [21]. This has prognostic indications as the mechanisms for continence in the female have been destroyed [17,23,24].

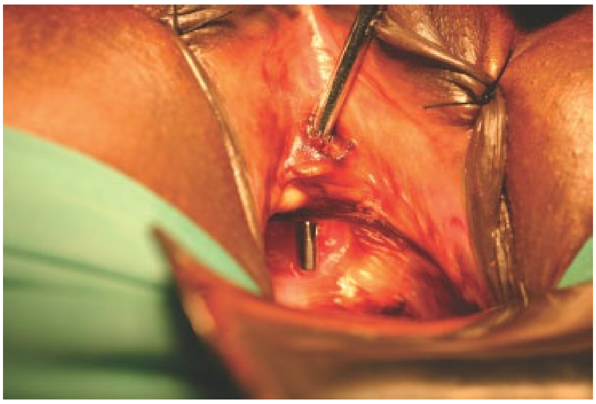

Figure 109.2 Fistula located lower, or more distally in the vagina, involving the urethra.

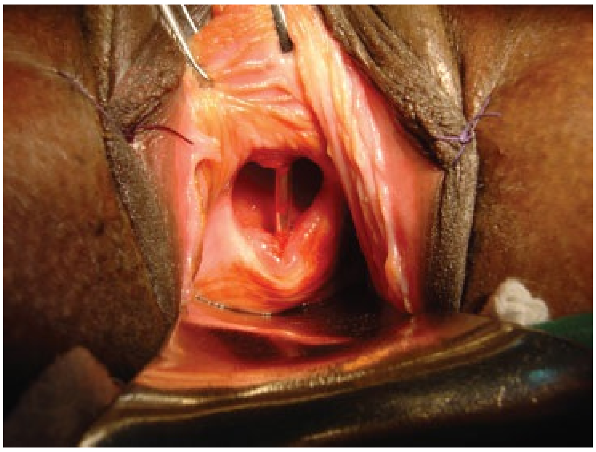

Figure 109.3 Midvaginal fistula, more proximal in the vagina, involving the trigone.

Ureteric Injury

In a small number of obstetric fistula cases, the lower part of the ureter can be involved. The whole ureterovesical junction is necrosed and sloughed away, leaving the vesicovaginal fistula with the ureter draining outside of the bladder straight into the vagina. It is becoming more common to see isolated ureterovaginal fistulae after cesarean section or cesarean hysterectomy, more commonly on the left, and these are iatrogenic, occurring at the time of operative delivery [2,25].

Rectovaginal Injuries

A rectovaginal fistula occurs if the presenting part is impacted against the sacrum during labor, causing ischemic necrosis of the rectovaginal septum. It has various reported prevalence and seems to vary geographically, ranging between 6% (B. Hancock, personal communication, Uganda) and 22% in Ethiopia [4]. If present, it usually occurs in conjunction with a vesicovaginal fistula, rarely presenting in isolation [4]. The status of the anal sphincter should always be noted as there may be residual flatal or fecal incontinence even after repair [26]. Neglected fourth-degree tears are also common (Figure 109.4).

Reproductive Tract

The tissues of the vagina are obviously injured, but in some cases, the whole vagina has necrosed, leaving little or no identifiable remaining vaginal epithelium (Figure 109.5). Overall, about 28% of patients will need some form of vaginoplasty [21]. The cervix is often torn or partly necrosed and fistula surgeons testify that it is rarely that one will see an uninjured cervix. Vesicouterine fistulae, although more uncommon, do occur and the uterus affected.

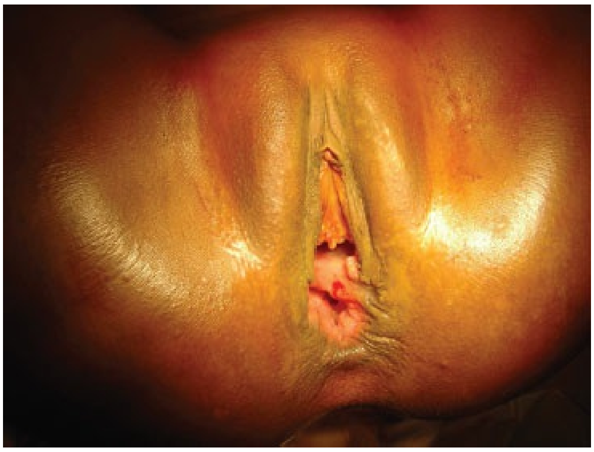

Figure 109.4 Concurrent fourth-degree tear. A reasonably common finding.

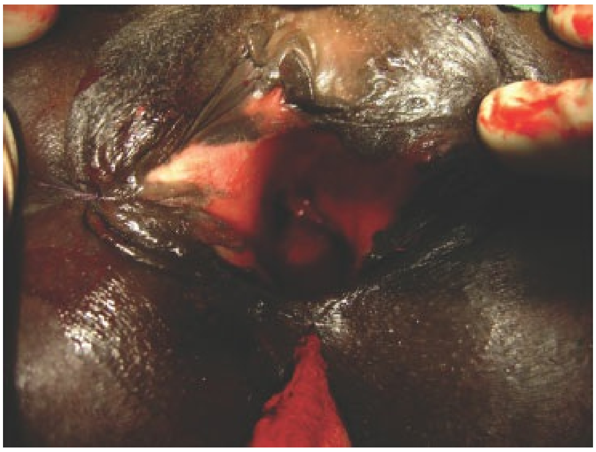

Figure 109.5 Severe injury with no urethra, no bladder, and no vagina remaining.

Muscles

The muscles of the pelvic basin are often affected by a neuropathy, directly weakened by the ischemic process or even completely destroyed. A recent ultrasound study of the levator muscle complex in obstetric fistula patients showed little muscle loss and little denervation [27], but certainly in extensive injuries, an “empty pelvis” is all that remains.

Bones

A series by Cockshott performed x-rays on 312 women with obstetric fistula and found that 32% had some x-ray abnormality, ranging from bony resorption, bony spurs, obliteration or separation of the symphysis pubis [28].

Nerves

It has been quoted that between 20% and 65% of obstetric fistula, patients will have some form of peroneal neuropathy manifesting as bilateral or unilateral foot drop [21,29]. There are currently three theories as to its etiology: a prolapsed intervertebral disc, direct compression of the fetus on the lumbosacral trunk during labor, or impingement of the common peroneal nerve as it transverses the head of fibula while the patient squats for prolonged periods during labor [30,31]. Waaldjik and Elkins commented that most patients do improve with time with 13% still showing some signs at 2 years [29].

Secondary Conditions

Social Consequences

The consequences of complete incontinence for a woman in the developing world, where the status of women is usually low, are far reaching. Over half are divorced by their husbands who feel that the affected woman is now unable to fulfill her marital duties and unable to bare children [4]. Her incontinence has other consequences as she is now in urine-soaked clothes, unable to clean herself or her attire. She is unable to interact socially; others find her presence unacceptable. She cannot go to church or mosque to worship, to the market, or to the well to draw water. She lives in isolation stripped of her dignity and place in society.

Mental Health

It is becoming more apparent that mental health issues in obstetric fistula patients are a significant disease burden [32–36]. The GHQ-28 shortened form of mental health questionnaire revealed a 93% positive screening for potential psychological disorder, and 100% of those patients interviewed in Ethiopia screened positive [32]. Similarly, in Kenya, 17% of patients had suicidal ideations before receiving treatment, 73% were depressed, and 26% severely depressed [35]. If, however, the patient is cured completely by the operation and has no residual incontinence, the percentage screening positive returns to the background positive rate from the general population [33,36].

Limb Contractures

There are often stories of patients being shut away in huts for months if not years. It is thought with time, disuse can cause limb contractures. This is seen in roughly 1%–2% of patients in Ethiopia. It is occasionally so severe that her legs are locked in the fetal position.

Malnutrition

Malnutrition results from isolation as the patient may be fed and cared for inadequately by a relative in a small room or hut. The average BMI from a small unpublished series from Ethiopia was 19 (A. Browning, unpublished work). Cases of severe malnutrition with hypoproteinemia are not uncommon.

Upper Renal Tract Damage

One study from Nigeria looking at intravenous pyelograms in women with fistula revealed 49% of patients sustained upper renal tract damage. The most common consequence is hydronephrosis (34% of women), but the damage may progress all the way to nonfunctioning kidneys [37]. This is presumably due to scarring partially or totally occluding the lower ureter causing obstructive uropathy and partly due to repeated ascending infections.

Bladder Stones

The constant leakage of urine leads many women to drink less water and, hence, produce less urine. The concentrated urine might collect in pockets of scar, vagina, or bladder and, with time, form calculi, causing pain, infection, and increased odor. Occasionally, the woman herself or perhaps a local healer will insert foreign bodies into the vagina to try and stem the flow. Such foreign bodies have included stones, rags, or plant material, acting as a nidus for calculi formation.

Urine Dermatitis

The leakage of urine, often concentrated, affects the skin. The ammonias and phosphates can encrust on the skin, causing excoriations, secondary infections, and areas of tender hyperkeratosis. Much thought has gone into treating this condition coined the “urine dermatitis,” but the most expedient way to just to ensure that the urine is not in contact with the skin is by applying barrier ointments such as Vaseline or better by closing the fistula, making the patient continent (Figure 109.6).

Reproductive Outcomes

After fistula occurrence, up to 44%–63% may suffer from amenorrhea [21,38,39]. This has a multifactorial causality most of which are not clearly delineated. Surely, some are due to stresses of the delivery and the resulting social isolation. Some patients do have their menses return following repair [38,39]. A low BMI is often be the cause. It is thought that some will have focal anterior pituitary necrosis from shock during the long labor [40]. A small unpublished series by Dosu Ojengbede from Nigeria looking at hysteroscopy showed intrauterine scarring is common, Asherman’s syndrome (L.L. Wall, personal communication). Others will have a cryptomenorrhea from an obstructed outflow tract with time causing a hematometra. If the patient does receive treatment, remarries, or returns to her husband, the subsequent fertility rates are quite desponding. A number of studies have shown that as few as 19% achieve a pregnancy [38,41,42] with perhaps a higher prematurity rate and infant mortality in those that do [43]. Subsequent deliveries are hazardous. One small series following the pregnancies in women delivering post–fistula repair showed an alarming 27% recurrence rate of fistula with a supervised vaginal delivery [41]. It is commonly recommended that any further deliveries should be performed by cesarean section. A series from Barhirdar, Ethiopia, confirmed that 49 deliveries after fistula repair with the delivery of 50 infants (1 woman delivered twins). All but three patients delivered by cesarean section, three infants died, two from premature delivery and one from an obstetric complication. There were no recurrences of the fistula. All of these patients presented to the fistula hospital and used the hospital as a maternal waiting area so a timely cesarean could be implemented. During the time period of the study, 24 women represented after trying to deliver a subsequent child at home, some of them reaching a health facility, but after a prolonged period of labor. All women delivered a stillborn child and all reopened their fistula. There were verbal reports of women dying trying to deliver at home and likely more. Likewise, there could have been some women who did deliver successfully at home, and there are many anecdotal reports of this occurring, but it seems a considerable risk [44].

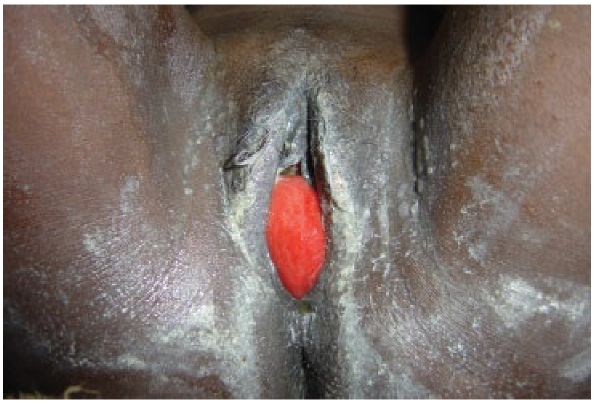

Figure 109.6 Urine dermatitis, note the bladder fundus prolapsing through the fistula and out through the introitus.

INVESTIGATION

The investigations of the fistula are kept simple, merely because most patients with obstetric fistulae present in areas where resources are limited.

The majority of obstetric fistula patients can be confidently diagnosed by history and examination alone—a history of a long labor (more than 1 day) with a stillborn child and complete incontinence of urine is the rule. Most obstetric fistulae can be diagnosed on simple digital vaginal examination—noting the site, size, and amount of scarring.

If the fistula is very small, it may not be palpable and a dye test must be performed. The classical teaching for this is to place three clean swabs into the vagina and insert 50–100 mL of dilute gentian violet via a catheter into the bladder. The swabs are left in the vagina for some minutes and then removed. A fistula is confirmed by the presence of dye on the gauze, and depending on which of the three gauzes are stained reveals the approximate site of the fistula. However, it is common in many centers to directly visualize the fistula by examining the patient with the aid of a Sims speculum, retracting on the posterior vaginal wall to expose the anterior wall, instilling the dye, and seeing where the dye leaks into the vagina. In some very small fistulae and some vesicouterine or vesicocervical fistula, the dye may take some minutes to find its way into the vagina. In these circumstances, it is best to insert a gauze swab into the vagina, instill 50–100 mL of dilute dye into the bladder, remove the catheter, and ask the patient to walk about for 15–30 minutes. It is surprising how many gauzes are stained with dye at the end of this time when the initial examination showed a negative test.

The posterior vaginal wall is examined digitally again noting the site, size, and any scarring associated with a rectovaginal fistula. The state of the anal sphincter is noted as is the distance of the fistula margin to the sphincter. A small number of patients will complain of flatal incontinence with or without incontinence of diarrhea through the vagina hinting that a small fistula is present, unrecognizable to the physicians’ digital examination. A dye test can also be performed by the installation of dilute dye into the rectum via a Foley catheter.

Routine urine tests, renal function tests, and intravenous urography are not warranted as the results do not often influence management, and these tests are expensive and are simply unavailable in most units where fistula surgery is usually performed.

PROGNOSTIC FACTORS AND CLASSIFICATION

There are several factors to the fistula injury that influence the outcome to surgery, both with being able to successfully close the fistula at operation and also the rate of ongoing urethral incontinence despite a closed fistula. These include (1) urethral involvement, which makes the repair more complex as the urethra needs to be reconstructed and continence maintained despite the loss of the continence mechanisms, (2) severe vaginal scarring, making access to the fistula for repair difficult or impossible without relaxing incision and increases the likelihood of ongoing incontinence, (3) the size of the fistula, and (4) finally, the amount of bladder tissue loss, reflected in a small remaining bladder capacity [23,45,46].

There is no universally agreed classification for obstetric fistula. There are two classification systems currently in use, the Waaldjik and the Goh. The Goh system has been validated and seems predictive of outcome [45,47,48]. It looks at the site of the fistula in relation to the external urethral meatus, its size, and the amount of scarring. This is based on three of the four known predictive factors for outcome (above). It is difficult to measure bladder volume before repair so site, size, and scarring are examined. The measurements of site and size are objective, but the measurement of scarring tends to be more subjective (site size scarring, Goh classification Table 109.1). The Waaldjik system concentrates more on the urethra and if it is a circumferential defect or not [49]. There has been one study comparing the prognostic value of both systems and concluded that the Goh system had significantly better predictive value of obstetrics fistula closure [50].

TIMING OF REPAIR

It has been commonly taught that a surgeon should wait for roughly 3 months after the injury before attempting repair [51]. The rationale behind this is to allow the necrotic tissue to slough away and the often suboptimal tissue that remains to recover before attempting to operate. There has been one compelling paper advocating earlier repair, to repair as soon as the dead tissue has come away, with active debridement while waiting. This affords a good success rate and enables the woman to regain health more quickly, before she is made an outcast [52]. However, the tissues are much more difficult to handle at this stage, with the tissues tearing and sutures cutting out. This series was done by an extremely experienced fistula surgeon and the results are yet to be replicated in other units and with more inexperienced surgeons. It would be prudent for the inexperience fistula surgeon to rely on the traditional teaching of waiting for 3 months.

Table 109.1 Classification for Cardozo Text

		Breakdown of repair (n = 987) (%)	**Ongoing incontinence despite repaired fistula (n = 987) (%)**
	Classification of genitourinary fistula with comparative outcomes		
Site			
Type 1	Distal edge of fistula >3.5 cm from the external urinary meatus	2	3
Type 2	Distal edge of fistula 2.5–3.5 cm from the external urinary meatus	1.6	20
Type 3	Distal edge of fistula 1.5 to <2.5 cm from the external urinary meatus	3	32
Type 4	Distal edge of fistula <1.5 cm from the external urinary meatus	3	46
Size			
a	Size <1.5 cm in the largest diameter	2	10
b	Size 1.5–3 cm in the largest diameter	0.5	22
c	Size >3 cm in the largest diameter	4	30
Scarring			
i	None or only mild fibrosis (around fistula and/or vagina) and/or vaginal length >6 cm, normal capacity	2	7
ii	Moderate or severe fibrosis (around fistula and/or vagina) and/or reduced vaginal length and/or normal capacity	2	24
iii	Special consideration, e.g., postradiation, ureteric involvement, circumferential fistula, previous repair	4	41
Overall results		2.7	23.2

	Classification of genitoanorectal fistulas
Site	
Type 1	Distal edge of fistula >3 cm from the hymen
Type 2	Distal edge of fistula 2.5–3 cm from the hymen
Type 3	Distal edge of fistula 1.5 to <2.5 cm from the hymen
Type 4	Distal edge of fistula <1.5 cm from the hymen
Size	
a	Size <1.5 cm in the largest diameter
b	Size 1.5–3 cm in the largest diameter
c	Size >3 cm in the largest diameter
Scarring	
i	None or mild fibrosis around the fistula and/or vagina
ii	Moderate or severe fibrosis
iii	Special consideration, e.g., postradiation, inflammatory disease, malignancy, previous repair

The pathology for iatrogenic fistula is different, being a discreet injury rather than ischemic over a broad area. These can be operated upon as soon as it is practical. If the fistula is iatrogenic in an ischemic operative field, such as a cesarean after 2 days of labor, it could be argued to follow the same guidelines as for obstructed labor fistula.

IMMEDIATE MANAGEMENT

If a patient presents within the first few weeks of injury, while the tissues are still raw, a large gauge catheter should be inserted and kept on free drainage for up to 4 weeks. With this management, up to 20%–40% of smaller vesicovaginal fistulae will heal [52,53].

ROUTE OF REPAIR

The route of repair, vaginal or per abdomen, traditionally depends on the experience and training of the surgeon. Doctors with gynecological training often favor the vaginal route, while doctors with urological training favor the abdominal route. The abdominal route might be found easier with high vault, juxtacervical, or vesicovaginal/vesicouterine fistulae. Even these cases can be confidently managed vaginally with experience, which has obvious benefits postoperatively. A recent publication comparing vaginal to abdominal route of repair showed that the abdominal route seemed to be associated with higher rates of closure. However, of the cohort, only 5% of cases underwent an abdominal repair and were more likely to be higher in the birth canal, which have a better outcome than those lower in the birth canal anyway [23,54]. The choice of route of repair seems to be reflected more on the surgeon’s training and experience.

TREATMENT

Many surgical techniques have been described, including the open transvesical and transperitoneal or combined techniques, fibrin glue, laparoscopic techniques, partial colpocleisis, and cauterization. The most popular “flap-splitting” technique will be described here.

At a meeting of “fistula surgery experts” hosted by the WHO in 2002, it was agreed that the flap-splitting technique should follow the principles of

1. Exposure of the fistula and protection of the ureters
2. Wide mobilization of the bladder off the vagina/cervix/uterus and surrounding tissues
3. Tension-free closure of the bladder
4. Dye test to confirm watertight closure of the bladder

Exposure of the Fistula and Protection of the Ureter

The patient is placed in the exaggerated lithotomy position with the patients’ buttocks over the end of the operating table. The table is placed in steep Trendelenburg, which will bring the anterior vaginal wall perpendicular to the surgeons gaze.

In up to 28% of patients, there is significant vaginal scarring that renders it impossible to insert a speculum [21]. Lateral relaxing incisions are necessary to release the scar, expose the fistula, and then be able to insert the speculum for adequate exposure.

In all trigonal and supratrigonal fistulae, except the very small, the ureters should be identified and catheterized (Figure 109.7). This can be done through the fistula and the catheter ends advanced through the urethra. This is to prevent inadvertent injury during dissection and inadvertent suturing of the ureter during repair.

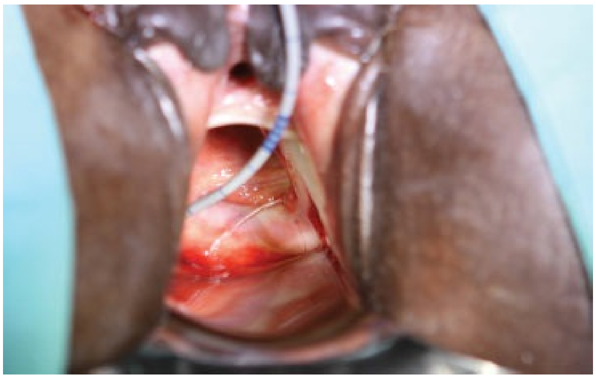

Figure 109.7 Right ureter catheterized, left ureter spurting urine at the edge of the fistula.

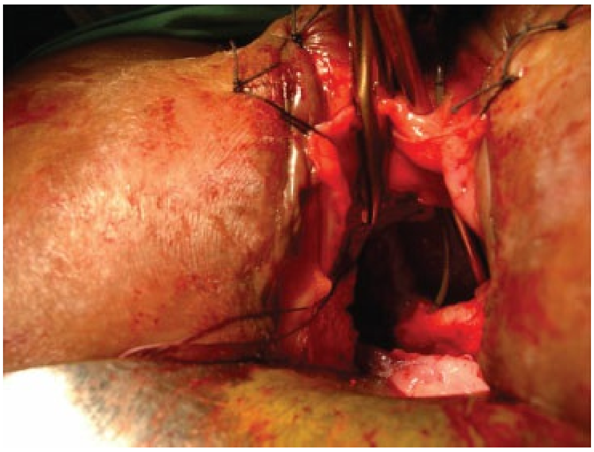

Figure 109.8 Wide mobilization of the bladder. Note mobilization along right lateral pelvis.

Wide Mobilization of the Bladder off the Vagina/Cervix/Uterus and Surrounding Tissues

The hallmark of successful vesicovaginal fistula surgery is wide mobilization of the bladder, releasing it from scarred attachments to the surrounding structures and excision of the scar tissue from the bladder and surrounds, so good viable tissue is approximated in the repair. Almost all mobilization IS obtained proximally, laterally and at times anteriorly into the cave of Retzius. The distal margin of the fistula usually involves the urethra WHICH is more fixed, so mobilization of the vaginal tissues off the urethra is merely enough to be able to place a suture in the urethra/bladder. (Figure 109.8).

Tension-Free Closure of the Bladder

Once the bladder has been successfully mobilized, the bladder is sutured together under no tension. If tension remains on the suture line, it runs the risk of disrupting. The initial sutures secure the angles of the fistula. The bladder is closed with interrupted sutures (2-0 polyglycolic acid) approximately 4 mm apart. Usually, this is done in a single layer to the bladder muscle.

Dye Test to Ensure a Watertight Closure

To ensure that a watertight closure has been achieved, 50–100 mL of dilute colored fluid (dilute gentian violet is often used) is instilled into the bladder (Figure 109.9).

To Graft

A contentious issue in fistula surgery is whether to use an interpositional graft. It has been traditionally taught this aids healing by bringing a fresh blood supply to the compromised tissues surrounding the fistula. It may also plug any undetected microleaks along the repair. The most common graft used is the Martius fibrofatty graft harvested from the labia majora. Other grafts have been described, being of the gracilis muscle, peritoneum, omentum, and broad ligament. One small study did show an increased success rate with using the Martius graft [55]. However, based on a large study done in Ethiopia [56], many fistula surgeons no longer use grafts routinely and note similar success rates to graft interposition. There are instances when a graft may be advantageous, such as for a patient who has had multiple unsuccessful operations or when the tissues are very thin and fragile, say with the complete reconstruction of a neourethra.

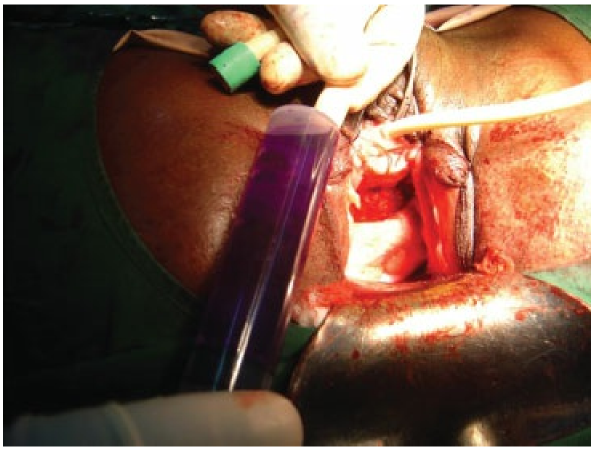

Figure 109.9 Tension-free bladder closure and testing the integrity of the closure with a dye test.

To form a Martius graft, an incision is made longitudinally along the bulge of the labia majora. The fat underneath is exposed and a flap of fat developed from anterior to posterior with the pedicle still being attached posteriorly. A tunnel is created into the vagina superficial to the inferior pubic ramus, beneath the bulbocavernosus and vaginal skin. The fat is introduced into the vagina and placed over the fistula repair with anchoring sutures (Figure 109.10).

The vaginal and labial skins are repaired, taking precaution to prevent hematoma formation.

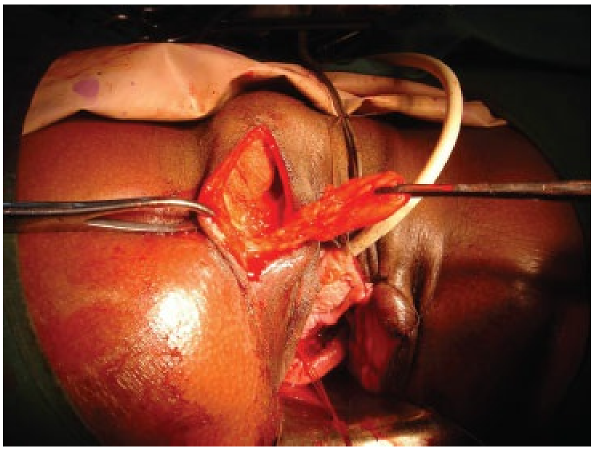

Figure 109.10 Martius graft/flap, harvested from the right labia majora, before tunnel formation and introduction into the vagina.

PARTICULAR SURGICAL PROBLEMS

Absent Urethra

Up to 5% of obstetric fistulae have the entire urethra sloughed, which poses one of the most difficult problems for the fistula surgeon [21,57]. An anatomical closure may be quite possible, but a functioning closure is very difficult. There are two ways commonly used. First, a new urethra may be created from the remaining paraurethral tissues. Initial incisions are made about 2.5–3 cm apart either side of where the new urethra will lie (Figures 109.11 and 109.12). Flaps are then created and sewn over a Foley catheter and this delicate structure is anastomosed to the bladder. A graft is sometimes placed to help support and nourish this frail construction, a gracilis graft has been described [58], but if a graft is used, the Martius graft is the common choice (as mentioned earlier). The vaginal epithelium is drawn over the repair.

Second, a new urethra may be created from an anterior flap of the bladder tissue. A longitudinal flap is created after dissecting the bladder off the symphysis pubis and then advancing this toward the urethral meatus. The flap sewn into a tube over a Foley catheter, a graft placed, and the vagina repaired [59]. This is often not possible with obstetric fistulae as these types of fistulae often result in much loss of the bladder tissue; this procedure will thus decrease the size of an already small bladder.

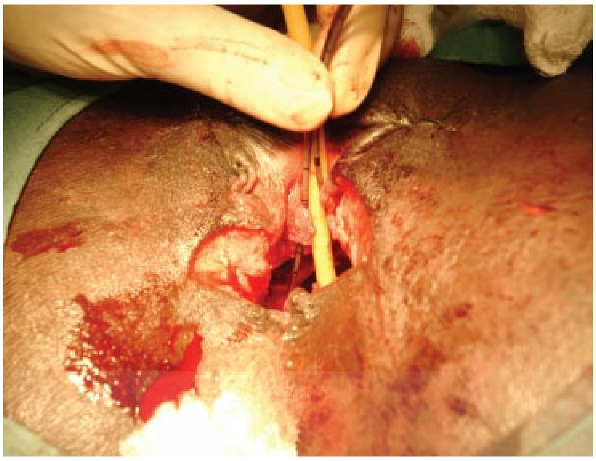

Figure 109.11 A patient with absent urethra. Mobilization of the remaining tissues to roll over a Foley catheter.

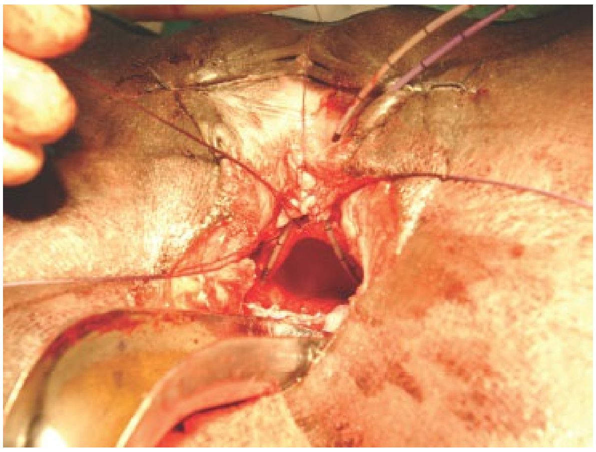

Figure 109.12 Neourethra in the same patient as Figure 109.11. She was able to be continent using a urethral plug.

When a new urethra is made from remaining paraurethral tissues, urethral strictures may form in the long term resulting in urinary retention and voiding disorders. There is also a high rate of residual incontinence after repair. This is presumably stress urinary incontinence. To help reduce this, a sling of levator muscle can be used to support the repair, taking a flap of levator from the right and left (or scar tissue, if there is no other tissue remaining), and sewn in the midline [60].

Circumferential Fistulae

A circumferential fistula occurs against the posterior pubic symphysis. In these cases, the bladder is completely detached from the remaining urethra (Figures 109.13 and 109.14) The bladder needs to be mobilized not only off the vagina and surrounding structures, but also off the pubic symphysis, dissecting high into the cave of Retzius. The bladder is then advanced on mass to the urethra and anastomosed to it.

Again, there is a high rate of residual urinary incontinence, presumably stress urinary incontinence. This may be improved by the use of a levator muscle sling employed at the time of repair [60,61] (Figure 109.15).

Rectovaginal Fistula

The techniques for repair are similar to that of the vesicovaginal fistula: flap splitting with wide mobilization, excision of scar tissue, repair of the fistula under no tension, and repair of vaginal epithelia. Grafts are rarely used for rectovaginal fistula, but the Martius graft may be employed if a long enough pedicle is developed for it to reach the operative site. Rectovaginal fistulae can be comfortably repaired per vaginum, but some surgeons may prefer to use the abdominal route for the high fistula adhered to the sacral promontory. Diverting colostomies were used liberally, but in more recent times, fistula surgeons have largely stopped using these with no appreciable difference in outcomes and saving the patient two extra procedures—opening and closing the colostomy. A diverting colostomy would still be advised for very large (>5 cm in diameter), high, and circumferential bowel fistulae, where a breakdown of repair could leak into the peritoneal cavity. Low, large rectovaginal fistulae can still be safely repaired without a colostomy. If there is a diverting colostomy, there is no need for the bowel to be prepared adequately before the operation.

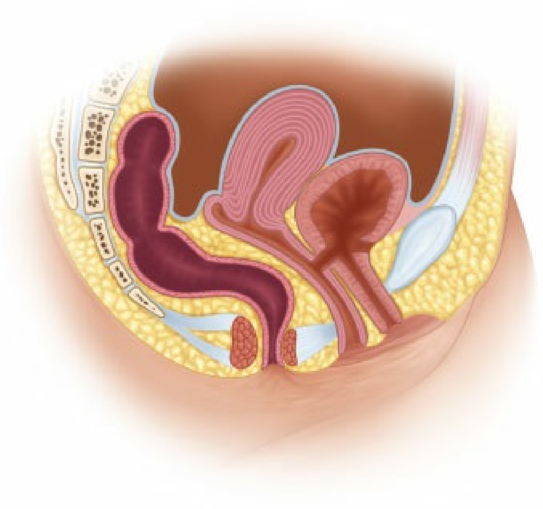

Figure 109.13 Circumferential fistula. There is complete detachment of the bladder from the urethra.

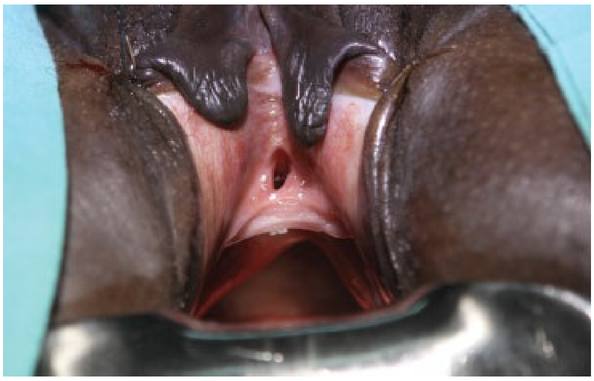

Figure 109.14 Circumferential fistula. Note small remaining “tag” of the urethra, then the anterior lip of the bladder, and some 4–5 cm proximally attached to the pubic bone.

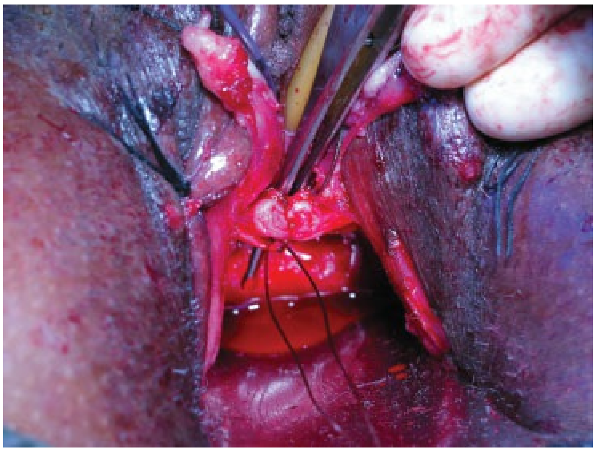

Figure 109.15 Supportive sling for urethral injuries. Made from the levator complex or if there is no levator remaining, from scar remnants.

No Vaginal Tissue Remaining

About 28% of cases will need some form of vaginoplasty due to vaginal skin loss and after repair, dyspareunia and apareunia can result [39,41]. Vaginoplasty may be anything from a simple Fenton-type procedure to release vaginal scarring to reconstruction of a new vagina from tissue flaps, anteriorly from the labia minora and majora and posteriorly with rotational flaps of the gluteal skin. This does result in a scarred vagina. Other options are a neurovascular flap of the tissue from the groin crease or a sigmoid neovagina [62]. Some have used a modified Martius graft with the overlying skin being swung in with the flap. However, this skin is hair bearing and can cause considerable discomfort.

POSTOPERATIVE CARE

The ureteric catheters can be removed upon completion of the operation if the ureteric orifices were far from the fistula margin. If they were close to <1.5 cm, or on the margin, they remain for 5–7 days to ensure that the ureters do not obstruct with postsurgical swelling. Occasionally, the ureters will need reimplanting; if so, the catheters remain in place for 10–14 days.

The Foley catheter remains on free drainage for 10–14 days postoperatively. For most injuries, the Foley catheter can be safely removed after 10 days. A small randomized controlled trial showed this to be as effective when compared to 14 days [63,64]. If a breakdown occurs due to poor surgical technique, it usually occurs soon after the operation, in the first few days. If it occurs from poor healing or infection, it usually breaks down on day 7–9. Hence, it seems wise to leave the Foley catheter in place at least until this later danger time has passed. This takes meticulous nursing as a full bladder will put pressure on the repair site and may even disrupt it. The patient should be educated that if their catheter is not draining or they experience bladder pain (indicating a full bladder), they should notify the nurse immediately and have the catheter either irrigated carefully or changed. There has been some cases that break later after the repair, after the patient has returned home, which can occur weeks to months after discharge [39,65].

A vaginal pack is usually placed at the end of the operation. This reduces the operative dead space and is removed the following day.

The patient should mobilize as soon as she is able; however, it is important that the indwelling catheter is secured with either a strong tape or a suture so that the balloon of the catheter does not pull on the fistula repair site while the patient is mobile.

A high fluid intake is encouraged to keep the bladder irrigated.

A normal diet is encouraged. The stools should be kept loose in cases of rectovaginal fistula with a rapid return to a normal diet and use of laxatives.

Spinal headaches are quite common as fine-pencil-point spinal needles are not available. This can be treated with nursing supine, simple analgesia, and caffeine.

RESULTS

The fistula can be closed in up to 94%–97% of cases with their first operation [4,39]. If a fistula is not closed successfully, repeat operations prove difficult. With the second operation, the success rate drops to 79% and with the third, 53% (A. Browning, unpublished work). Successful closure, however, does not necessarily equate to a functional cure. Rates of postoperative incontinence, largely stress urinary incontinence, vary between 5.6% and 33% [4,60].

The postoperative incontinence rate appears to be decreased by using a supportive sling of levator muscle or scar tissue if there is no muscle remaining. This is done at the time of primary repair for all significant urethral injuries [60] (Figure 109.15).

This ongoing incontinence rate of 5.6%–33% is observed at short-term follow-up, within the first few days of catheter removal. With time and bladder retraining and strengthening of pelvic floor muscles, this may improve with time. In northern Nigeria, patients have been followed up over a period of 6 months and 15% of closed fistula patients still have some incontinence at time of final follow-up (K. Waaldjik, personal communication). At the Addis Ababa Fistula Hospital, patients are asked to return in 6 months if they are still experiencing leakage; however, only 8% of patients do [4], probably because the journey is long, difficult, and expensive. In a more rural fistula hospital in Ethiopia, 70% returned for follow-up, and 50% of those patients discharged with mild urethral incontinence (leakage of walking and/or coughing or straining) were cured of their symptoms with 6 months of conservative therapy. Only 18% of patients suffering with more severe urethral incontinence, leaking with walking, sitting, and/or lying, were improved after 6 months of conservative therapy [39]. The latter group were therefore encouraged to use the urethral plug to keep them dry, and all were encouraged to return to hospital for follow-up and a secondary incontinence procedure if it was still needed [39,66].

The rectovaginal fistula seems to have a lower initial success rate at 73% [21]. A more recent but unpublished series of nearly 1000 fistula patients with 111 rectal fistulae put the success rate higher at 98%. However, with subsequent operations, it is almost always possible to get a successful closure although the patient may have some remaining anal flatal and/or stool incontinence from a poorly functioning anal sphincter [26].

POSTOPERATIVE COMPLICATIONS

Ongoing Incontinence

The most concerning complication of fistula surgery is residual incontinence. This is thought mainly to be stress urinary incontinence in type, but detrusor overactivity must also play a role. One study of 22 women with severe incontinence following fistula closure underwent urodynamic assessment and 41% had urodynamic stress incontinence (USUI), 14% had USUI and poor compliance, 41% had USUI and detrusor overactivity, and 4% had voiding disorder and overflow incontinence [67].

There have been several operations described for women suffering urethral incontinence after fistula repair. The pathology is quite different to stress urinary incontinence seen in the west as the pathology usually includes tissue destruction of the urethra, so repairing the fistula can restore the anatomy, but not the function. Operations concentrate on supporting and at times, obstructing the urethra.

The use of synthetic material has been discouraged due to expense, the ethical consideration of placing material that may cause complications later in areas where women cannot easily receive medical help, and when artificial urethral slings have been used in these patients, the results have been discouraging. One trial in Niger compared fascial slings and synthetic slings, outcomes were similar, but there was a significant problem with erosions in the synthetic arm, and for both arms, the success was lower than other series (see the following texts) [68].

A sling operation was described by Carey and Goh in which urodynamically selected patients have a tension-free sling of rectus sheath inserted beneath the midurethra. This is done with open dissection into the space of Retzius and the sling inserted under direct vision. The open step is necessary due to the often dense retropubic scarring and high risk of bladder perforation if done as closed procedure with use of a trocar to pass the sling retropubically. A flap of omentum is inserted between the freed urethra and symphysis pubis to try and prevent further scarring. This procedure has a 66% cure rate at 14 months but in carefully selected and screened patients [66].

Simpler methods include merely vaginal mobilization of the urethra and bladder neck off from the pubic ramus and plication of the lower bladder, bladder neck, and urethra in an attempt to elongate the urethra. Most patients who do return with ongoing incontinence problems have a short urethra of only 1.4 cm. This can elongate the urethra to 3.1 cm. A sling of levator muscle or scar tissue is used if there is no muscle complex remaining. This gives a 70% complete cure rate with no ongoing incontinence and 15% improved in their continence and 15% have no change [69]. This improvement is maintained in a 6-month follow-up but longer-term follow-up is not available. Those not improved or improved slightly but not satisfactorily can use the urethral plug as the urethra is now longer and narrower.

Urinary Retention

After removal of the catheter on day 10 or 14 after fistula repair, up to 8% of patients will have urinary retention with overflow. All patients should have a residual urine volume checked after their catheter is removed. It is usually treated with recatheterization with “bladder training,” that is, clamping the catheter and releasing every 2 hours. After 48 hours, 70% of patients are voiding normally and the remaining will need a time of self-catheterization.

Frequency and Voiding Disorders

It has been noticed that on removing the catheter patients often complain of frequency of micturition and some voiding problems. It was often thought that this may resolve with time and could have been secondary from a prolonged catheterization; however, recent evidence from Ethiopia shows this problem is ongoing in at least some women. Of the 35 women studied with persistent incontinence despite fistula closure, 77% had more than eight episodes of voiding in 24 hours and 51% voiding more than 15 times. This was at 6-month follow-up [70]. A further 13 persistently incontinence women were studied and this revealed a significant number of voiding dysfunctions with low flow rates, prolonged voiding times, and the average voided volume of only 72 mL [71].

Sexual and Reproductive Complications

Other ongoing problems include dyspareunia in 11% of those sexually active (only 35% were sexually active at 6 months follow-up), 30% of women will have ongoing amenorrhea at 6 months, and nearly half of whom do not have an obvious cause, such as being postmenopausal, had a cesarean hysterectomy at the time of delivery, being pregnant, or on a long-acting progesterone contraception [39]. These “less obvious” reasons could be Sheehan’s or Asherman’s syndrome.

Social and Mental Health

Most patients return to their normal living arrangements once they are cured and start to attend social functions and return to work. Several recent studies have shown improvements in social, physical, and mental health once they are cured [33,34,36]. Some, however, do not and still suffer ongoing mental health problems and difficulties with reintegrating back into their communities. Further measures need to be taken to help women return to a normal life.

FAILED REPAIRS

One study examined 71 failed repairs. All of the 71 cases had a fistula described as complicated, meaning that they had one or more of the following: excessive scarring, total destruction of the urethra, ureteric orifices outside the bladder or at the edge of the fistula, a small bladder, both recto- and vesicovaginal fistulae in conjunction, or the presence of bladder stones. Patients were more likely to have a failed repair if they (1) had a ruptured uterus at the time of labor, (2) had a previous failed repair, (3) presented with limb contractures, (4) presented malnourished or in poor health, (5) had a fistula described as complicated, and (6) had blood transfusion [72]. If a patient's repair has broken, it is important to counsel the patient appropriately as there are likely to be discouraged and tearful. It is usually recommended that you should wait for 3 months before attempting another repair. Provisions need to be made for the patient to return to the hospital or if the patient is suffering severely, they can stay within the hospital and wait for their second repair.

IRREPARABLE FISTULA

The term irreparable fistula may be misleading, but some injuries are so severe that no bladder tissue remains to be repaired. The only option for these women to have any quality of life is either to have a bladder augmentation or a urinary diversion operation.

Bladder augmentations are not without their problems. Patients who have such severe injuries often have their urethra affected, so even with a good reservoir, they are still unable to hold their urine. If the urethra is intact, then self-catheterization may be needed to effect full drainage of the bladder as the augmented bladder cannot contract, or mucous secreted from the bowel lining may block the urethra. This may be unmanageable for a woman living in the developing world, far from a supply of catheters and clean equipment.

The diversion operations commonly used are direct ureterosigmoidostomy, Mainz II pouch, or ileal conduit. The former two options require an intact anal sphincter and the woman to agree to pass urine through the anus. The Mainz II shows promise for these women in developing nations as there are perhaps less long-term complications following this procedure as compared to the direct ureterosigmoidostomy [73–75].

The ileal conduit restricts a patient to living near a service that can supply the conduit bags, which are often rare in the developing world. The patient also needs to be close to a health center that knows how to deal with any complications. The ureters and kidneys in these women are often dilated and compromised and ascending infections can be common.

There are anecdotal cases of ileal conduits being performed on patients, and then the patient has been unable to access bags, leaving her in a worse state than she was to start with.

THE FUTURE

Obstetric fistula, like many morbidities suffered by women during labor, is preventable. This should be an attainable dream in the twenty-first century and this suffering is placed in medical texts of yesteryear. The task, however, is immense with up to many thousands of new obstetric units being required for Africa alone to supply adequate maternity care [76]. In tandem with this, roads need to be built, transport systems put in place, and, most importantly, men and women educated. Until all this is achieved, the obstetric fistula patient will still need our caring attention.

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Urethral Diverticulum and Fistula

Kathleen C. Kobashi

INTRODUCTION

A urethral diverticulum (UD) is a periurethral cystic structure that may or may not communicate with the urethra [1]. UD presents a diagnostic and therapeutic challenge to the clinician. They may be completely asymptomatic or exceedingly symptomatic. They may be anatomically simple or complex and are associated with a range of conditions that may need to be addressed concomitantly.

Incidence

The incidence of female UD is estimated to be approximately 0.02%–6% [2–5]. However, it is believed that this represents an underestimate and, with increased clinical suspicion and improved diagnostic techniques, the true incidence may prove to be higher [6] at least in symptomatic women. Indeed, UD has historically been an underdiagnosed condition. In 1953, Novak was quoted as saying, “This is a relatively rare condition and no gynecologist will see more than a few in a lifetime” [7]. However, the frequency of diagnosis has increased with more sensitive imaging modalities.

History

The existence of UD has been known since at least the early nineteenth century, when Hey reported the first case in 1805 [8]. In 1938, Hunner reported three cases associated with calculi and commented on the rarity of the condition [9]. In 1956, Davis and Cian reported 50 cases; more than had been reported previously in the entire history of the Johns Hopkins Hospital [10]. They also developed a double-balloon catheter to be used in conjunction with positive-pressure profilometry to facilitate the diagnosis of UD.

BACKGROUND

Etiology and Pathophysiology

Patients typically present in the third to sixth decades of life, with a mean age of 45 years [11]. Rarely, UD has been diagnosed in neonates and children [12,13]. A racial predilection has been suggested, with diagnosis in African-American women being 2–6 times that in white women [14]; however, Ganabathi et al. [11] found no racial differences. A concomitant UD has been incidentally noted in 1.4% of women diagnosed with stress urinary incontinence (SUI) [15,16].

Periurethral glands are tubuloalveolar structures located posterolaterally beneath the periurethral fascia in the proximal two-thirds of the urethra. They drain into the distal third of the urethra [17]. There are two main schools of thought regarding the etiology of UD—acquired and congenital. The most widely accepted theory is UD formation due to infection of the periurethral gland. Infection leads to obstruction of the glands, local abscess formation, and eventual rupture into the urethral lumen, as first described by Routh [18].

Trauma secondary to childbirth or forceps delivery remains a problem in developing countries, possibly contributing to UD formation [19]. However, with current obstetric technology, traumatic delivery is no longer a prevalent factor in developed nations. In fact, 15%–20% of patients diagnosed with UD are nulliparous, thereby refuting this as a sole etiology [13].

Although there has been some evidence supporting a congenital etiology, this theory seems less likely to be the principle etiology given that two large series included no patients younger than 10 years of age [14,20]. Faulty union of primordial folds, genesis from cell rests or Gartner’s duct remnants, and Müllerian remnants causing vaginal cysts have all been suggested as possible etiologies of UD, and it may be possible that a congenital defect, while not a direct cause of UD formation, may place one at risk for developing a UD later in life [4]. The discovery of mesonephric adenoma and adenocarcinoma has implicated Gartner's duct remnants. Paneth cell metaplasia lining a UD also supports a congenital basis [21]. Blindending ureters resulting from an aborted ureteral duplication may rarely lead to an anterior UD [22]. Other suggested etiologies of UD include high-pressure voiding against outlet obstruction, urethral calculi, instrumentation, and complications of previous anterior vaginal surgery [23]. UD has been described following transurethral collagen injection therapy for SUI [24,25]. Clemens et al. [24] hypothesized that the collagen injections resulted in obstruction of the periurethral glands resulting in the gradual accumulation of glandular secretions and subsequent development of noncommunicating diverticula.

Associated Conditions

Symptoms or sequelae associated with UD include incontinence, infection, stones, and malignancy. Urinary incontinence is common in patients with UD. Ganabathi et al. [11] reported a 65% incidence of SUI among patients with UD (57% with SUI as the presenting complaint). These patients may also suffer from urgency incontinence or "paradoxical incontinence," in which urine stored in the UD is lost during stress maneuvers [4].

Approximately 25%–33% of patients with UD present with recurrent urinary tract infections (UTIs), including some who suffer from systemic infections. The most common infecting organisms of UD are *Escherichia coli*, chlamydia, and gonococcus; however, multiple organisms have been cultured [4,26]. Up to 13% of patients present with calculi in the UD, and this can be confirmed by plain radiograph [27,28]. Stones form secondary to stasis, infection, and chronic inflammation in the UD [29] (Wittich, 1987). Stones can be multiple, and in some cases, quite large. A 5 × 6 cm stone was discovered in the UD of an elderly woman during workup for a firm vaginal mass. Urethrovaginal fistula (UVF) secondary to rupture of a UD is also a potential complication [30,31].

Table 110.1 Frequency and Outcome for Treatment Modalities Used for Carcinoma in a Urethral Diverticulum

Treatment	**Patients (*n*)**	**Disease-free (%)**	**Local recurrence (%)**	**Death/metastasis**
Diverticulectomy	27	9 (33)	13 (48)	5 (19)
Radiation	10	2 (20)	5 (50)	2 (20)
Diverticulectomy + radiation	16	8 (50)	5 (31)	3 (19)
Anterior exenteration	26	19 (73)	1 (4)	6 (23)

Source: Shalev M et al., *Urology*, 59, 773iii, 2002.

Although the vast majority of UDs are benign, malignant change has been reported [32]. Approximately 100 cases of neoplasm within a UD have been reported in the world literature [33–37]. There have also been reports of nephrogenic adenoma, a benign metaplastic condition [32,38–44]. Malignancy must be considered whenever a UD is diagnosed, particularly when accompanied by hematuria, induration or firmness of a UD on physical examination, noncalcified filling defects within the UD on radiography, or a visible lesion on cystoscopic examination. Despite the fact that squamous epithelium lines most of the urethra in addition to the fact that squamous carcinomas are the most frequently diagnosed histopathologic malignancy in the female urethra, adenocarcinoma is by far the most common histopathological condition demonstrated within UD, specifically [39,45]. This lends further support to the theory that UDs develop from glandular origins. More than 80% of the diverticular cancers seen are either adenocarcinoma (61%) or transitional cell carcinoma (27%) [45–47]. Squamous cell carcinoma is rare, comprising only 12% of UD malignancies [47]. When identified within a UD, squamous cell carcinoma appears to be very aggressive, with a mortality rate of 78% at 3 years [48]. One case of a high-grade serous carcinoma, a histopathology that typically arises in the uterine corpus or in the Fallopian tubes/ovaries has recently been reported [49].

Treatment of diverticular carcinoma includes wide local excision for localized disease (Seballos et al., 1995). Adjuvant radiation therapy or chemotherapy may also be indicated for extensive malignancy or for nonsurgical candidates [50,51]. Survival is a function of stage [51] and grade [50] of the disease. Squamous cell carcinomas are typically diagnosed at an advanced stage, with all reported cases presenting at stage T2 or higher, and require a more aggressive treatment approach [50,52–55]. Because of the relative rarity of carcinoma in UD, it has been difficult to develop a common definitive treatment strategy (Table 110.1) [56]. Among 79 patients reviewed by one center with follow-up ranging from 6 months to 10 years, anterior pelvic exenteration appeared to offer the highest likelihood of prolonged disease-free survival [48]. Both laparoscopic radical cystectomy and robotic anterior exenteration have reportedly been performed for clear cell adenocarcinoma in a UD [57,58].

PRESENTATION AND DIAGNOSIS

Clinical Symptoms

Patients with UD present with a variety of symptoms ranging from irritative voiding complaints to pelvic pain and dyspareunia (Table 110.2) [4,59]. The classic triad of UD is known as the “3 Ds”—dysuria, dyspareunia, and dribbling. However, few patients with a UD actually have the full triad, [60] and many patients are completely asymptomatic. Urinary urgency, frequency, and hematuria may also occur with UD [61]. Nevertheless, the diagnosis is often not straightforward and UD may mimic other pelvic floor disorders, resulting in diagnostic delay [62].

In a review of 46 consecutive cases of UD, the mean interval between onset of symptoms to diagnosis was 5.2 years [62]. Frequently, patients receive an initial, erroneous diagnosis for which a variety of treatments are considered or attempted (Table 110.3). A high index of suspicion is required in order to diagnose UD because many patients may not be overtly symptomatic upon initial evaluation. In cases of persistent irritative voiding symptoms, pelvic pain, and urinary incontinence unresponsive to therapy, UD should be kept in mind and excluded [62].

Table 110.2 Signs and Symptoms of Urethral Diverticula

Symptoms	Signs
Vaginal or pelvic mass	Recurrent UTI
Pelvic pain	Hematuria
Urethral pain	Vaginal or perineal tenderness
Dysuria	Urinary retention
Urinary frequency	Vaginal mass
Postvoid dribbling	Expression of urethral
Dyspareunia	discharge with stripping of
Urinary urgency	the anterior vaginal wall
Incontinence	
Urinary hesitancy	
vaginal or urethral discharge	
Double voiding	
Sense of incomplete emptying	

Source: Rovner ES, Chapter 78: Bladder and urethral female diverticula, in: Wein AJ et al., eds., *Campbell-Walsh Urology*, 10th ed., Saunders, Philadelphia, PA, 2012, pp. 2262–2289.

Table 110.3 Most Common Initial Diagnoses and Subsequent Treatments Given to Patients before Identification of a Urethral Diverticulum

Diagnosis	Treatment
Chronic cystitis trigonitis	Long- or short-term antibiotics
SUI	Anti-incontinence surgery
Urge incontinence	Anticholinergics
Interstitial cystitis	Hydrodistention
Idiopathic pelvic pain syndrome	DMSO instillation
syndrome	Tricyclic antidepressants
Urethral syndrome	Urethral dilation
Vulvovestibulitis	Vaginal creams—antifungal/antibiotic

Cystocele	Surgery
sensory urgency	Anticholinergics
Psychosomatic disorder	Psychotherapy

Source: Aspera AM et al., *Urol Clin North Am*, 29, 617, 2002.

Physical Examination

Patients with UD will often have anterior vaginal wall tenderness, with or without a concomitant palpable suburethral mass [62]. Digital pressure along the urethra may demonstrate expressible purulence or blood from the UD that can be seen emanating from the urethral meatus (Figure 110.1) [63]. Firmness of the area may be indicative of a diverticular stone or neoplasm. Rarely, some patients are without any pertinent physical findings, and workup is pursued only on clinical suspicion based on the patient's history. Importantly, the clinician should also evaluate urethral mobility and examine for evidence of SUI, which can be addressed at the time of repair of the UD if deemed necessary.

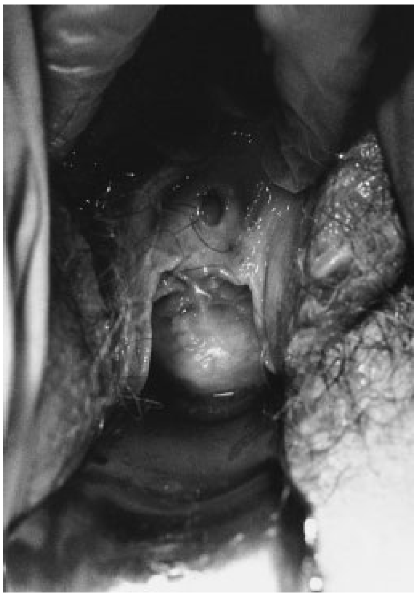

Figure 110.1 Urethral diverticulum presenting as an anterior vaginal mass. (Reproduced from Ganabathi K et al., *J Urol*, 152, 1445, 1994. With permission.)

Differential Diagnosis

The differential diagnosis of urethral and meatal/perimeatal masses (Figures 110.2 and 110.3) is illustrated in Tables 110.4 and 110.5, respectively. Note that Table 110.5 includes conditions that occur in locations distal to the location of the majority of UD; however, they should be considered in the differential diagnosis [64].

Classification System

Leach et al. [65] created a system for classification of female UD known as the L/N/S/C3 system. This acronym represents location, number, size, configuration, communication, and continence. The system aims to facilitate preoperative assessment of UD and standardize the classification, thereby simplifying comparisons between series. Table 110.6 illustrates the classification of 63 patients.

EVALUATION

Endoscopic Examination

A blunt-tip female urethroscope with a short sheath beak and a 0° or 30° lens is used to evaluate the urethra. The anterior vaginal wall is compressed with a finger in the vagina, and the urethral lumen is inspected for any expression of effluent from the floor or the roof of the urethra (Figure 110.4). Fifty percent of patients will have multiple diverticula, and more than half of the UDs will communicate with the urethra in its middle third [3]. Cystoscopy is the only diagnostic tool that allows direct inspection of the urethra and bladder and, in some cases, may facilitate diagnosis of a diverticular neoplasm or calculus; however, the value of cystoscopy as a diagnostic tool has been questioned [66].

The ostium of the diverticular neck can be difficult to visualize between collapsed urethral folds, and noncommunicating diverticula (periurethral cysts) will not have a visible orifice [67,68]. Cystoscopy does not provide any information regarding size, shape, or appearance of the diverticulum or the diverticular wall [69]. Additionally, cystoscopy is invasive and carries the risk of UTI and may cause significant pain in a woman with a diverticulum. Furthermore, a negative finding on cystoscopy does not rule out the absence of a UD. Imaging studies should be considered as cystoscopy will frequently fail to diagnose UD.

Urodynamic Evaluation

Urodynamic studies are not required in the evaluation of all patients with UD but may be useful for patients with symptoms of SUI or bladder dysfunction [70–72]. These symptoms may include urinary leakage with increased intra-abdominal pressure, urgency incontinence, or spontaneous loss of urine that may represent intrinsic sphincter deficiency, paradoxical incontinence (i.e., loss of urine that has “pooled” in the UD), or poor emptying. Identification of these problems is critical in proper surgical planning. In patients with SUI, appropriate correctional surgery can be considered at the time of diverticulectomy. The urodynamic findings in 55 women studied by Leach and Ganabathi [70] are noted in Table 110.7.

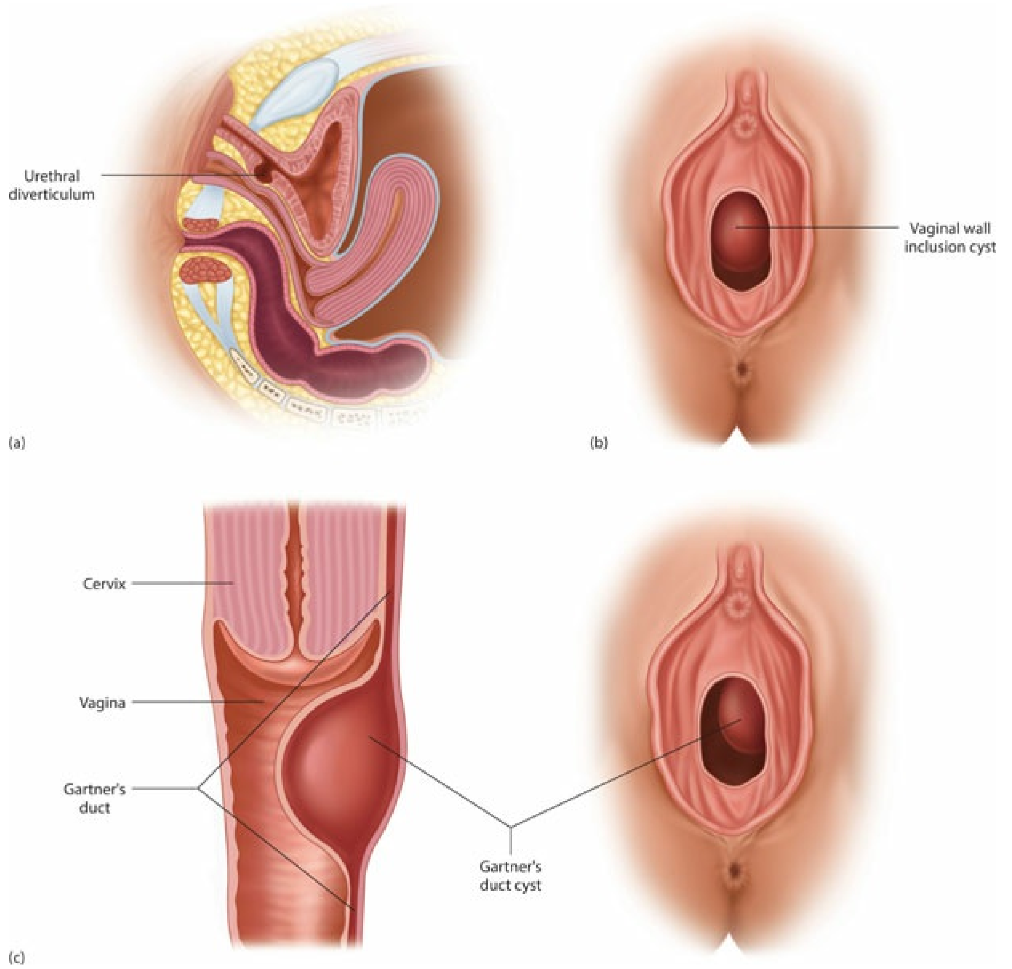

Figure 110.2 Differential diagnosis of urethral and anterior vaginal wall masses: (a) urethral diverticulum, (b) vaginal wall inclusion cyst, and (c) Gartner’s duct cyst.

Radiological Studies

Careful evaluation of UD can facilitate optimal treatment planning. Proper imaging plays an important role in determining the anatomy of the UD as well as its spatial relationship to its surrounding structures and its position along the length of the urethra. Numerous imaging modalities are available and each has its own strengths and weaknesses [73].

Voiding Cystourethrogram

The *voiding cystourethrogram* (VCUG) is performed under fluoroscopic visualization with the patient standing (Figure 110.5). The assessment of the bladder neck and proximal urethra as well as bladder neck competency is imperative to document incontinence that may be treated at the time of diverticulectomy. Filling defects within a UD may represent tumor or stones (Figure 110.6) [4]. An air–fluid level in the UD may indicate a UD that is much larger than it appears radiographically.

Fifty percent of patients have multiple UDs. Proper and thorough preoperative evaluation is critical to ensure complete excision of all components of the UD. VCUG has historically been considered the study of choice for the diagnosis of UD (Figure 110.5). Some studies have challenged the sensitivity and specificity of a VCUG in the diagnosis of a UD as the study depends upon the patient voiding during the study to provide a complete study. A 3-year experience comparing VCUG to positive-pressure urethrography (PPUG) in the evaluation of UD found that the positive predictive value of VCUG after PPUG was only 60% [68]. Overall, reported sensitivity of VCUG has ranged from 44% to 95% [70,74]. Once considered the gold standard for diagnostic evaluation, VCUG is now used mainly as a screening test. Should it fail to adequately characterize or identify UD and there is still high suspicion that the entity exists, other imaging modalities should be applied [68].

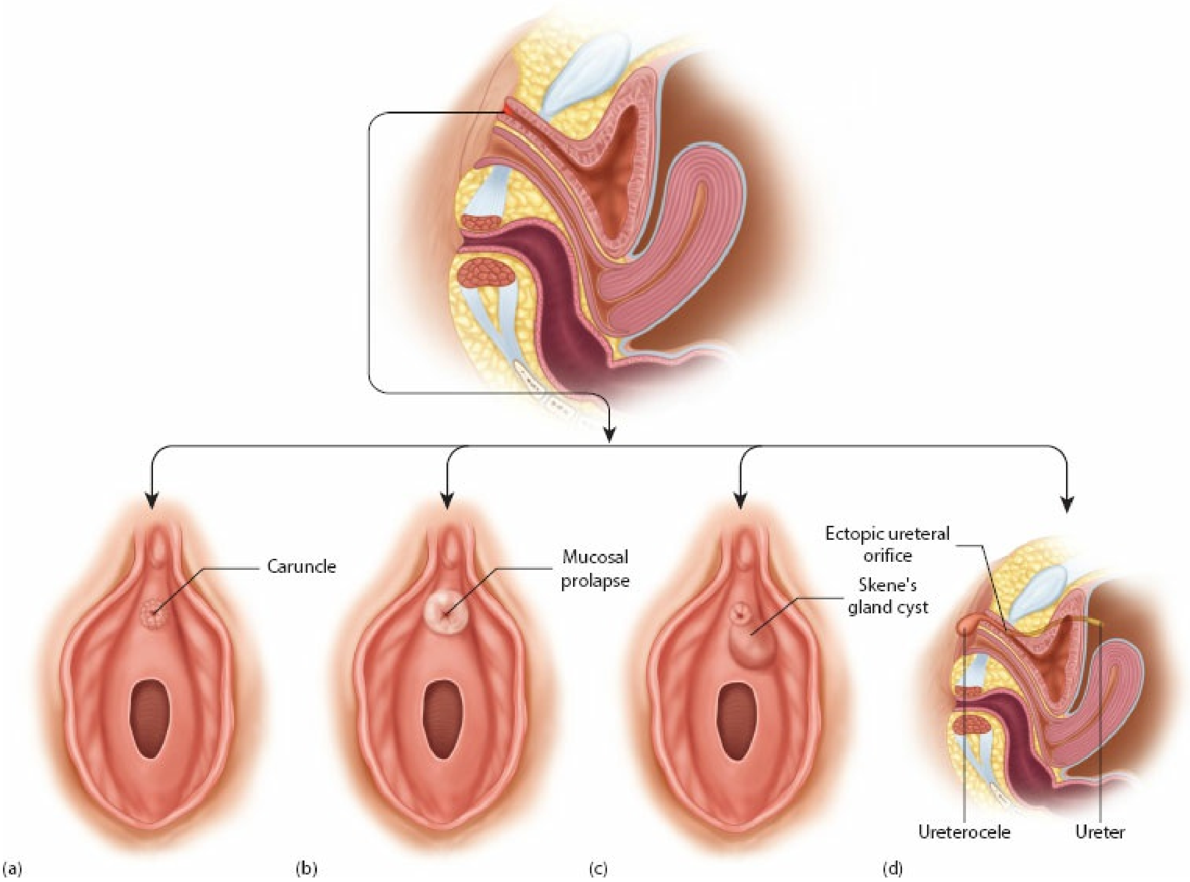

Figure 110.3 Differential diagnosis of meatal and perimeatal lesions: (a) caruncle, (b) mucosal prolapse, (c) Skene’s gland (or duct) cyst, and (d) ureterocele.

Intravenous Pyelography

Intravenous pyelography (IVP) is now a rarely utilized modality and has been replaced in many parts of the word with CT urography. IVP or CT urogram can be useful to evaluate the upper tracts and rule out an ectopic ureterocele [75–78]. An ectopic ureterocele may be considered when there is an abnormal protrusion into the urethra or from the meatus. It is important to obtain a low pelvic view in order to visualize the urethra completely (Figure 110.7).

Retrograde Positive-Pressure Urethrography

Retrograde PPU was once considered the optimal study for the diagnosis of UD. It was reported by Robertson [3] to have a 90% accuracy. Additional studies have reported superior sensitivity of PPU over VCUG for the diagnosis of UD [74,79]. However, this technique is now rarely utilized and is mentioned here primarily for historical purposes. In present-day urological practice, PPU may be employed only as a last resort, when high-quality VCUG or magnetic resonance imaging (MRI) is not available.

PPU is a painful procedure for patients, often necessitating anesthesia. It is also a technically difficult study that requires a special catheter known as the Davis or Trattner catheter [3,80] (Figure 110.8). This catheter has two balloons—one of which is placed just inside the bladder neck and the other at the external meatus. The distal balloon is wedge shaped to fit snuggly into the urethral meatus. Injection of contrast through a separate channel that contains a side port between the occlusive balloons allows for filling of the urethra under slight pressure to facilitate filling of the UD (Figure 110.8).

Table 110.4 Differential Diagnosis of Urethral and Anterior Vaginal Wall Lesions

Lesion	**Location**	**Symptoms/physical exam**	**Cystoscopy/radiography**	**Comments**
Urethral diverticulum	Anterior vaginal wall, midline	UTI, dysuria, dyspareunia, postvoid dribbling, cystic mass	Orifice of diverticulum visible on urethral floor, VCUG opacifies lesion.	May be multilocular
Vaginal wall cyst	Anterior vaginal wall, midline or eccentric	Cystic mass; may be loculated	None or extrinsic compression.	
Gartner's duct cyst	Anterolateral vaginal wall	Cystic mass	None or extrinsic compression; IVP may indicate ectopic ureteral drainage.	Rule out ectopic ureter prior to excision
Müllerian remnant cyst	Midline	Cystic mass	None.	
Ectopic ureterocele	Anywhere in bladder, urethra, vagina (upper third), uterus, fallopian tubes	Cystic mass	May be seen on IVP, US, or cystoscopy.	
Leiomyoma, hamartoma	Vaginal wall	Solid mass	None or extrinsic compression.	Rule out malignancy
Malignant urethral or vaginal neoplasms	Urethral or vaginal wall or hematuria	Solid mass; may have pain, may be seen on cystoscopy	None or extrinsic compression; ± adjuvant therapy erythema, obvious lesion or tumor growing from the diverticulum into the urethral lumen.	Wide local excision, radiation, combination, anterior pelvic exenteration

Source: Adapted from Dmochowski RR et al., J Urol, 152, 1943, 1994.

Abbreviations:UTI, urinary tract infection; VCUG, voiding cystourethrogram; IVP, intravenous pyelography; US, ultrasonography.

Table 110.5 Differential Diagnosis of Meatal and Perimeatal Lesions

Lesion	**Location**	**Presentation**	**Comments**

Caruncle	Inferior to meatus	Asymptomatic or dysuria/pain with atrophic or ischemic mucosal changes	Postmenopausal age group
Skene's gland cyst or abscess	Inferior and lateral to meatus	Painful, orifice of duct visible at urethral meatus	
Mucosal prolapse	Circumferential mucosal prolapse with central meatus	Pain and dysuria, atrophic or ischemic mucosal changes	Young girls or postmenopausal women
Prolapsed ureterocele	Submeatal, prolapsed through meatus	Glistening mucosa, may be fluid filled, may be ischemic, may be asymptomatic	IVP to evaluate upper tract status

Source: Adapted from Dmochowski RR et al., *J Urol*, 152, 1943, 1994.

Abbreviations:IVP, intravenous pyelography.

Table 110.6 L/N/S/C3 Classification System Applied to 63 Patients with Urethral Diverticula

Location (L)	Number (N)	Size (S)	Configuration (C1)	Communication (C2)	Continence (C3)
Proximal, beneath bladder neck (9)	Single	0.2 × 0.2 cm–6.0 × 4.5 cm	Multiloculated (22)	Proximal urethral (16)	Complete (26)
Proximal urethra (7)	Multiple		Single (41)	Midurethra (35)	SUI only (30)
Midurethra (36)			Saddle-shaped (14)[a]	Distal urethra (12)	Urge incontinence only (3)
Distal urethra (11)					SUI and urge incontinence (4)

Source: Adapted from Leach GE et al., *Neurourol Urodyn*, 12, 523, 1993.

Note:These patients are also included in the “simple” or “multiloculated” groups.

Abbreviation:SUI, stress urinary incontinence.

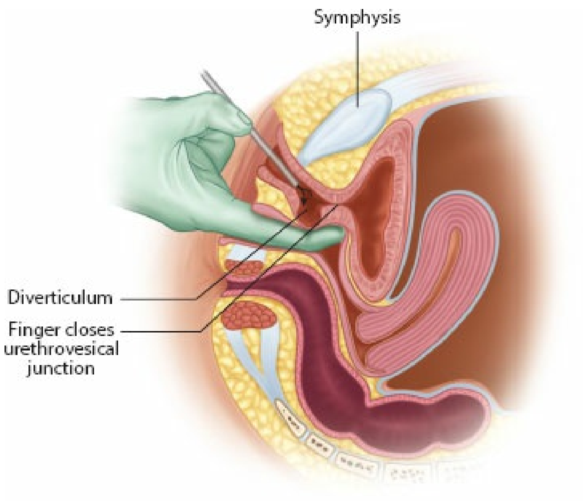

Figure 110.4 The technique of endoscopic examination of the urethra while “milking” the anterior vaginal wall and urethral roof.

Table 110.7 Urodynamic Findings in 55 Women with Urethral Diverticula

Urodynamic finding	***n* (%)**
Normal	22 (40)
SUI alone	18 (32.7)
SUI + DI	8 (14.5)
DI alone	5 (9)
Sensory urgency	1 (2)
Myogenic decompensation	1 (2)

Source: Leach GE and Ganabathi K, Atlas Urol Clin North Am, 2, 73, 1994.

Abbreviations:DI, detrusor instability (now termed detrusor overactivity); SUI, stress urinary incontinence.

Ultrasonography

Ultrasonography is used in the evaluation of the upper tracts or, occasionally, in conjunction with VCUG to confirm the number and size of diverticula, especially in those cases in which the UD does not completely filled during urethrography [28,81,82] (Figure 110.9). Vargas-Serrano et al. [82] advocated transrectal ultrasonography (TRUS) as the most sensitive tool in the diagnosis of female UD. Keefe et al. [81] support transperineal or transvaginal sonography, reporting 100% sensitivity in their small series and stressing the noninvasive nature of the technique. Wang and colleagues advocate for 2D and 3D transvaginal ultrasound as an accurate and cost-effective imaging modality for the assessment of lower urinary tract perineal masses [83].

Multiple approaches to ultrasonography have been employed, including transvaginal [84,85], translabial [86], suprapubic [80], perineal [81], and TRUS [81]. Dai et al. [87] described a contrast-enhanced transvaginal ultrasound as a technique to facilitate the diagnosis of a female UD. Contrast was injected into the urethra of 14 women suspected of having a UD. Cross-sectional, sagittal, and dynamic images were obtained and color Doppler was applied, and the flow of microbubbles into the UD was tracked. The sonographic findings correlated well with the intraoperative findings, and the authors concluded that this technique provides a tool for the identification of the size, location, configuration, and ostia of the UD.

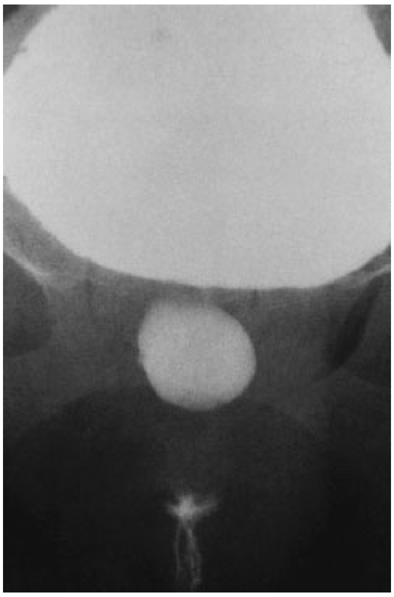

Figure 110.5 A voiding cystourethrogram demonstrating a multiloculated diverticulum. (Reproduced from Jensen LM et al., *Acta Obstet Gynecol Scand*, 75, 748, 1996. With permission.)

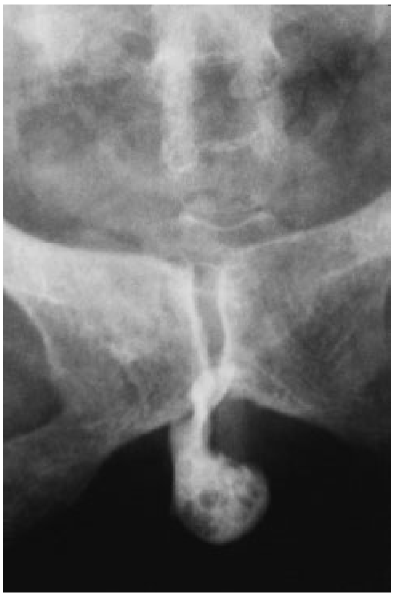

Figure 110.6 A postvoid film demonstrating filling defects within a urethral diverticulum suggestive of stones or tumor. (Reproduced from Leach GE and Ganabathi K, *Atlas Urol Clin North Am*, 2, 73, 1994. With permission.)

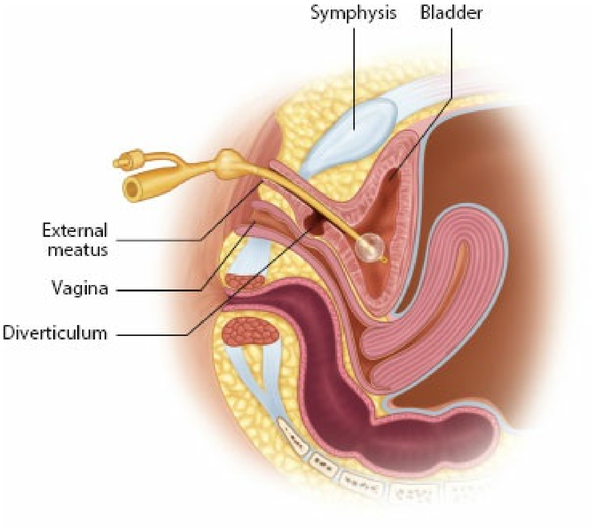

Figure 110.7 Placement of a Trattner/Davis double-balloon catheter for positive-pressure retrograde urethrography.

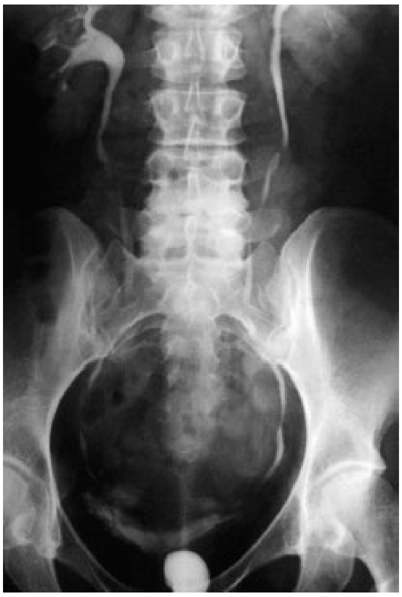

Figure 110.8 Intravenous pyelogram demonstrates the urethral diverticulum and the upper tracts.

Intraoperative endoluminal ultrasonography has been described for localization of the UD [88,89]; however, this is very difficult to perform. One limitation is that the modality is dependent on the technical skills of the operator. Advantages include real-time evaluation and the ability to clarify the spatial relationships between the diverticulum and the urethra [67]. Ultrasound is less expensive compared to other diagnostic tools including VCUG, MRI, and cystoscopy [67].

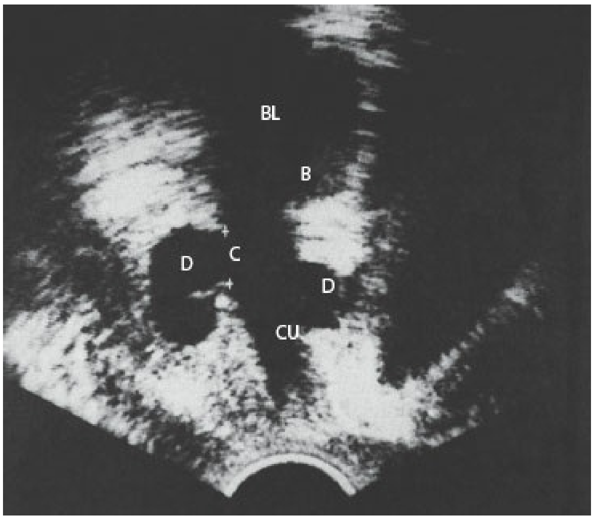

Figure 110.9 Transvaginal ultrasonography demonstrating a multiloculated urethral diverticulum opening into the proximal urethra. BL, bladder; B, Foley catheter balloon; C, diverticular communication; D, diverticulum; CU, intraurethral Foley catheter. (Reproduced from Ganabathi K et al., *J Urol*, 152, 1445, 1994. With permission.)

Magnetic Resonance Imaging

MRI is considered by many to be the most useful diagnostic tool for UD due to its high sensitivity for identifying fluid-filled cavities [38,90–94]. The caveat is that the decompressed UD may not be easily visualized in light for the fact that this study is not performed while voiding, and therefore, the cavity may not be filled to provide for optimal detection. Endorectal and endovaginal coil MRI techniques differ from surface or body coil MRI to that of the former; the coil is placed within the body cavity adjacent to the tissue of interest. This results in improved signal-to-noise ratio and higher-resolution imaging of the urethra [93].

Kim et al. [95] reported 100% sensitivity of MRI in the detection of UD, though others have reported up to a 24% discrepancy between MRI and surgical findings [96]. The signal intensity of fluid is high on T2-weighted images and isointense on T1-weighted images (Figure 110.10). MRI is helpful in defining the extent of a UD and differentiating it from other urethral or vaginal masses, such as malignancy, paraurethral cysts, and Gartner's duct cysts. Endorectal coil MRI can also provide for the diagnosis of periurethral fibrosis and other periurethral pathology [97]. Foster et al. reported on 27 patients with a UD in whom MRI altered the treatment plan in 15% [98]. When compared to VCUG, MRI has been touted to have a higher sensitivity and better characterization of size, location, and complexity of the diverticulum [99]. The superior imaging also may facilitate surgical planning by accurately delineating the extent of the diverticulum.

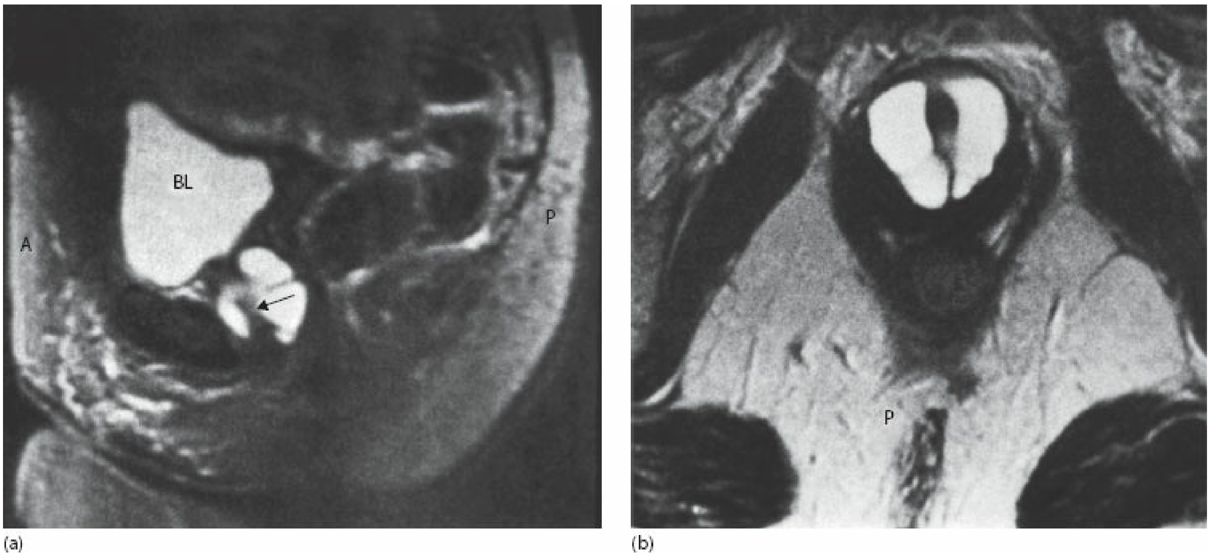

Figure 110.10 T2-weighted magnetic resonance imaging illustrates a multiloculated diverticulum (arrow) posterolateral to the urethra: (a) sagittal view and (b) axial view. (BL, bladder; A, anterior; P, posterior.) (Reproduced from Martensson O and Duchek M, *Scand J Urol Nephrol*, 28, 101, 1994. With permission.)

The high cost of MRI is a detraction compared to other modalities. Endovaginal coil MRI may also be uncomfortable for patients but probably not much more so than VCUG or PPU. Portnoy et al. [100] reported on a retrospective review that showed a high correlation between PPU and MRI in 14 women who underwent both studies. MRI may also provide alternative diagnoses or additional information about surrounding structures that would not be noted on a PPU.

TREATMENT

History

Numerous techniques for the identification and repair of UD have been described. To facilitate identification of a UD, intradiverticular placement of a sound [9,101], a Foley catheter [102], a Fogarty catheter [103], gauze [104], silicone, or blood products [105] have been utilized. Repair has been performed endoscopically and transvaginally by the incision of the urethral floor with layered reconstruction [42], marsupialization [106,107], packing of the UD with various materials to obliterate the cavity [108,109], and transvaginal flap creation with layered closure [70,102,110,111].

Observation

Surgical resection and reconstruction is frequently necessary in the treatment of UD [112]. However, observation is an option in the asymptomatic or very small UD. Marshall reported that UD in young girls may regress spontaneously; therefore, in this rare situation, observation may be a reasonable option [113].

Endoscopic Treatment

Endoscopic treatment should be considered only for distal UD to avoid injury to the proximally located continence mechanism. Transurethral saucerization with incision of the urethral floor [114,115] or of the anterior urethra overlying the UD [116] with a Collins' knife through a pediatric resectoscope can be performed with minimal risk of complication. The major risk is incontinence, which can be minimized by limiting the use of this technique to distal UD [4]. This risk also applies to transvaginal marsupialization (Figure 110.11) of a UD, an outpatient procedure also known as the Spence procedure [3]. One blade of the scissors is placed in the vagina and the other in the urethra; the incision results in marsupialization of the cavity.

Excision with Vaginal Flap Technique

The authors prefer the transvaginal flap technique for all midurethral or proximal UD. This technique allows complete resection of the UD with a three-layer closure and avoidance of overlapping suture lines. An autologous fascial pubovaginal sling can easily be performed concomitantly when deemed necessary (in cases of demonstrable SUI) [117].

Preoperative Preparation

Preoperatively, the risks of a diverticulectomy including bleeding, infection, recurrence, UVF formation, and persistent or worsening urinary incontinence are explained to the patient in detail. It has been recommended that patients have a documented negative urine culture, though many advocate for a short course of oral antibiotics for several days just prior to the day of surgery [4]. All patients receive appropriate perioperative intravenous antibiotics.

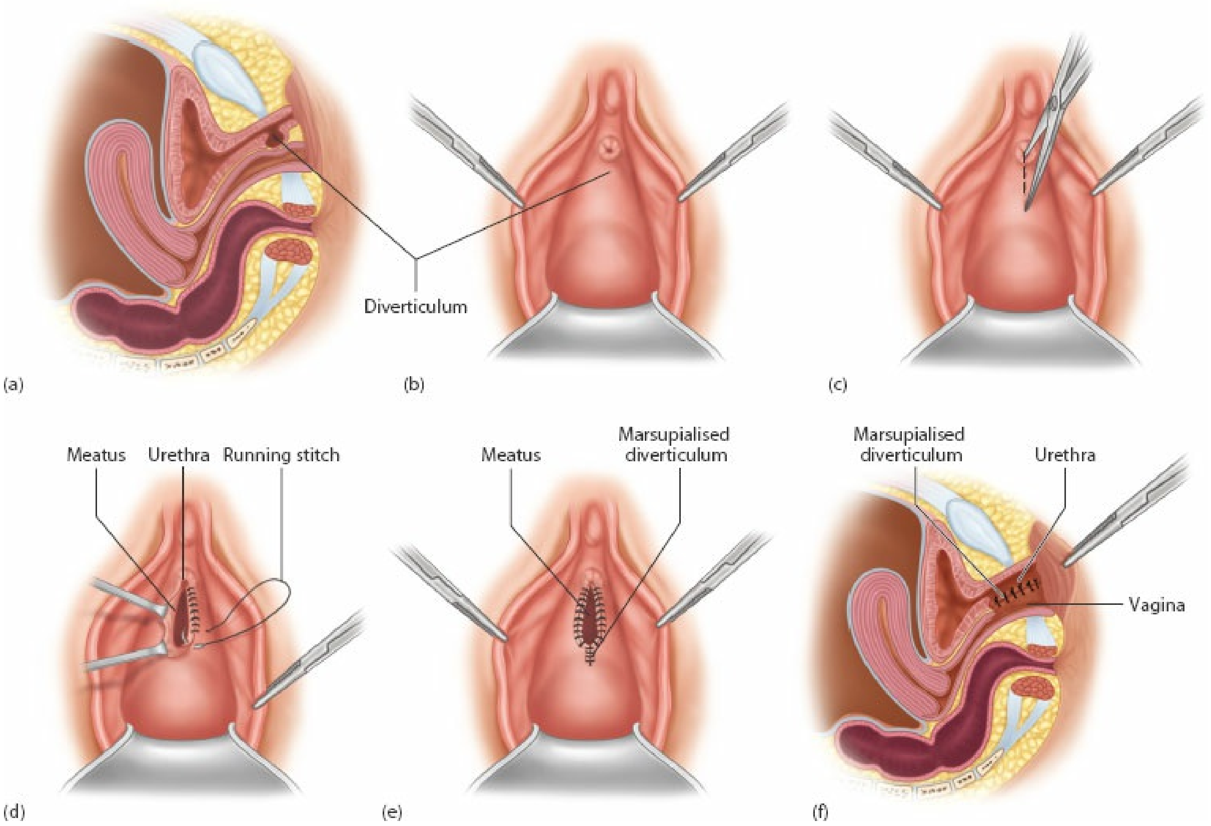

Figure 110.11 The Spence technique for marsupialization of a urethral diverticulum (UD): (a/b) sagittal and vaginal views showing the distal location of the diverticulum and the proximity of the diverticulum to the urethral meatus. (c) One blade of the scissors is inserted into the UD and the other into the vagina. The full thickness of the diverticular septum is incised and (d) a running locking absorbable suture ensures hemostasis. (e/f) This results in a urethral meatus that extends from the diverticulum to the original meatus.

SURGICAL TECHNIQUE

The patient is placed in the low lithotomy position, and prepared and draped, exposing the lower abdomen and perineum. Cystoscopy is performed to examine for the neck of the UD in the urethral lumen. We prefer to place a 12 Fr/5 cc suprapubic tube (SPT), which is secured to the skin and plugged. If a concomitant pubovaginal sling (PVS) is to be performed, the SPT placement is delayed until the harvest and closure of the rectus fascia is complete (see Figure 110.12). A 14 Fr or 16 Fr urethral Foley catheter is passed into the urethra and a weighted vaginal speculum and a Scott ring retractor facilitate exposure. The anterior vaginal wall (Figure 110.12) is infiltrated with saline to facilitate dissection in the proper plane. A U-shaped incision is made with the apex located distal to the UD (Figure 110.13).

In the case of a concomitant PVS, the vaginal dissection is extended laterally to the undersides of the pubic rami bilaterally. The endopelvic fascia is perforated with the bladder completely emptied, and the retropubic space is developed. A strip of rectus fascia is harvested through a Pfannenstiel incision, and the fascia is closed. Helical #0 Vicryl sutures are placed in the ends of the fascial strip, the sling is placed into antibiotic irrigation, and the low abdominal incision is packed with a moist sponge until the sling is placed later in the procedure (see section titled “Concomitant Anti-Incontinence Procedures”).

The diverticulectomy is continued with creation of a vaginal flap via sharp dissection in the white shiny layer of the vaginal wall. *Dissection in the wrong plane can result in significant bleeding or inadvertent entry into the periurethral fascia or the UD, which can render the remainder of the dissection very difficult*. Mobilization of the vaginal flap toward the bladder neck, followed by a transverse incision in the periurethral fascia (Figure 110.14), exposes the UD, which lies directly beneath this layer. The periurethral fascia is then sharply dissected off the UD (Figure 110.15) by developing flaps proximally and distally. The UD is then exposed circumferentially until the diverticular neck is encountered (Figure 110.16). *Difficulty identifying the urethral communication site can result in incomplete resection of the UD and subsequent recurrence. Identification can be facilitated by insertion of a pediatric sound or Fogarty catheter into the UD.*

Complete excision of both the UD and its neck can leave a significant urethral defect (Figure 110.17), while incomplete resection of the diverticulum can lead to recurrence. In cases of a large and/or circumferential UD, the surgeon must be cognizant that extensive dissection beneath the trigone can endanger the ureters and the base of the bladder, sometimes obliging the surgeon to consider leaving the most proximal portion of the UD behind. In these cases, careful cauterization of the inner epithelial surface can be utilized to facilitate obliteration of the cavity. The urethral defect is closed longitudinally without tension over a urethral catheter using a full-thickness #4-0 Vicryl stitch, with care to incorporate the urethral mucosa in each stitch (Figure 110.18).

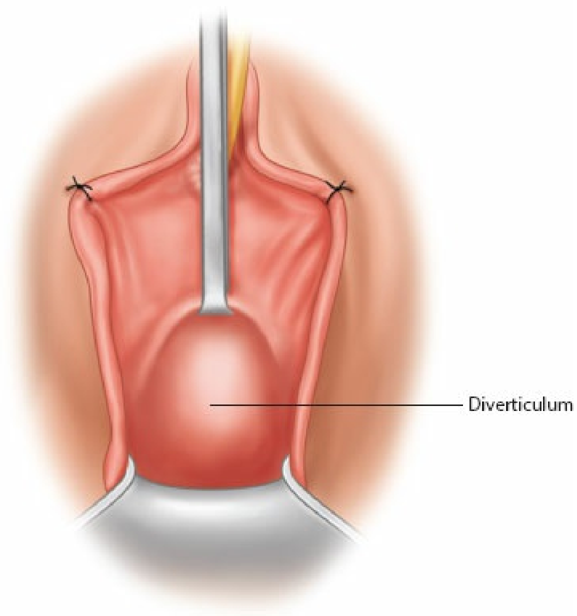

Figure 110.12 Anterior vaginal wall and urethral diverticulum. (Reproduced from Leach GE and Ganabathi

K, *Atlas Urol Clin North Am*, 2, 73, 1994. With permission.)

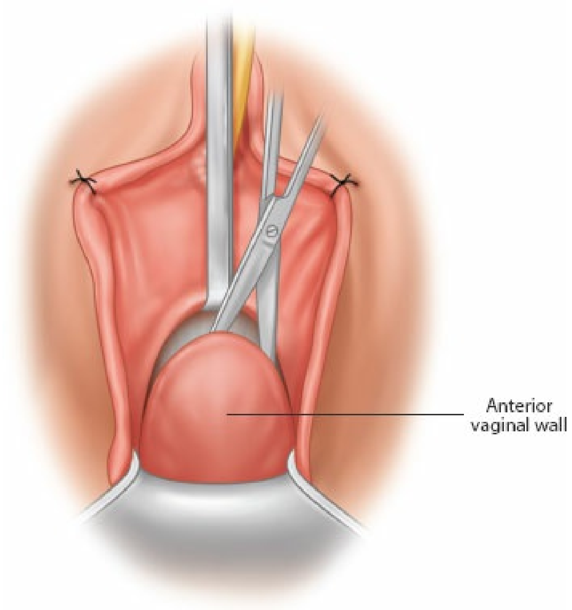

Figure 110.13 An inverted U-incision is made in the anterior vaginal wall, and the vaginal wall is dissected off the underlying periurethral fascia.

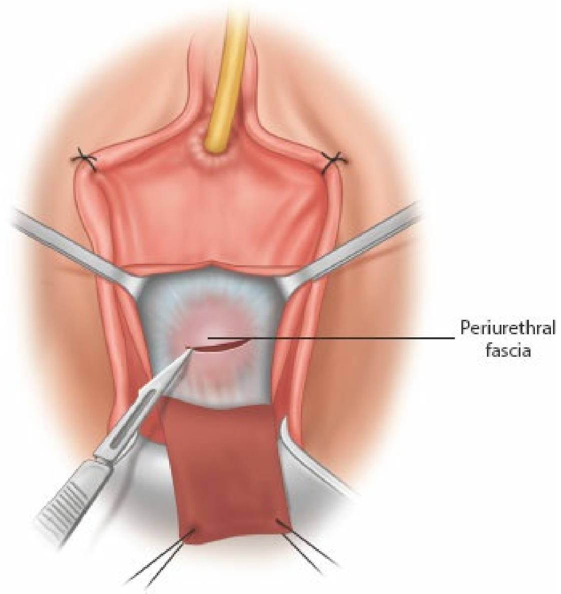

Figure 110.14 The periurethral fascia is incised transversely.

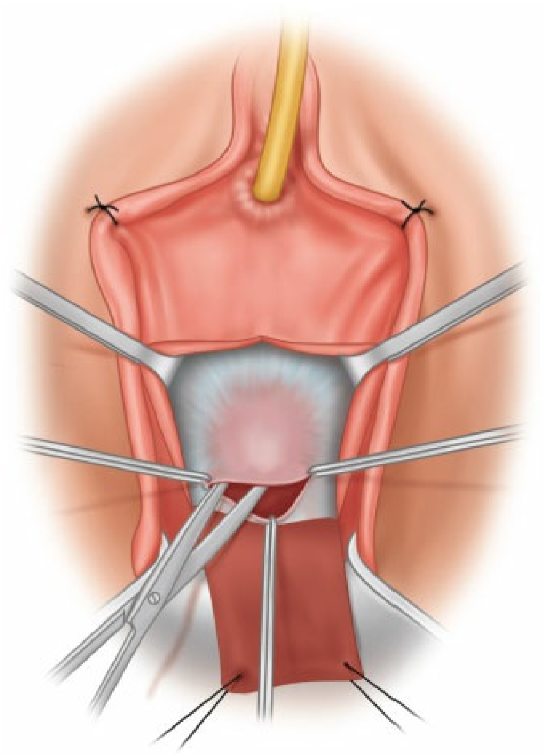

Figure 110.15 The periurethral tissue is dissected from the diverticulum.

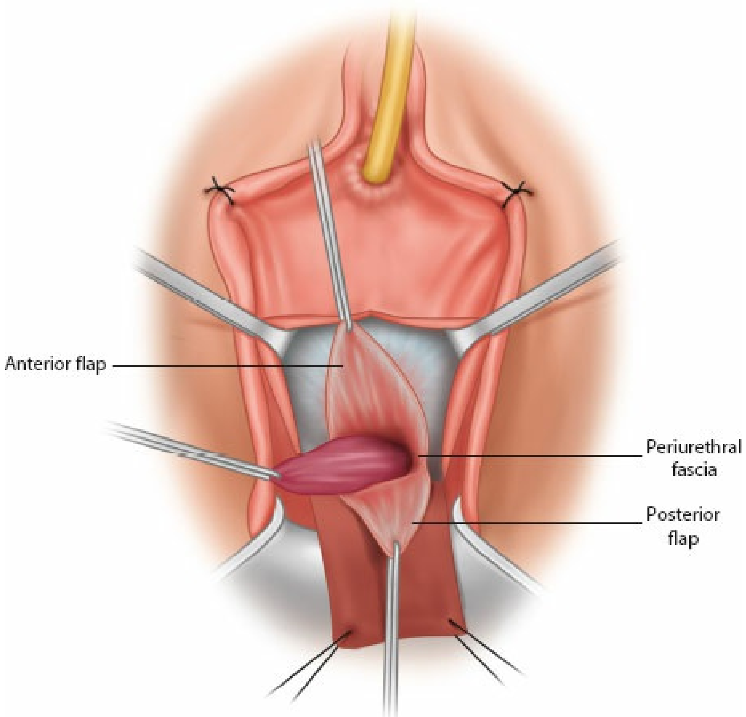

Figure 110.16 The diverticulum is isolated and carefully dissected until the communication is identified.

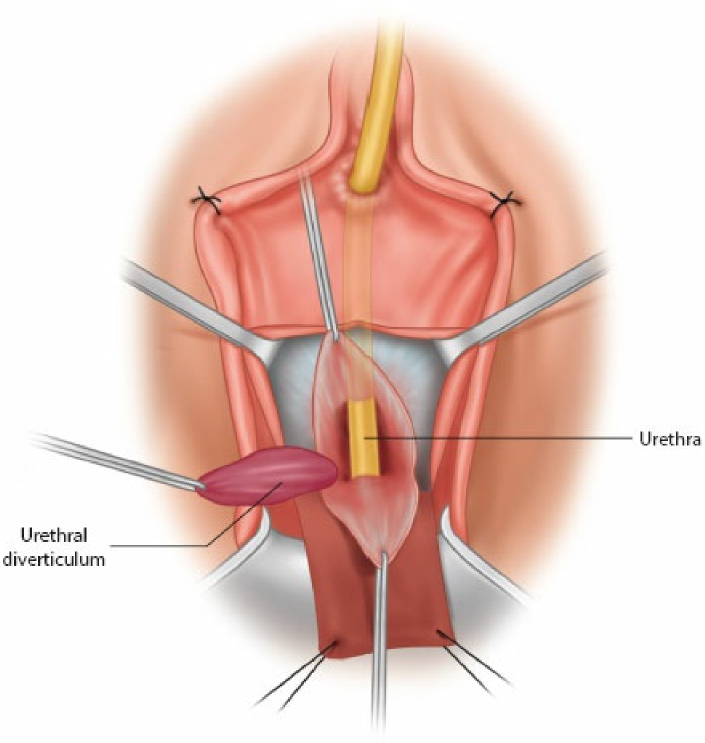

Figure 110.17 The diverticulum is amputated at its communication site, thereby exposing the urethral Foley catheter and leaving a urethral defect.

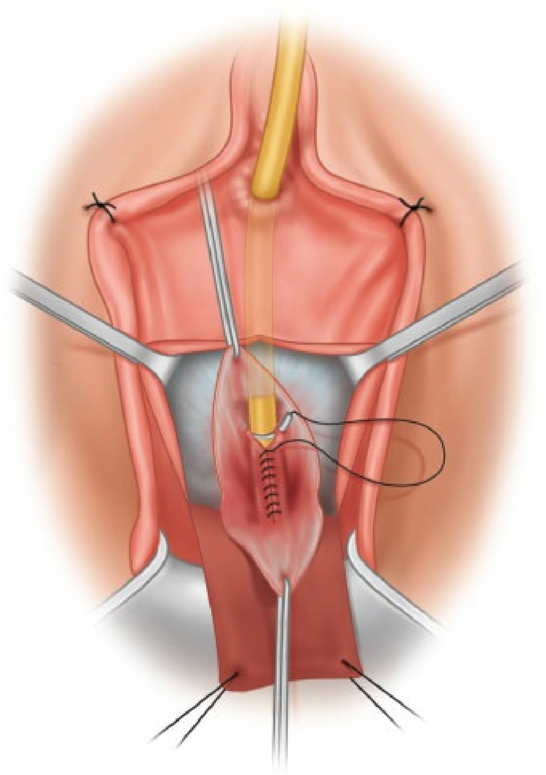

Figure 110.18 The urethra is reapproximated longitudinally with 4-0 absorbable suture.

In cases in which the tissues are tenuous or fibrotic (e.g., due to previous surgery, radiation, or smoking), a well-vascularized 8–12 cm Martius fat pad graft can be placed between the vagina and urethra. The periurethral fascia is closed transversely with running #3-0 Vicryl (Figure 110.19). Dead space should be obliterated beneath this layer. A Martius flap, if utilized, is placed between the periurethral fascia and the vagina. The third and final layer of closure is the inverted U-incision in the vaginal wall, which is closed with #2-0 absorbable suture. The three layers of closure include the urethral wall longitudinally, the periurethral fascia transversely, and the vaginal U-incision. There are no overlapping suture lines (Figures 110.20 and 110.21). Vaginal packing moistened with antibiotic solution or estrogen cream is inserted, the Foley catheter is placed to gravity drainage, and the SPT is plugged.

Complex Diverticula

Anteriorly or dorsally located horseshoe-shaped and circumferential UD presents unique challenges to the pelvic surgeon. Because of their complexity, they frequently present as recurrent diverticula that have been operated on previously. The tissue planes may be obscured complicating the dissection. The anterior location is also challenging to access transvaginally.

Anterior UD can attain large size, leading to difficulty filling the dead space created after excision. The subsequent urethral defect can be quite large (>2 cm). Clyne and Flood [118] described an approach to anterior horseshoe-shaped UD using a suprameatal incision. The authors utilized a double-wrapped porcine xenograft to aid in filling of dead space. Retropubic approaches have also been described [119]. However, for circumferential diverticula, a separate vaginal incision would also be necessary to excise the ventral portion of the diverticulum (Figure 110.22). A parasagittal vaginal incision has been described with detachment of the urethra from the inferior pubic ramus laterally to facilitate anterior dissection [120]. Rovner and Wein [121] introduced a novel technique for excision and reconstruction of dorsal or circumferential UD by dividing the urethra to access the anterior portion of the diverticulum. Once excised, an end-to-end urethroplasty or diverticular sac urethroplasty is performed [121]. Martius flap interposition was performed in nearly all patients in their series to help with closure of dead space (Figures 110.27 and 110.28).

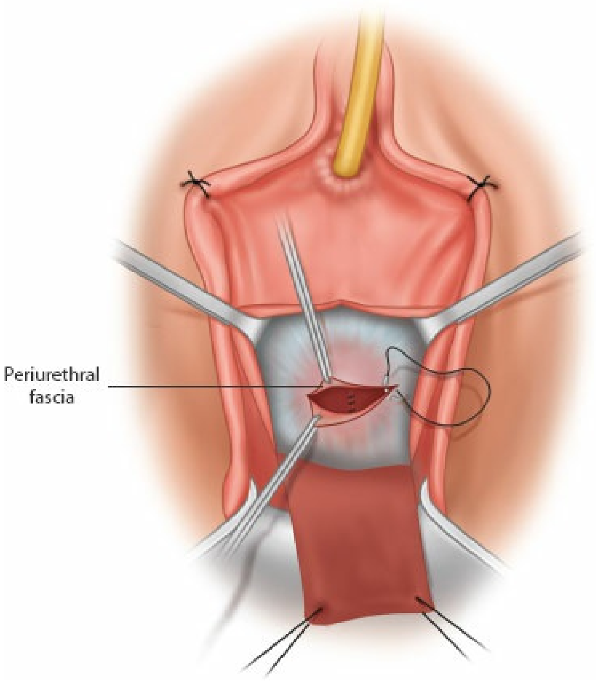

Figure 110.19 The periurethral tissue is closed transversely with 3-0 absorbable suture.

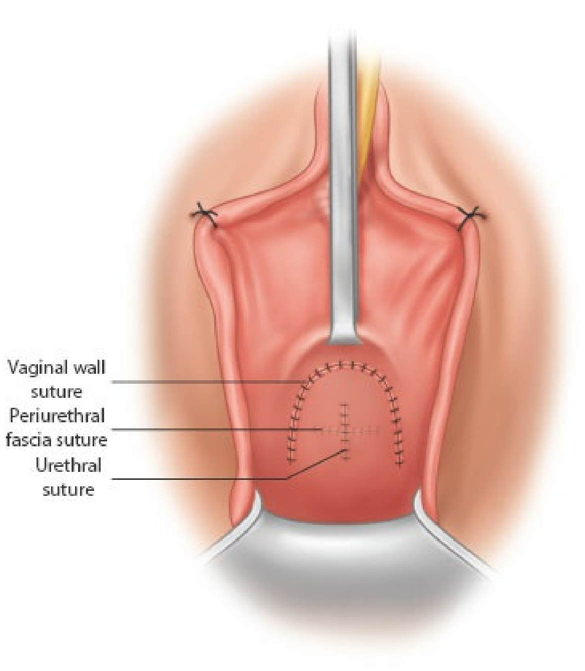

Figure 110.20 The vaginal wall flap is closed, resulting in a three-layer closure with no overlapping suture lines.

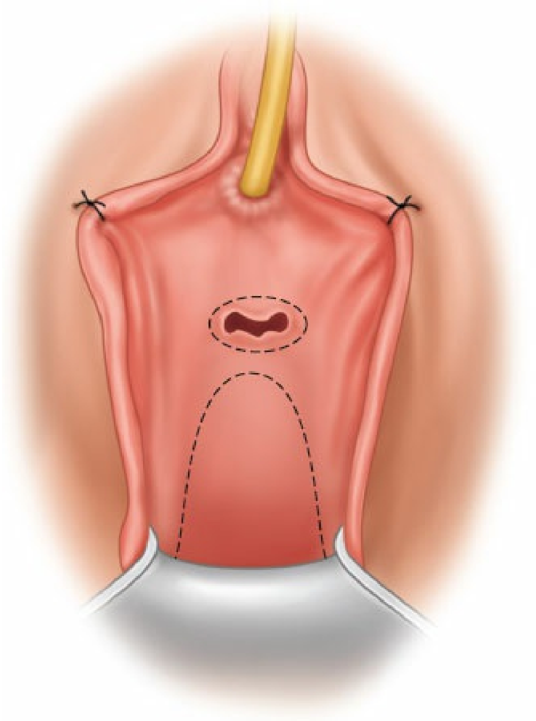

Figure 110.21 An inverted U-incision is made in the vaginal wall with the apex just proximal to the fistula.

Concomitant Anti-Incontinence Procedures

If a PVS is being placed, it is placed over the periurethral fascial layer. If a Martius flap is also being utilized, the sling is generally placed over the Martius fat pad. The dilemma is the need for cystoscopy following retropubic passage of the needles used to deliver the sling sutures from the vaginal to the suprapubic incision to ensure that the sling passers have not entered the bladder or urethra (Figure 110.23).

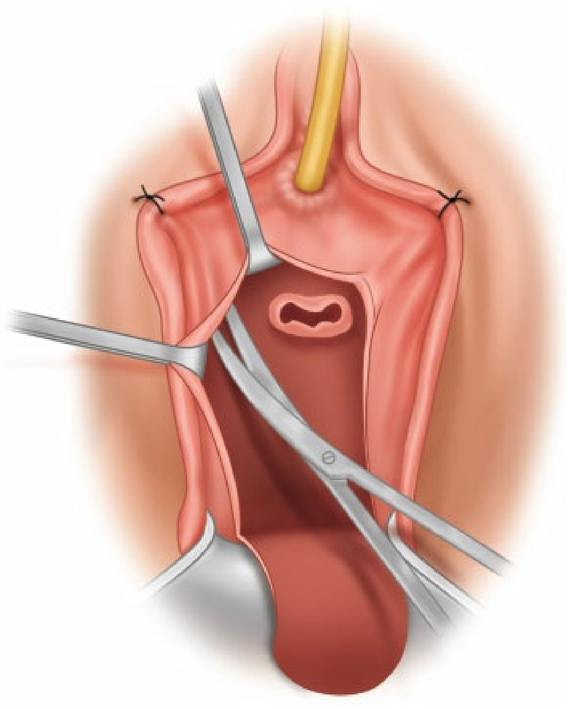

Figure 110.22 The fistula is circumscribed but not excised. The avascular plane beneath the lateral vaginal wall is developed.

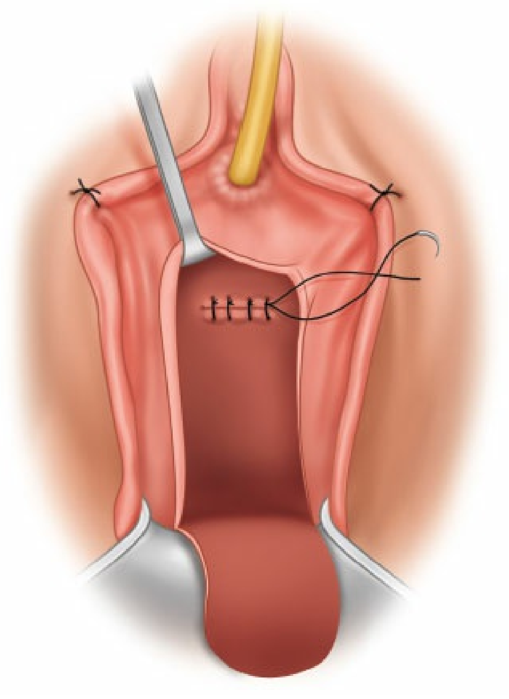

Figure 110.23 The fistula is closed with absorbable suture.

Many advocate for passing the sling prior to the diverticulectomy or following excision of the diverticulum, but prior to the urethral closure. If placed prior to the diverticulectomy, the sling can be carefully packed into the vaginal incision out of harm's way or permitted to hang loosely while the urethra is addressed. In this fashion, gentle cystoscopy can be performed prior to opening the urethra to avoid enlarging the urethral defect or injuring the urethral tissues. The advantage of passing the sling sutures prior to the diverticulectomy is that the cystoscope does not have to be passed over an open urethrotomy or urethral reconstruction; however, the presence of the diverticulum can make the retropubic needle passage difficult. Conversely, while the passage of the needles may be easier if the diverticulectomy has already been completed, cystoscopy with a urethral disruption requires a skilled touch to avoid enlarging the urethral defect. Finally, some will proceed with completion of the diverticulectomy and closure of the first two layers prior to passing the sling, understanding the risk of passing a scope over a fresh urethral closure. While there is no single correct approach, surgeons must be aware of the pros and cons of each alternative.

A synthetic sling should never be utilized in the face of a diverticulectomy due to the risk of urethral erosion, though one group did report placement of a synthetic sling over a biological graft interposed between the urethra and the sling [122]. Consideration of a synthetic sling in patients who have undergone a diverticulectomy in the past and at what interval postdiverticulectomy remains controversial. Historically, bladder neck suspensions (BNSs) could be performed concomitantly with a urethral diverticulectomy [11,123] as there was no suburethral component to the anti-incontinence technique and therefore minimal risk of disruption of the urethral reconstruction by the anti-incontinence procedure. However, BNS are no longer routinely utilized due to the suboptimal outcomes and durability. Consideration of a Burch urethropexy is reasonable in this situation, though it is limited by the necessity to enter the abdomen (Figure 110.24).

Postoperative Management

The vaginal packing is removed no later than the morning of postoperative day 1. All patients receive 24 hours of intravenous antibiotics. Antimuscarinics are used to minimize bladder spasms but are discontinued 24 hours prior to a VCUG that is performed 14–21 days postoperatively. At the time of this first VCUG, approximately 50% of patients have some extravasation from the urethral reconstruction site [4]. When extravasation is evident, the SPT is placed to gravity drainage; the urethral catheter is *not* reinserted. A follow-up VCUG is obtained 7–10 days later. This pattern is repeated with intervals at the discretion of the surgeon until there is no extravasation, at which time the SPT is clamped, and a postvoid residual (PVR) is checked. If it is 100 mL or less, the SPT is removed; if the PVR exceeds 100 mL, the SPT is left in place until this volume decreases (Figure 110.25).

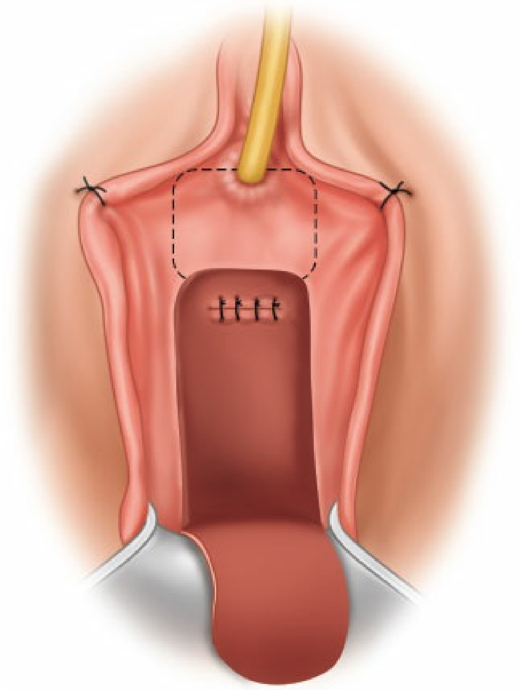

Figure 110.24 Two longitudinal incisions are made to create medially based flaps.

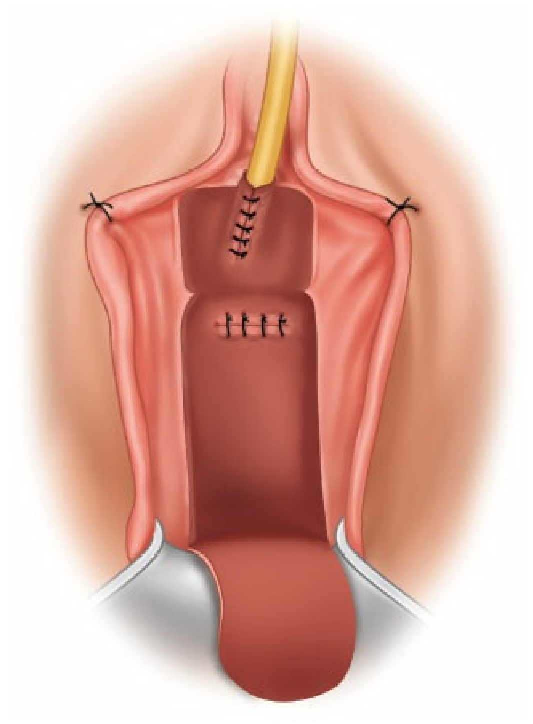

Figure 110.25 The flaps are rolled over a 14-F urethral catheter.

Table 110.8 Complications of Transvaginal Urethral Diverticulectomy

Complications	**% Range of reported incidence**
Urinary incontinence	1.7–16.1
UVF	0.9–8.3
Urethral stricture	0–5.2
Recurrent UD	1–25
Recurrent UTI	0–31.3
Other • Hypospadias/distal urethral necrosis • Bladder or ureteral injury • Vaginal scarring or narrowing, dyspareunia, etc.	

Source: Rovner ES, Chapter 78: Bladder and urethral female diverticula, in: Wein AJ et al., eds., *Campbell-Walsh Urology*, 10th ed., Saunders, Philadelphia, PA, 2012, pp. 2262–2289.

Results and Complications

Potential complications following a urethral diverticulectomy include incontinence, UD recurrence, UVF, irritative symptoms, urethral stricture, and general postoperative complications [4] (Table 110.8).

Ganabathi et al. [11] reported on 63 women who had been treated for UD between 1982 and 1992. Fifty-six were treated operatively including 29 who received a diverticulectomy alone and 27 who underwent a concomitant BNs. seven were observed, among whom three declined surgery and four had small asymptomatic diverticula. Complications included recurrent diverticula in two, UVF requiring surgical repair in one, early postoperative UTI in six, and suprapubic tenderness in one who had undergone a concomitant BNs. The two recurrences of the UD occurred distal to the initial repair site. The majority of patients in this series were completely continent with 80.4% dry or requiring no pads and only 1/56 (2.8%) reporting severe incontinence, defined as requiring several pads a day. A greater percentage of the patients who underwent diverticulectomy alone were reported as continent than were those who underwent diverticulectomy with concomitant BNS (Table 110.8). It was reported that incontinence was more frequently secondary to SUI than to detrusor overactivity (i.e., urgency), despite the presumed increase in bladder neck support (Figure 110.26).

Reeves et al. [16] reported a more contemporary series of 89 patients who underwent diverticulectomy by one of two surgeons over an 8-year period with follow-up ranging from 3 to 20 months. Seventy-two percent were continent postoperatively, with 13 (14.6%) experiencing de novo SUI, 3 (3.4%) had recurrent diverticula. Two had abnormal pathology within the diverticulum, including one with leiomyoma and the other with squamous cell carcinoma.

The largest series was reported by Ingber et al. [124]. One hundred and twenty-two patients underwent urethral diverticulectomy over the course of 12 years. Thirteen percent had recurrence of their UD requiring further surgery; a significant number of whom had had previous pelvic surgery excluding diverticulectomy prior the excision of their UD. Other risk factors for recurrent UD were multiple UD or proximal UD. Sixty-one (50%) of the patients responded to a questionnaire at a mean follow-up of 50.4 months. Thirty-nine percent had a UTI within the previous year and 23% had three or more UTIs over the same time period. Twenty-six percent reported persistent pelvic pain or pain with urination.

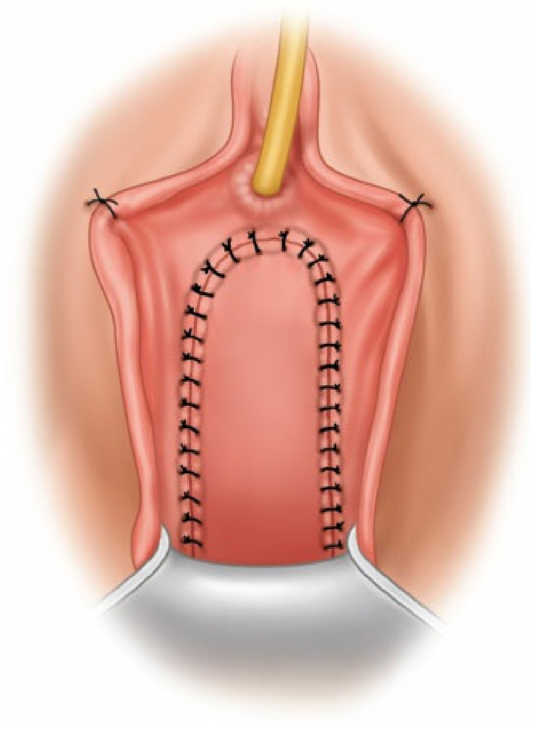

Figure 110.26 The vaginal flap is closed with a running, locking absorbable suture.

Postoperative incontinence may represent persistent SUI that was present preoperatively. De novo SUI has been reported in up to 49% of patients who underwent a urethral diverticulectomy [125,126]. This situation can be avoided by a comprehensive preoperative evaluation such that, if indicated, urinary leakage can be addressed at the time of diverticulectomy [4,11,16]. Incontinence can also result from UVF, recurrent diverticulum with paradoxical loss of urine with stress, infection, persistent or de novo detrusor overactivity, or new onset SUI. The first two conditions may require surgical intervention. New onset SUI may be a result of the urethral dissection, which can compromise urethral support, or secondary to dissection beneath the proximal urethra and bladder neck, which is often necessary when removing a large UD.

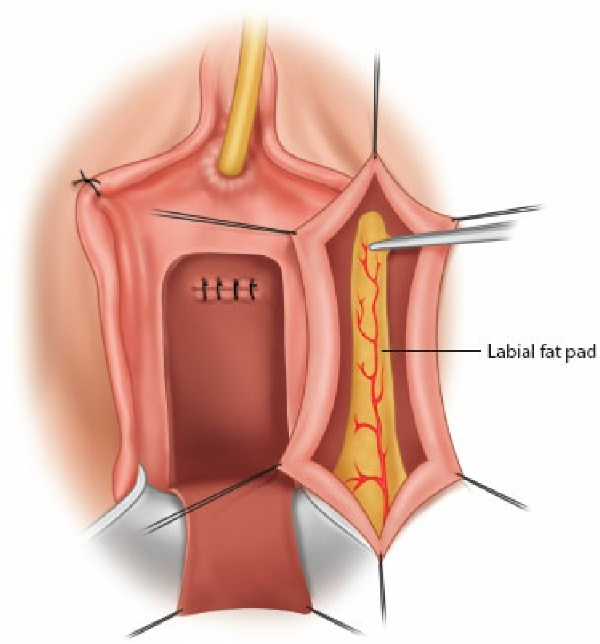

Figure 110.27 The labium majus is incised, and the Martius fat pad graft is mobilized with care to preserve the posteriorly located pudendal vessels.

Though preoperative urinary urgency and frequency symptoms tend to abate in most patients following urethral diverticulectomy, some patients will have persistent symptoms (Stav, 2008). In such cases, the urgency and overactive bladder symptoms should be addressed based upon the American Urological Society/Society of Urodynamics, Female Pelvic Medicine, and Urogential Reconstruction OAB Guidelines [127]. First-line therapy includes behavioral therapy and dietary modification and second-line therapies include antimuscarinic or beta-3 agonist pharmacotherapy (Figure 110.27).

Recurrent UD is often a result of failure to identify multiple UD preoperatively, secondary to lack of either suspicion or proper high-quality studies [11,16]. Incomplete excision of the diverticular neck and faulty closure of the urethral defect are also possible causes. This problem, if anticipated intraoperatively based on tissue quality, can be managed with interposition of a Martius fat pad graft between the vagina and urethra [11]. For small, distal recurrences, endoscopic saucerization or Spence marsupialization may suffice [4]; however, caution must be exercised not to injure the proximally located continence mechanism. UVF formation, another potential complication, is managed in much the same manner and may be prevented by intraoperative Martius flap if tissues appear tenuous or if there is any tension in the urethral closure (Figure 110.28).

Finally, urethral stricture may result from extensive excision of the urethral wall at the time of diverticulectomy and can be prevented by a tension-free urethral closure over a 14 or 16 Fr catheter. If this is not possible, reconstruction using vaginal wall or other pedicalized or free flaps can be contemplated, again with consideration of a Martius labial fat pad graft (Figures 110.29 and 110.30).

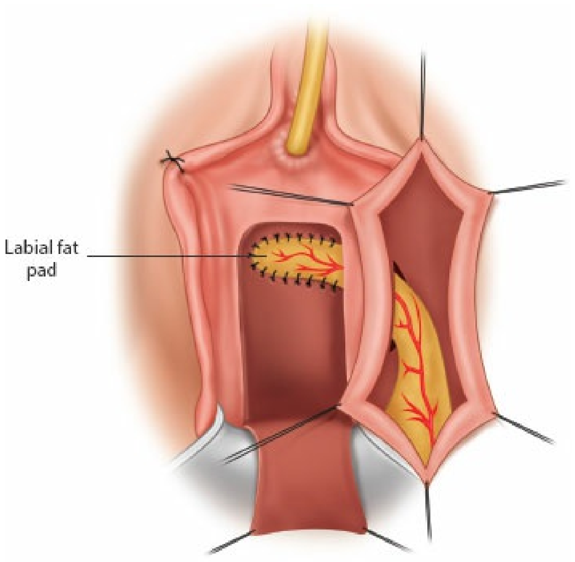

Figure 110.28 The labial fat pad is passed through a medial tunnel and secured over the fistula repair site.

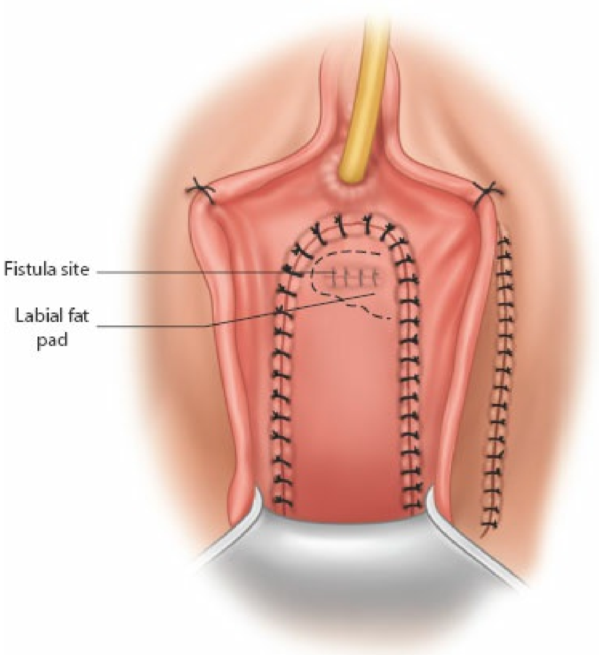

Figure 110.29 The vaginal wall flap is advanced over the fat pad graft, resulting in closure with no overlapping suture lines.

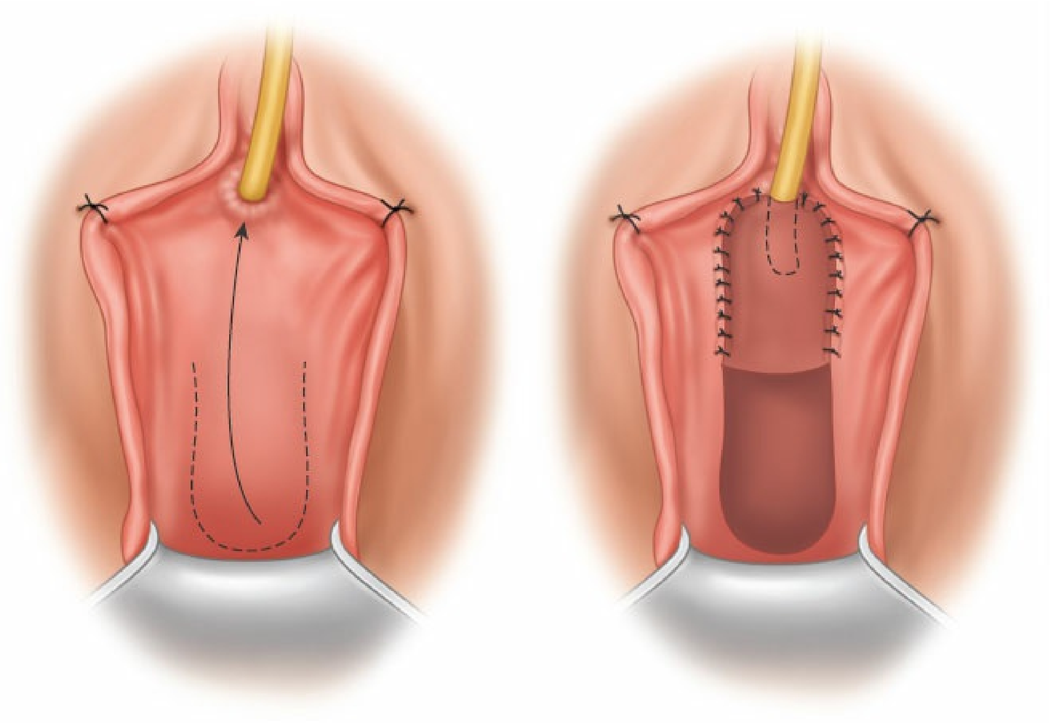

Figure 110.30 A meatus-based vaginal flap is rotated distally.

CONCLUSION

UD is likely an underdiagnosed entity, though improved imaging techniques have improved their detection over the years. While asymptomatic UD does not need to be excised, symptomatic UD can prove to be a diagnostic and therapeutic challenge. Careful and thorough evaluation is imperative to allow for consideration of other associated conditions, and meticulous surgical technique can provide excellent results for our patients.

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111 Diagnosis and Management of Female Urethral Stricture Disease

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INTRODUCTION

Urethral stricture is a true narrowing or scarring of the urethra that can result in bladder outlet obstruction with subsequent decreased urine flow, elevated postvoid residual (PVR), and a variety of lower urinary tract symptoms (LUTSs). Less common urethral strictures can cause urinary retention, renal failure, hydronephrosis, and pyelonephritis [1,2]. Like any cause of obstruction, patients may present with voiding symptoms and/or storage symptoms (frequency, urgency, urgency incontinence). The incidence of true female urethral stricture is not known, and treatments for it have not been extensively studied. In 2013, Osman et al. performed a systematic review of all surgical techniques for the treatment of female urethral strictures and found only 114 patients reported in the world literature [3]. Despite the relatively sparse data on treatment of female urethral stricture, the diagnosis accounted for 1.2 million office visits in the United States from 1992 through 2000 and had an annual expenditure of $69 million in 2000 [4]. This apparent discrepancy is likely the result on of over diagnosis of women without true stricture disease and underutilization of surgery to treat true urethral strictures. Fortunately, the concept of the “narrow” yet unscarred urethra as a cause of LUTSs and recurrent urinary tract infections is not as popular as it once was, and the practice of urethral dilatation has decreased. In more contemporary series, urethral stricture has been reported to be the cause of urodynamically proven bladder outlet obstruction in 4%–13% of women [5–7].

ANATOMY

Urethral stricture may occur anywhere along the length of the urethra from the bladder neck to the urethral meatus. The female urethra is approximately 3–4 cm in length. It is comprised of an inner mucosal epithelium layer with numerous infoldings, creating an effective seal against the passive loss of urine. Beneath the mucosa lies a rich, vascular network that includes elastic tissue. The proximal 75% of the urethra has two smooth muscle layers, an outer circular and inner longitudinal layer. These layers thin as they traverse distally, and terminate before the urethral meatus. Outside of the smooth muscle layer lays the striated urethral sphincter muscle, which extends the whole length of the urethra and is critical to the continence mechanism. It is horseshoe shaped, more dense dorsally, and is thickest in the middle third of the urethra. Surrounding this is a collagen-rich fibromuscular envelope comprising the periurethral fascia. Other important structures to consider during surgical treatment of urethral structures are the clitoral tissue that surrounds the urethrovaginal complex and supports the urethra along its dorsal aspect, and the neurovascular bundles that traverse along the ischiopubic ramus [8].

There are two primary fascial attachments that provide support to the urethra, the pubourethral ligaments and the periurethral fascia that makes up the suburethral hammock that attaches to the tendinous arch of pelvic fascia on each side. The pubourethral ligaments are a band of fascia that supports the urethra dorsally between the vagina and pubic symphysis. These “ligaments” often serve as a point of anatomic demarcation of the midurethra. The suburethral hammock is comprised of two layers of fascial condensation, the endopelvic fascia and the pubocervical fascia, providing lateral attachment to the tendinous arch. The midurethra is thought to be the center of continence where the striated sphincter complex maintains both active and passive tone.

ETIOLOGY

There are multiple causes of urethral stricture in women. These include infection, inflammation (vulvar dystrophy, lichen sclerosis) radiation, trauma, instrumentation, and prior urethral surgery and aging. However, many times urethral strictures are idiopathic without any obvious cause. Traumatic endoscopic exam or even catheter placement may result in stricture formation. Urethral dilation, one of the treatments of strictures or urethral “narrowing,” may actually cause or worsen strictures. Urethral dilation can result in edema, bleeding, and urinary extravasation that can cause periurethral fibrosis that is often found in pathological specimens of urethral stricture [9]. Rarely strictures may result from estrogen deficiency, usually at the meatus (meatal stenosis). Urethral destruction/ablation may result from urethral trauma, chronic indwelling urethral catheterization (usually in a patient with decreased or absent sensation) or as a complication of urethral surgery.

DIAGNOSIS

The diagnosis of urethral stricture usually requires a high index of suspicion. As with many diagnoses, that suspicion starts with a proper history. The assessment of voiding and storage symptoms (frequency, urgency, incontinence, slow or interrupted stream, hesitancy, incomplete emptying, dysuria), UTI history, and any possible causes of stricture (history of trauma, surgery, catheterization, instrumentation, prior urethral dilation, or urethrotomy) are important. For women with complaints of difficult voiding, slow or hesitant urinary stream, or incomplete bladder emptying, a noninvasive uroflow and PVR can be helpful. Typically, urethral strictures result in a reduced maximum flow rate with a flattened appearance to the flow curve, rather than the typical bell shape. Sometimes, a straining pattern may be noted.

Often, but not always, a significant PVR may accompany the reduced flow. Physical exam may show inflammation or atrophy around the urethral meatus and/or the surrounding vulva. In cases when there is a high suspicion of urethral stricture, one can attempt catheterization (or calibration), and this can be done as part of the physical exam. Some authors have defined failure to admit a 14 French catheter as an inclusion criterion for urethral stricture [10–12]. We usually start with a small 10–12 French catheter. If there is any resistance, the process is stopped, and further, more definitive testings are recommended. In a patient with a true urethral stricture, a 10 French catheter often will not pass [13], but its passage does not rule out a stricture.

Radiographic evaluation of urethral stricture is best accomplished with voiding cystourethrogram; however, in order to perform this test, a catheter must be passed into the bladder. For this, a small 6–8 French catheter can be used if a larger catheter will not pass. In special circumstances, the bladder can be filled via a suprapubic catheter. Sometimes, radiographic evaluation is done as part of a videourodynamics (VUDS) test, where the diagnosis of urodynamic obstruction and localization of the stricture can be made. Typically, one will see distal urethral narrowing with proximal urethral ballooning [1]. Also, for more proximal strictures, VUDS or cystogram allows one to determine the level or point of continence. For example, if the bladder neck is closed with Valsalva, that is usually the level of continence. However, if with straining the bladder neck opens and the level of continence is at or near the stricture, there may be concern for posturethroplasty incontinence.

When malignancy, periurethral or extraurethral pathology is suspected (e.g., palpable mass, prior or current history of genitourinary malignancy), further evaluation of the urethra and surrounding structures may be warranted. In such cases, we prefer MRI as the radiographic test of choice, though CT scan may also be considered.

Finally, endoscopic evaluation can be helpful to evaluate the extent of the stricture. It is often necessary to use a pediatric cystoscope or ureteroscope. If not possible, endoscopy can be deferred until repair. Gentle dilatation of the stricture can be performed to facilitate endoscopy, especially if a biopsy is desired. It is often done with the patient under anesthesia.

TREATMENT OF URETHRAL STRICTURE

The treatment algorithm for female urethral stricture is not as well defined as in the male. Perhaps, this discrepancy is attributable to the relative rarity of stricture disease in women, combined with the more varied causes of strictures in women. In men, urethral strictures are commonly caused by blunt trauma; however, due to the female urethra’s short length, its anatomic position behind the pubic arch, and its relative mobility, the incidence of stricture following trauma in females is low (range of 0%–6%). More commonly, stricture disease in women is seen following endoscopic or open urethral surgery, urethral dilatation, and pelvic radiation therapy for gynecological malignancies.

Treatment of urethral strictures can be divided into four categories:

1. Conservative management—urethral dilatation and/or self-catheterization
2. Endoscopic
3. Urethroplasty
4. Salvage procedures (bladder neck closure and/or urinary diversion)

The driving factors for treatment of female urethral stricture will often be based on the patient's degree of obstruction, bothersome symptoms, and emptying patterns. In cases in which a patient is adequately emptying and not encumbered with bothersome symptoms, they may be offered the option to be conservatively monitored with routine follow-up. In cases in which treatment is warranted, the course of treatment should be based on the degree of urethral stenosis and/or retention, the functionality of the bladder, and the risk for any upper tract dysfunction. Additionally, if the underlying mechanism of stricture formation can be ascertained, such as radiation, this should be kept in consideration. Ultimately, if there is suspicion for urethral stricture in a woman, it is imperative to fully assess them in order to make an accurate diagnosis for which a proper treatment course may be offered. For example, in cases of pelvic floor dysfunction or dysfunctional voiding, it may present and appear as a urethral stricture, but the treatments are profoundly different. Counseling the patient is very important throughout the process, as symptoms of frequency and urgency may persist even after treatment of a stricture [13].

CONSERVATIVE MANAGEMENT

Conservative options for management of female urethral strictures include self-catheterization or urethral dilation. Selfcatheterization involves teaching the patient how to perform intermittent catheterization at various intervals based on the degree and timing of scarring. If a stricture is diagnosed early, self-catheterization can likely be initiated without requiring urethral dilations or surgical therapies. The patient should be followed at regular intervals to ensure no problems with or worsening symptoms between catheterizations. If a patient fails intermittent self-catheterizations or elects to have more definitive therapy, a discussion regarding other conservative and surgical options should be initiated with the patient.

Urethral dilation gained rapid popularity in the 1960s when it was proposed to dilate a "contraction ring" noted in the urethras of young girls up to 32–45 French [14]. This notion as a treatment for "urethral syndrome" in those with recurrent urinary tract infections and chronic urethritis subsequently expanded. Since then, studies have demonstrated that in the absence of a true stricture, urethral dilation does little in the way of helping with urinary symptoms of frequency and urgency [15,16]. In general, emerging literature advocates against the use of urethral dilation in the absence of a true urethral stricture. This change in management trends is reflected in surveys given to practicing urologists, with those trained within the 10 years prior to 1999 considering dilation to be as largely unsuccessful, contrasted by 21% of those trained more than 10 years before 1999 considering it to be very successful [17].

Despite changes in perception, however, it is still a common practice. Osman et al. recently performed a systematic review of the literature on female urethral stricture and found that 107 of the 221 women studied underwent urethral dilation, making it the most commonly performed procedure for urethral strictures [3]. Of these, one-third had already failed a prior dilation. Another recent British survey found that 69% of urologists still regularly perform urethral dilation despite data to suggest its lack of efficacy [18]. It is unclear why this practice continues, and it has been suggested that generous reimbursements by Medicare may play a role. Analysis of public datasets estimate an annual cost of $61 million for treatment of stricture disease in women, of which the majority (67%) were for ambulatory surgery visits [19]. Diagnosis of urethral stricture in a woman averages a cost of $8444 in health-care costs compared to $4658 in those with similar complaints without that diagnosis.

Long-term data on outcomes of dilation are scarce, and many studies are performed in the absence of the diagnosis of a true urethral stricture. Three recent case–control studies provide some input. Smith et al. evaluated seven patients with stricture less than 14 French diagnosed from findings on cystoscopy and/or VUDS [20]. They were dilated to 30 French, left with a catheter for 1 week, and then asked to intermittent catheterized once a day for 6 months. At a mean follow-up of 21 months, there was an improvement in AUA symptom score by 10.7 points, but three of seven required repeated dilations. Takao et al. [20] evaluated 17 women diagnosed with true urethral stricture that underwent serial dilation over 6 months to 30 French and studied with uroflow 1 week after their last dilation. They found that the urethral calibration increased to a mean of 23.5 French from 18.1 French and the mean uroflow increased to 11.2 mL/s from 9.4 mL/s. Blaivas et al. [21] retrospectively evaluated data for 17 women over a period of 12 years diagnosed with urethral stricture by cystoscopy, urethral obstruction per the Blaivas–Groutz nomogram on urodynamics, and urethral circumference less than 17 French. All women had at least one prior dilation prior to presentation, and of those that underwent another dilation, nearly all had a recurrence (16 of 17 patients) subsequently requiring another dilation or urethroplasty. Success rate at a mean follow-up of 2 years was a meager 6%, thereby prompting the authors to conclude that urethral dilation is very rarely effective. The review by Osman et al. found a mean failure time of 12 months, of which redilations were performed in 56% [3]. At a mean follow-up of 43 months, the urethral dilation success rate was 47% with higher rates of success in those that had not had a prior dilation (58%) than if they had a prior dilation (27%). The authors concluded that in cases of repeat dilation, it often serves primarily a palliative purpose rather than as a cure likely due to extension of the scarring.

Imaging has been used as an aid to dilation. The use of fluoroscopy or transvaginal ultrasound (US) may be required to ensure proper placement and dilation. A case report of the use of transvaginal US during dilation described urethral strictures as having a hypoechoic center that represents the mucosa and a surrounding hyperechoic region that correlates to the nondistensible spongiofibrosis of the periurethral tissue [22]. In this report, 1 month after dilation, a follow-up US showed a normal urethra. In addition to aiding in dilation and other treatments, US may serve as a tool in the future to evaluate for early recurrence or degree of fibrosis and scarring.

A recent study was conducted by Heifari et al. to compare outcomes between intermittent scheduled dilations and on-demand dilations [23]. Women with primary urethral stricture diagnosed by uroflow, elevated PVR (>60 mL), and US were randomized to either undergoing intermittent dilation every 2 months for a total of three dilations or on-demand dilation in case of recurrence. At 6 months, the on-demand group demonstrated no recurrences requiring repeat dilation, and there were similar improvements in PVRs and uroflow between both groups. The group concluded that on-demand dilations are superior because they provide similar outcomes with less urethral manipulation.

Finally, adjunctive therapy with vaginal estrogen in order to improve atrophy and improve tissue either pre- or posttreatment can be considered [13,24]. Atrophic vaginitis and other postmenopausal changes that often cause LUTSs or meatal stenosis are also often helped with topical vaginal therapy and may also be an option to consider [25].

ENDOSCOPIC MANAGEMENT

In the cases in which dilation fails or the patient elects to undergo other therapies, some have considered endoscopic management with either direct visual internal urethrotomy (DVIU) or laser treatment of the scar. Very scant literature exists on endoscopic management of urethral strictures in women. Massey and Abrams in 1988 reported 80% success in women that underwent dilation or DVIU [26]. Alternatively, a laser could be used to endoscopically incise a stricture (CO_2, argon, KTP, Nd:YAG, holmium:YAG, excimer lasers) with the goal being to vaporize tissue without causing significant harm to surrounding tissue. Most of the existing literature for lasers is for the treatment of male urethral strictures and as with literature in female strictures is sparse [27,28].

URETHROPLASTY

There are a number of procedures that can be performed to reconstruct the strictured urethra. These range from meatoplasty to vaginal inlay flaps for distal strictures, more extensive vaginal flap urethroplasty for midurethral strictures, and onlay grafts for mid and proximal urethral strictures. We will describe examples of each of these techniques based on the anatomic location of the stricture. Successful urethral reconstruction, no matter where the location of the stricture, is based on several principles including identification of the entire stricture, tension-free reconstruction, and adequate drainage/stenting when necessary.

Meatal stenosis and stricture of the distal urethra are two of the most common indications for urethral reconstruction. The distal urethra is particularly susceptible for stricture from instrumentation, trauma, radiation, and aging. The two most common types of urethral reconstruction that we utilize for distal urethral stricture are (1) distal urethrectomy with advancement meatoplasty for very distal strictures (usually involving the distal 1 cm of the urethra) and meatal stenosis and (2) a proximally based distal vaginal flap urethroplasty (Blandy urethroplasty) for lesions 1–2 cm proximal to the urethral meatus. Stricture and other lesions of the midurethra often result from iatrogenic injury associated with urethral diverticulectomy, incontinence surgery or urethral instrumentation, and endoscopic trauma. They can be associated with urethrovaginal fistulae or loss of the mid to distal urethra that can occur as a result of long-term indwelling catheters. For midurethral lesions, beyond the limits of a Blandy urethroplasty, we will typically employ a vaginal flap urethroplasty or, in cases when suitable vaginal tissue cannot be found or is not appropriate, a free graft using buccal mucosa. For proximal strictures and strictures involving the entire urethra, the buccal mucosal graft is our procedure of choice.

Distal Urethrectomy with Advancement Meatoplasty

Meatotomy can be performed to treat distal stenosis by simple ventral incision of the meatus and suturing the cut end of the meatus to the vaginal wall. However, in our experience, circumferential, distal urethrectomy and advancement meatoplasty work best for distal strictures and urethral prolapse. It can be applied to meatal stenosis and strictures within approximately 1 cm from the meatus, but works best for true meatal stenosis [29].

To start, the extent of the stricture is identified to make certain that distal urethrectomy is appropriate. If desired, interrupted absorbable sutures can be placed in the more proximal, healthy urethral mucosa (at least 2 mm proximal to the strictured segment), at the 6 and 12 o’clock position, so that the mucosa does not retract inward. Identification of healthy mucosa can be aided with a nasal speculum. Sometimes, a small ventral urethrotomy is necessary to determine the proximal extent of the stricture. The procedure is described in Figure 111.1. Depending on the degree of reconstruction, a urethral catheter may be left in place for 1–3 days postoperatively. This is particularly useful as postoperative swelling can cause urinary retention.

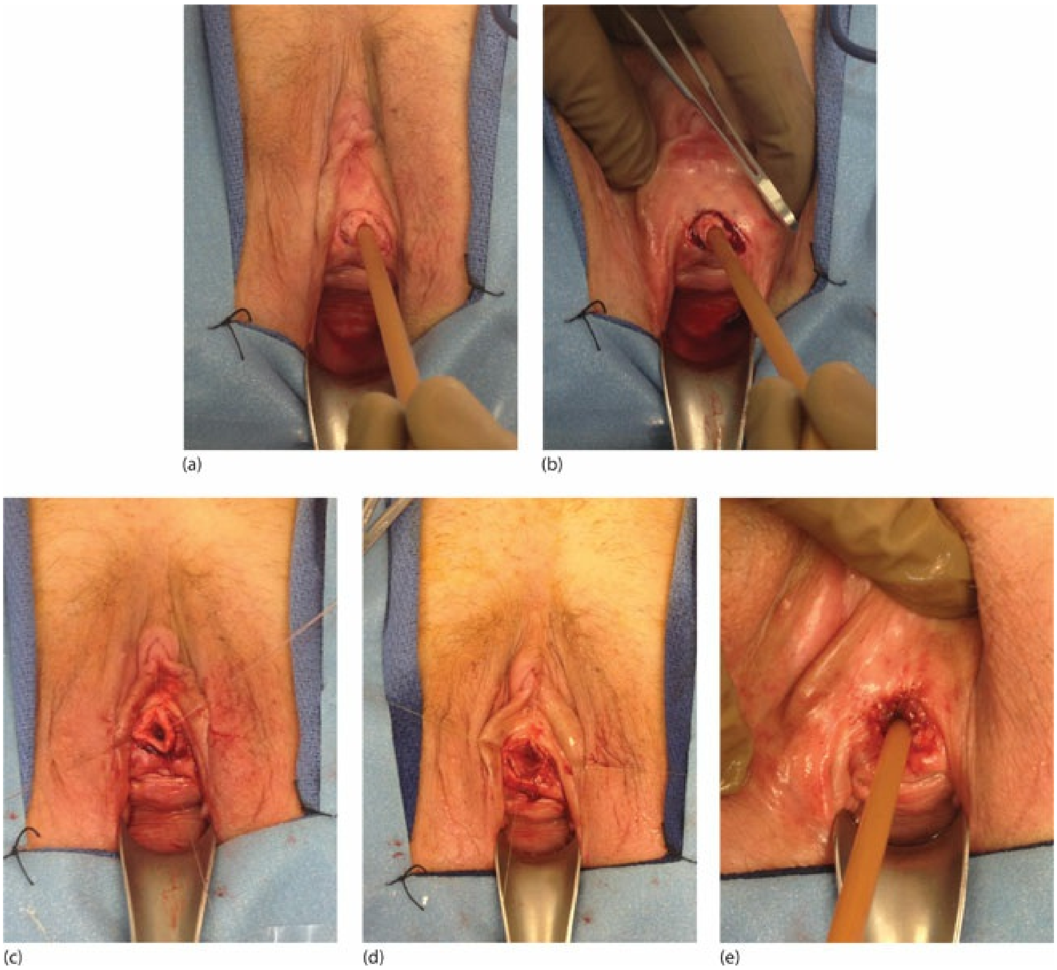

Figure 111.1 Distal urethrectomy with advancement meatoplasty. (a) A circumferential incision is made around the urethra at the mucosal/epithelial junction. (b) The urethra is dissected off of the periurethral fascia for the extent of the stricture. (c) Stay sutures of 4-0 delayed absorbable suture (polyglycolic acid or Monocryl) can be placed proximal to the portion of the urethra to be excised. (d) The distal urethra is excised and the stay sutures are brought through the vaginal epithelium. (e) Circumferential suturing of the urethral mucosa to the vaginal epithelium completes the meatoplasty.

Distal Urethroplasty with Vaginal and Vestibular Inlay Flaps

For distal strictures that have a proximal limit of up to 2 cm from the urethral meatus, a Blandy urethroplasty or proximally based vaginal pedicle inlay flap can be done. The procedure was originally described but never reported by Blandy, but was subsequently reported on by Schwender et al. [30]. This procedure recreates the ventral portion of the urethral meatus and replaces the distal ventral urethra with a flap of vaginal wall. The procedure is described in Figure 111.2 [29]. As with any stricture, the first step is identifying the proximal extent of the stricture. After completion on the urethroplasty, a 14–16 French Foley catheter is left indwelling for several days. Montorsi et al. [32] described a similar procedure where the distal urethra is incised dorsally and a vestibular pedicle is sutured to the dorsal distal urethra. Here, the blood supply of the flap is distally based.

Outcomes for Distal Urethral Reconstruction

Early postoperative complications of distal urethral reconstruction are generally self-limiting and include bleeding, transient urinary retention secondary to swelling, and urinary tract infection. There is little in the literature regarding the outcomes for distal urethral reconstruction. Schwender et al. [30] reported an 89% success rate (no further treatment necessary) for eight women undergoing distal ventral vaginal flap inlay urethroplasty. Onol et al. [31] reported 100% objective success in 10 patients. Using a similar vestibular flap inlay pedicle, Montorsi et al. reported that 88% of 17 women had relief of obstruction [32]. Regarding distal urethrectomy and advancement meatoplasty, we would expect similar success rates. When this procedure occasionally fails, it is usually due to the reformation of scar tissue caused by inadequate resection at the initial procedure.

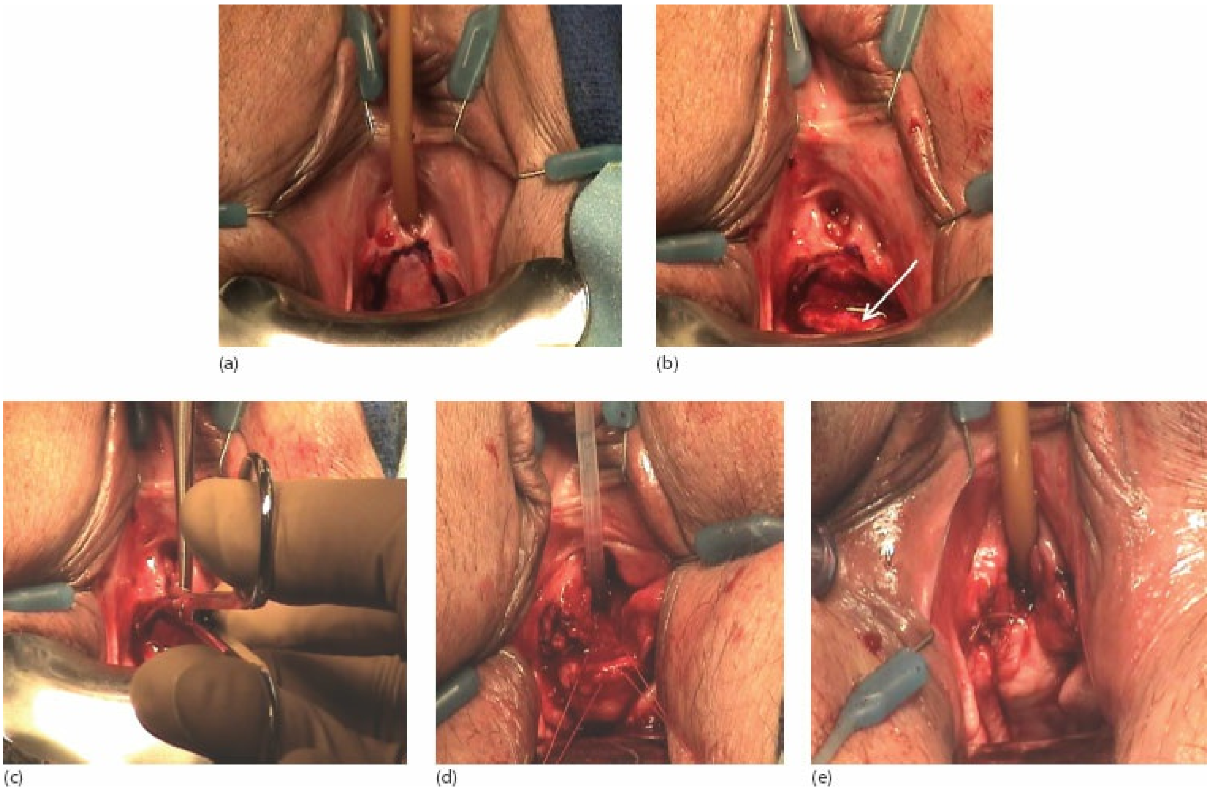

Figure 111.2 Distal urethroplasty with vaginal inlay flap (Blandy urethroplasty). (a) The vaginal inlay flap is

outlined with a marker. (b) An inverted-U incision is made in the anterior vaginal wall with the apex of the U at the urethral meatus, and using sharp dissection, a proximally based vaginal flap is raised that is slightly longer than the length of the stricture, usually 2–3 cm. (c) The ventral urethra is incised ventrally at the 6 o'clock position, from the meatus through the stricture into normal urethral mucosa. (Cystoscopy can also be used to aid in the identification of the limit of the stricture.) (d) The apex of the vaginal flap is advanced to the apex of the incised ventral urethra and is secured with 4-0 polyglycolic acid or Monocryl sutures. (e) The edges of the vaginal flap are approximated to the urethral mucosal edges using an interrupted, 4-0 polyglycolic acid or Monocryl sutures completing the urethroplasty. (From Nitti VW and Rosenblum N, Female urethral reconstruction, in: Nitti WW, Rosenblum R, and Brucker BM, eds., Vaginal Surgery for the Urologist, Elsevier Saunders, Philadelphia, PA, 2012, pp. 137–154. With permission.)

Vaginal Flap Urethroplasty

The mid or proximal segment of the female urethra, between the true bladder neck and pubourethral ligaments, contains the striated sphincter complex and levator ani insertion. The most critical components of both active and passive continence are located in this important segment of urethra. The Blandy proximally based vaginal flap urethroplasty (described earlier) can be used to treat some midurethral strictures, particularly those that are at the more distal portion of the midurethra. In cases of strictures that are isolated to the midurethra and do not include the distal urethra, one may also consider a free graft, such as buccal mucosa (see section "Onlay Urethroplasty Using a Free Graft" and Figure 111.5).

Vaginal flap urethroplasty, popularized by Blaivas [33], can be utilized to recreate a functional urethra by way of local, healthy tissues. It can be used for strictures as well as ablation/erosion of the mid to distal urethra. This technique can also be applied in cases of a shortened urethra associated with vaginal voiding in order to improve urethral length. In cases of urethral stricture, a longitudinal incision is made in the anterior vaginal wall directly beneath the urethra. The urethra is exposed and a longitudinal incision is made in the ventral urethra exposing the entire segment of strictured or diseased urethra, until more proximal, viable tissue is identified. This will become the dorsal plate of the urethra. In cases of urethral ablation, the vaginal wall distal to the urethra meatus becomes the ventral plate of the urethra.

There are two variations of the vaginal flap urethroplasty that we commonly employ. In the first, a flap of full thickness vaginal wall, including the epithelium, in a U configuration can be employed as a patch or ventral plate of neourethra (Figure 111.3). The second, for cases of urethral ablation, where there is compromised anterior vaginal wall tissue proximal to the urethra, medially based flaps can be created from the vaginal wall distal to urethra. In both cases, an autologous rectal fascia pubovaginal sling can be done simultaneously if there is coexisting stress urinary incontinence (Figure 111.4). In both cases, a Foley catheter is left indwelling for 10–14 days after the surgery.

Outcomes for Vaginal Flap Urethroplasty

Success rates for vaginal flap urethroplasty are quite good. In the largest series in the literature, Flisser and Blaivas reported successful anatomic repair in 93% of 72 women [33]. Sixty-two of the patients were incontinent and underwent simultaneous pubovaginal sling with a success rate of 87%. Incontinence occurred postoperative in 25% of women who were continent preoperatively. Potential complications of vaginal flap urethral reconstruction include recurrent urethral stricture/meatal stenosis, vaginal flap necrosis, de novo stress or urgency incontinence, vaginal shortening, and dyspareunia. Simonato and colleagues used a distal C-shaped flap for midurethral strictures [11]. The procedure is similar to that described in Figure 111.4. The distal to midurethral is incised from the meatus through the stricture, and the vaginal wall is mobilized from one side on a laterally based pedicle to create a new ventral mid to distal urethra. They reported "normal voiding" at a mean follow-up of 70.8 months in all six patients who had the procedure, but one needed to do intermittent self-catheterization. Overall, the success rate was 83%.

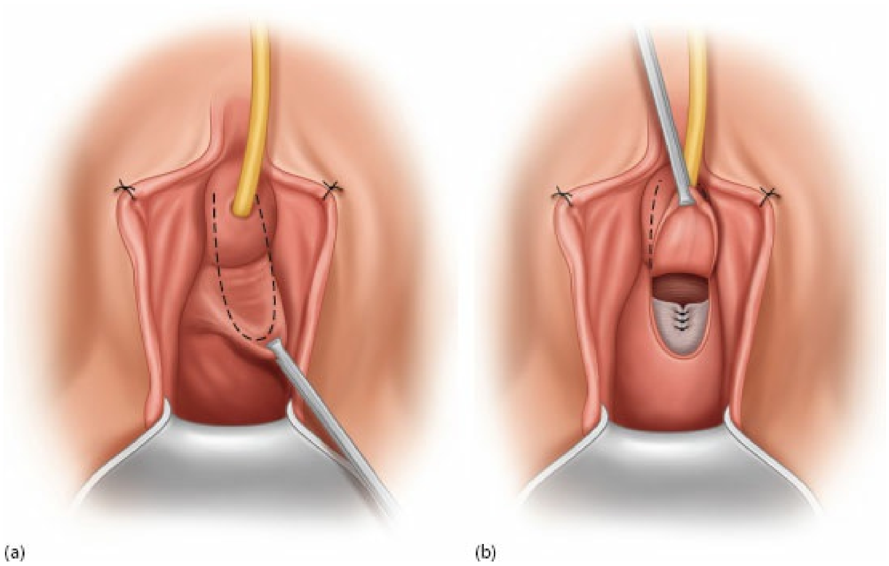

Figure 111.3 Proximally based vaginal flap urethroplasty. (a) U-shaped incision is made in the anterior vaginal wall. The dimensions of the U are approximately 1–1.5 cm wide and 2–3 cm long. In cases of stricture, where the opened urethra will be used as the dorsal plate of the neourethra, the top of the U is at the level of the proximal part of the opened urethra. In cases of urethral ablation (shown here), the top of the U extends to where the neomeatus will be. (b) The flap is then flipped up and sutured to the edges of the open distal urethra (stricture) or proximal vaginal wall (ablation) using a running 4-0 PDA suture on each side. Lateral vaginal wall flaps are made so that the anterior vaginal wall can be closed primarily, creating a second layer of tissue beneath the newly created urethra. If desired, an autologous fascia or biological pubovaginal sling can be placed at the bladder neck. (Adapted from Nitti VW and Rosenblum N, Female urethral reconstruction, in: Nitti WW, Rosenblum R, and Brucker BM, eds., *Vaginal Surgery for the Urologist*, Elsevier Saunders, Philadelphia, PA, 2012, pp. 137–154. With permission.)

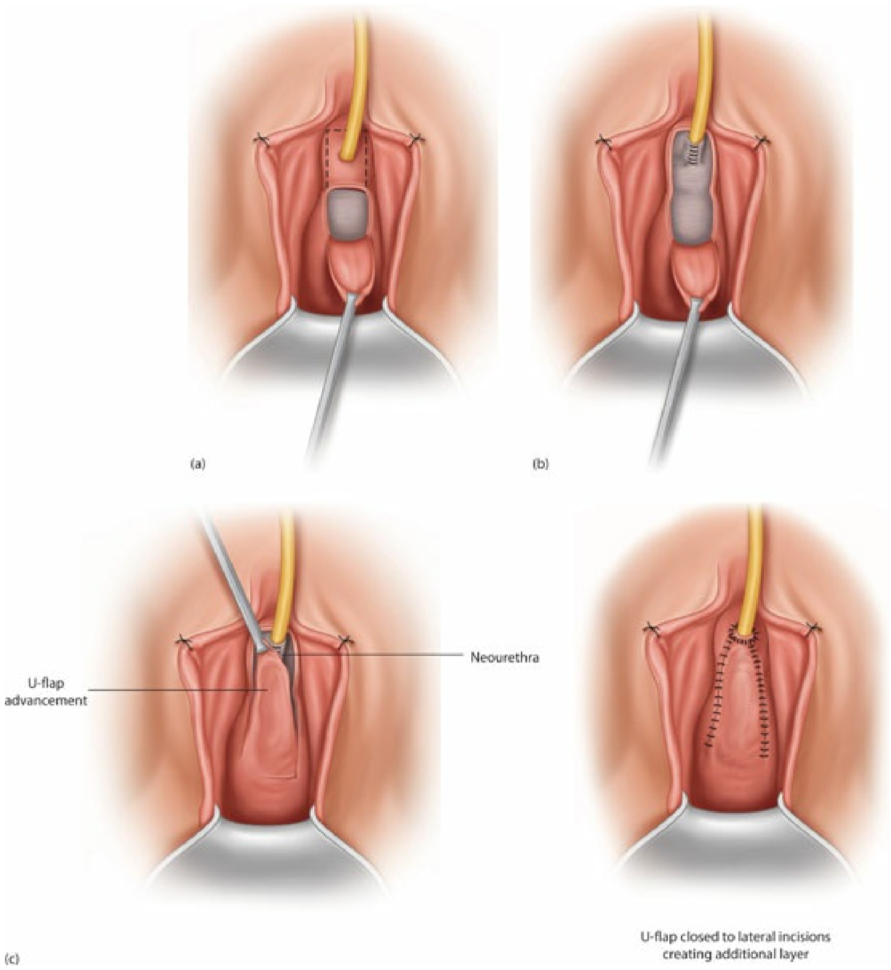
(a)
(b)
U-flap advancement
Neourethra
(c)
U-flap closed to lateral incisions creating additional layer

Figure 111.4 Distally based vaginal flap urethroplasty. (a) A rectangular or square island of vaginal wall is created by making lateral, vertical, proximal, and distal lateral incisions around the urethral meatus. In addition, an inverted-U incision is made with the apex of the U at the level of the lower border of the rectangle flap. (b) The flap is then dissected medially on both sides so that the vaginal wall can be tubularized over a catheter, creating a neourethra using 4-0 polyglycolic sutures. This is usually done over a 14 French Foley catheter. (c) The proximal inverted-U flap is then advanced over the neourethra and closed to the lateral incisions where the rectangular flap was taken, as an additional layer of tissue. If desired, a pubovaginal sling can be placed prior to advancement of the inverted-U flap. (Adapted from Nitti VW and Rosenblum N, Female urethral reconstruction, in: Nitti WW, Rosenblum R, and Brucker BM, eds., *Vaginal Surgery for the Urologist*, Elsevier Saunders, Philadelphia, PA, 2012, pp. 137–154. With permission.)

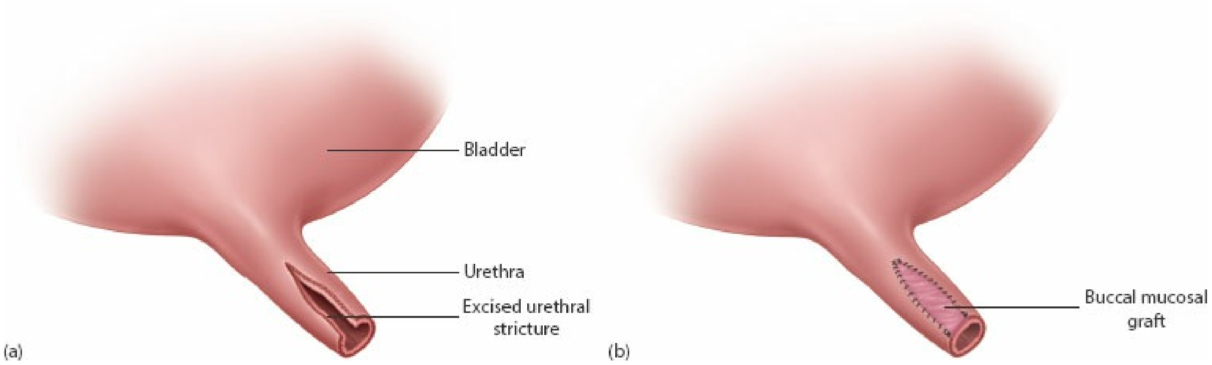

Figure 111.5 Dorsal onlay urethroplasty. (a) The urethra is incised dorsally at 12 o'clock through the entire length of the stricture. (b) The mucosal surface of the graft is placed into urethral lumen and sutured with running 4-0 or 5-0 delayed absorbable sutures to the open urethral edges. (Adapted from Nitti VW and

Rosenblum N, Female urethral reconstruction, in: Nitti WW, Rosenblum R, and Brucker BM, eds., *Vaginal Surgery for the Urologist*, Elsevier Saunders, Philadelphia, PA, 2012, pp. 137–154. With permission.)

Onlay Urethroplasty Using a Free Graft

When suitable vaginal tissue is not available or practical for urethral reconstruction, we prefer using a free graft to patch the urethra. It is our procedure of choice for proximal and panurethral strictures. Buccal mucosa, which has been used extensively in male urethral reconstruction, is currently the most widely used free graft in female urethral reconstruction as well. Some authors have used lingual mucosa harvested from the ventral–lateral aspect of the tongue claiming that it has many of the same properties as buccal mucosa, and avoid potential injury to the parotid duct and mental nerve. Free grafts can be placed dorsally or ventrally. We prefer dorsal placement primarily because graft is well supported mechanically and rests on a well-vascularized bed. Also, sacculation and the risk of urethrovaginal fistula can be minimized.

A stepwise description of the procedure is as follows:

1. The urethra is cannulated with a small catheter (5–6 French).
2. A suprameatal inverted-U incision is made to expose the dorsal urethra. Traction sutures may be placed in the urethral mucosal at the meatus at the 3 and 9 o’clock positions.
3. The urethra is sharply dissected from the vulvar epithelium, and a plane is developed between the urethra and clitoral cavernosal tissue with care so as not to damage the bulb, clitoral body crura, or the anterior portion of the striated sphincter that should be reflected upward.
4. The urethra is incised dorsally at the 12 o’clock position from the urethral meatus through the stricture, to normal unscarred urethral mucosa (Figure 111.5a). A stay suture of 4-0 or 5-0 polyglycolic acid or Monocryl can be placed at this point.
5. The stricture is measured so that an appropriately sized length of buccal (or lingual) mucosa approximately 1.5–2 cm wide can be harvested.
6. The graft is fixed to the apex of the stricture with the previously placed stay suture.
7. The sides of the graft are sutured to the urethra with 4-0 or 5-0 polyglycolic acid or Monocryl sutures over a 14–18 French Foley catheter (Figure 111.5b).
8. The graft is fixed dorsally with one suture, and the augmented dorsal urethra is quilted to the clitoral body to cover the new urethral roof.
9. The vulvar epithelium is closed.

Outcomes for Free Graft Onlay Urethroplasty

Outcomes for buccal and lingual musical onlay grafts come from relatively small series (1–15 patients) but are quite good in the short term with a mean follow-up 6–27 months [31,34–38]. Success rates for dorsal onlay are 93%–100% in 28 patients from combined studies [31,34–37], compared to 50%–100% for 4 patients with ventral onlay [31,38].

SALVAGE PROCEDURES

In cases of complete urethra destruction or refractory stricture, one may consider bladder neck closure or total urinary diversion. The bladder neck can be closed via a vaginal or abdominal approach. We prefer the transvaginal approach. It must be combined with either a suprapubic tube or a continent (e.g., catheterizable stoma such as a Mitrofanoff procedure) or incontinent (e.g., ileal chimney) urinary diversion. Although there are not a large number of reports on bladder neck closure in the literature, success rates are high. Zimmern et al. [39] reported 100% success in six women. One potential consequence of this procedure is bleeding from retropubic vessels, which can be difficult to control. When this happens, the case should be completed expeditiously. Other complications include ureteral injury (which can be minimized by giving intravenous dye that is excreted by the kidney or by urethral stenting) and vesicovaginal fistula formation. Alternatively, the surgeon and the patient may opt for a complete urinary diversion (with or without cystectomy) if there is a concern that the bladder neck closure will not heal, e.g., in cases of severe radiation damage.

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Ureteral and Bladder Reconstruction

Nadir I. Osman, Altaf Mangera, and Christopher R. Chapple

INTRODUCTION

Complex reconstructive surgery aims to restore function to the lower urinary tract (LUT) in patients with congenital or acquired disorders. The success of this type of surgery is dependent upon a sound and comprehensive preoperative evaluation of LUT function based upon urodynamic investigation, endoscopy, and radiological techniques. In addition, it is imperative that the operator is familiar with pelvic anatomy and the abnormalities associated with pathological or iatrogenic insult that are encountered. The application of the surgical tenants applicable to any form of reconstructive surgery is essential, including the excision of ischemic tissue, obliteration of dead space, interposition of vascularized tissue, avoidance of infection and hematoma, and tension-free anastomosis.

Although in contemporary practice complex reconstructive surgery is often restricted to the tertiary specialist setting, the basic underlying principles are fundamental to the practice of all surgery. In addition, it is essential that the surgeon is knowledgeable of and is able to apply the full gamut of available reconstructive techniques that may be appropriate for the given situation.

This chapter presents a brief exposition of complex reconstructive surgery in urogynecological practice including the reconstruction of ureteric, bladder, and urethral injuries in addition to the surgical management of severe detrusor overactivity (DO) refractory to conventional treatment.

URETERIC INJURY

The ureter is rarely injured as result of external trauma due to its elasticity and well-protected passage in the retroperitoneum. Most injuries are iatrogenic sustained during abdominal or pelvic surgery. The potentially lethal sequelae of sepsis and renal failure demands that any ureteric injury undergoes careful appraisal and timely intervention.

Iatrogenic Ureteric Injury

The overall incidence during abdominal surgery was found to be 0.4% in a series that included 4665 operations [1]. However, the actual incidence of ureteric injury is likely much higher due to the occurrence of occult injuries.

A systematic review of benign gynecological surgery estimated that ureteral injury ranged from 0.2 to 7.3 per 1000 surgeries [2]. In gynecologic oncologic surgeries, the incidence is much higher at 30%–35% [3–7].

Traditionally, gynecological surgery accounted for approximately two-thirds of iatrogenic injuries to the ureter. The vast majority sustained during hysterectomy, surgery for ovarian tumors, or incontinence surgery. Injuries are also sustained during colorectal surgery (15%), endoscopic ureteric procedures (2%–17%), vascular surgery (6%), laminectomy/spinal fusion (1%), bladder neck suspension procedures (3%), appendicectomy (1%), and cesarean section (1%) [8].

With the rise of laparoscopic approaches in contemporary gynecological surgery, laparoscopic injuries are becoming more common accounting for as many as 25% of all gynecological injuries to the ureter [9]. A similar rise can be seen in urological practice with the advent of more sophisticated endoscopes that allow better manipulation in the ureter for the treatment of urolithiasis. In a recent review of 165 ureteric injuries, urological surgery accounted for 42% compared to 34% and 24% for gynecological and general surgery, respectively. Most urological injuries were attributable to endoscopic procedures (79%) [10].

Risk Factors for Iatrogenic Injuries

Several factors are thought to increase the risk of iatrogenic injury to the ureter. These include congenital abnormalities such as ureteric duplication and ectopic ureter. Inflammatory or fibrotic conditions include the following: endometriosis, retroperitoneal fibrosis and pelvic infections, prior pelvic surgery or irradiation, and resection or large bulky tumors [11,12].

Types of Iatrogenic Injury

The pelvic ureter is involved in 80% of iatrogenic ureteral injuries, making it by far the most commonly involved segment [13]. The mechanisms of injury include the following:

1. *Avulsion*: Avulsion occurs when the ureter is forcefully retracted particularly if the tissues are weakened by infection or necrosis.
2. *Transection*: This occurs due to sharp injury by scissors or a scalpel, especially when the ureters are enveloped within tumor or fibrous tissue. Common sites of such injuries during gynecologic surgery include the following:
   a. The pelvic brim, where the vascular pedicle to the ovary is in close proximity to the ureter
   b. The broad ligament, where the ureter is crossed by the uterine artery
   c. The ureteric canal in the cardinal ligament, 1 cm lateral to the supravaginal cervix and 1 cm above the lateral vaginal fornix
3. *Ligation*: This occurs when the ureters are mistaken for bleeding vessels. It can also occur during vaginal hysterectomy when the uterine arteries are being ligated and in procidentia when the ureters prolapse with the uterus.
4. *Crushing*: This may occur when clamps are used blindly to control hemorrhage and is seen at the sites similar to transection injury, especially during radical hysterectomy for cancer. Necrosis and ultimately stricture or fistula formation can result.
5. *Devascularization*: This occurs when extensive or overenthusiastic dissection of the ureter is performed. The ureter is supplied in 80% of individuals by a single artery along its entire length with anastomotic feeding vessels at each end and in the middle. Devascularization results in ischemic necrosis, which ultimately leads to fistula or stricture.
6. *Perforation*: This is commonly caused by ureteroscopy and associated endoscopic manipulation for ureteric stones. The edematous tissue surrounding the stone and the tissue traumatized by lithotripsy are predisposing factors. Needle injury during open surgery may result in perforation but is rarely a cause of problems in healthy tissues.
7. *Fulguration*: This can occur during transurethral resection of the bladder cancers resected close to the ureteric orifices and then extensively diathermied. Laparoscopic diathermy and laser treatment of endometriotic lesions are an increasingly important cause of thermal injury to the urinary tract that has seen an increase in parallel with the rise of laparoscopic surgery in gynecology.
8. *Fistula formation*: This can follow transection, ischemic necrosis, or perforation if the distal end of the ureter is not in continuity or is obstructed. The urine will then discharge from the vagina, operative wound, or drain site or into the peritoneal cavity or retroperitoneal space.
9. *Stricture formation*: This can follow any of the aforementioned injuries and ultimately lead to obstruction of the ureters, hydronephrosis, and renal damage.
10. *Kinking*: This can occur when the tension is placed on ureteral wall or periureteric tissue. This is commonly seen in certain apical prolapse repairs.

Noniatrogenic Ureteric Injury

Ureteric injuries, not due to iatrogenic injury, are rare but potentially lethal injuries due to the potential for sepsis and high incidence of concomitant injuries (>90%) including the colon (51%), small intestine (49%), and large blood vessels (38%) [14,15]. A recent retrospective analysis of the 22,706 genitourinary injuries found ureteral trauma responsible for 2.5% [15].

A recent review of the data from the U.S. National Trauma Data Bank found that 62% of ureteric injuries are penetrating in nature, while 38% are blunt [15]. This is interesting as traditionally it was thought that blunt injuries are relatively much rarer. Penetrating injuries typically occur due to gunshot or stab wounds, whereas blunt injuries are typically sustained during motor vehicle accidents or falls. A 25-year review from San Francisco General Hospital showed that ureteral injuries in 70% cases involved the upper ureter [16].

Radiation injury to the ureters is rare and can occur in radiotherapy for cervical, bladder, rectal, and other pelvic tumors. Most postirradiation ureteral strictures, however, are due to recurrent tumor. Presentation may be from 3 months up to 10 years, usually with a long threadlike stenotic lesion or a localized constriction about 4–6 cm from the bladder. These are thought to be due to endarteritis obliterans resulting from radiotherapy. Subsequent surgery on such poor-quality tissues also predisposes to a higher complication rate involving the ureters [17].

Presentation

Ideally, any iatrogenic ureteral injury should be identified and dealt with intraoperatively; however, 50%–70% are diagnosed postoperatively [18,19]. Diagnostic delays can vary from 2 days to 12 years [20,21]. Early signs of ureteral injuries are subtle and usually missed, the injury being discovered several days or weeks later when a complication occurs. In urological surgery, however, where injury is most commonly associated with ureteroscopic procedures for stone disease, 77% are diagnosed intraoperatively. Of these ureteric injuries, 91% occur in the lower third, 7% in the middle third, and 2% in the upper third.

Diagnosis

Injuries recognized and repaired intraoperatively carry a better prognosis of cure than those that become manifest postoperatively as a result of complications [10,20,22,23]. In a review of 165 ureteral injuries by Selzman and Spirnak, the number of procedures required to repair urological injuries was 1.2 for those diagnosed intraoperatively compared to 1.6 for those diagnosed postoperatively [10]. Compared to 16% in gynecological surgery and 56% in general surgery, 77% of injuries were diagnosed intraoperatively. This difference is mainly due to the different procedures that cause such injuries in these specialties in presumably the greater familiarity with ureteric anatomy among urologists.

Features of postoperative presentation can be nonspecific and therefore a ureteral injury must first be suspected to be detected. The symptoms and signs include persistent fever, flank pain, ileus, abdominal mass, and excessive drain output or wound or vaginal leakage. Flank pain occurs in 36%–90% of cases of hydronephrosis [21,22,24]. Fistulae of the vagina and skin tend to be present 7–10 days after surgery with urinary leakage [18,20–22,24]. Excessive wound drainage or leakage per vagina may be collected and analyzed for urea and electrolyte levels to determine if it is urine.

In contemporary practice, a CT intravenous urogram (CT-IVU) is mandatory whenever ureteric injury is suspected postoperatively. This will usually demonstrate the site of injury as well as associated pathology such as hydronephrosis and ureteric fistulation and urinomas in addition to allowing the assessment of other associated abdominal and pelvic injuries. Should the CT-IVU be inconclusive, cystoscopy and retrograde pyelogram or antegrade nephrostogram is often useful; higher concentrations of contrast in these studies allow demonstration of leakage and will establish the diagnosis in most cases.

Prevention

Iatrogenic injuries are best managed by preventive rather than corrective measures. Avoidance of ureteric injury is invariably the principle of all good surgical practice and begins with a thorough knowledge of the course of the ureters, the nature, and the site of potential ureteric injuries and an adequate preoperative evaluation. This may include a CT-IVU or IVU to define anatomy if major pelvic or retroperitoneal surgery is planned. A preoperative IVU allows for comparative studies should a postoperative IVU become necessary. However, preoperative IVUs have not been shown to be of value prior to routine hysterectomy and cannot substitute for good surgical technique and identification of anatomic landmarks [18,25].

Congenital anomalies, ectopic ureters, and ureteric duplications should be recognized in advance and may be defined on preoperative imaging. Where radical surgery is being carried out and the ureters are involved or displaced by the pathology, their course should be mapped and the necessary precautions taken. Identification of the length of ureter within the operative field should significantly reduce the risk of damage. The ureters are recognized by the glistening appearance of their sheaths, peristalsis on stimulation, and characteristic feel on palpation. Dissection of the ureters may be necessary, especially when in close proximity to resection margins. Sharp dissection along the line of the ureter, incorporating a generous cuff of periureteric adventitia, should reduce the risk of ischemic injury.

The close anatomical relationship of the uterine artery and the last 3 cm of the ureter make it vulnerable to injury when mass ligature and blind clamping of an injured artery occur. Proper identification and isolation of the uterine artery before ligation and digital compression of the internal iliac artery to control hemorrhage can avoid the need for blind clamping. Most unexpected hemorrhage can be controlled by suitable compression of the bleeding point until the ureter is identified.

If ureteric injury is suspected during open surgery, indigo carmine dye may be useful in identifying the presence and site of the lesion. Contrast solution with intraoperative imaging is more useful during ureteroscopic procedures.

Preoperative ureteral stenting has long been advocated as a method of making intraoperative identification of the ureters easier in order to avoid ureteral injury. However, a recent randomized trial that compared preoperative ureteral stenting *versus* no stenting for major gynecologic surgery, a rate of injury of less than 1% occurred in each group with no statistical difference between the groups [26]. Illuminated or lighted stents have been advocated in laparoscopic practice given the lack of tactile feedback. In recent series of 145 complex laparoscopic surgeries in which theses stents were used, no ureteral injuries occurred [27]. If the efficacy of lighted stents in preventing injury is established, this would need to be balanced against the risks of ureteral stenting (e.g., hematuria and postoperative renal impairment due to ureteric edema) and the additional costs incurred.

Management of Ureteric Injury

The management of a ureteral injury depends on its extent and location, its etiology, associated injuries, and the time of its recognition.

Timing of Surgery

Ureteral injuries discovered intraoperatively and repaired immediately have excellent results, probably due to the absence of sequelae following urine leak and complications such as infection [10,28]. If the injury is incurred during a ureteroscopic procedure, an internal stent placed retrograde across the defect may be all that is required. Small perforations usually heal within 1–2 weeks, whereas larger defects and thermal injuries require up to 6 weeks of internal stenting. If immediate stenting is impossible, initial percutaneous nephrostomy and subsequent antegrade placement of the ureteral stent is indicated [9].

Injuries diagnosed postoperatively may initially be managed conservatively using nephrostomy drainage and/or subsequent ureteric stenting if the ureteric defect is short (<2.5 cm) and a stent can be passed across the defect, either retrograde or antegrade. About half of all ureteric injuries can be treated by such endoscopic stenting, whereas the remainder will require an open procedure for definitive repair. In a series of 165 iatrogenic ureteric injuries, 49% were treated with 6 weeks of internal stenting, 89% showing no evidence of obstruction on follow-up lasting 1–20 years (mean of 8.5 years) [10]. A further series of 50 ureteric injuries reported that endoscopic treatment performed for defects of <2 cm required less operating time, had fewer complications, and shorter hospital stays compared with those undergoing open surgery [29]. No recurrences were noted over a 2-year follow-up period. However, 14 of the 30 patients selected for endoscopic treatment failed ureteric stenting and subsequently required open repair (all were ureteric injuries diagnosed 3 weeks or more after injury). The authors concluded that endoscopic management of ureteral injuries should be carried out only in those with defects < 2 cm in length diagnosed within 3 weeks of injury.

In a further series of 27 patients, it was reported that percutaneous nephrostomy alone or in conjunction with ureteral stenting was successful in treating 11 (65%) of the 17 ureteral injuries considered suitable for endoscopic stenting [18]. As reported by Cormio et al. [29], only 1 of 20 attempted retrograde ureteral stenting was successful in those with delayed diagnoses. All ureteric fistulae required ureteric stenting for healing, and percutaneous nephrostomy was successful only in those with demonstrable ureteric obstruction. These cases presumably represent ligation or crush injuries requiring time for dissolution of sutures and tissue healing. Ureteric obstruction persisting after 8 weeks of percutaneous drainage will require open exploration and repair [18]. In a series of 20 patients with ureteric injuries who had percutaneous nephrostomy with or without a stent as a primary procedure, 80% had spontaneous recovery of the injured ureter without further intervention. Morbidity and reoperation rates were reduced compared with 24 ureteric injuries treated by immediate open ureteric repair [30].

For those that require open surgical correction, immediate repair has increasingly been shown to have similar if not better results compared with the traditional approach of waiting for 6 weeks to 3 months before definitive repair. A number of series support early surgical intervention within 3 weeks [20,22,23,31–34]. Selzman and Spirnak also found that complications were five times higher in the group treated by delayed compared with immediate repair for urologically injured ureters [10].

Open Surgical Management

Ureteral transection is best repaired by immediate spatulated ureteroureterostomy. This should be carried out with a tension-free anastomosis using interrupted absorbable sutures. Sutures should not be too close together in an attempt to achieve a watertight anastomosis, as ischemia and subsequent stricture formation may result. A ureteral stent is often used as a splint and removed between 2 and 6 weeks. Ligation injuries are simply deligated, but crush injuries may be of greater extent due to ischemia and must be handled carefully [24]. If doubt exists as to the viability of the ureter, partial excision and spatulated reanastomosis may be required (Figure 112.1).

For injuries at or below the pelvic brim, an antireflux ureteroneocystostomy is the treatment of choice, for which various methods have been described. In the event of a gap between the end of the ureter and bladder, extra length can be obtained with a psoas hitch [35]. Alternatively, a Boari flap may be employed to achieve a tension-free anastomosis [36,37] (Figure 112.2). A graft length to width ratio of 3:2 is necessary, using a vascular pedicle based on the superior vesical artery. As the tubularized flap has no functional activity, the tube should be openmouthed for adequate drainage [38]. The theoretical advantage of the psoas hitch is the better preservation of the blood supply that may be more precarious in the Boari flap. Other practical advantages include the relative ease of closure of the incision in thick-walled bladders. The incision is relatively smaller to produce an equivalent length of tube, thereby facilitating a nonrefluxing reimplantation, and the subsequent ureteric positioning facilitates ureteroscopy.

For ureteric defects above the pelvic brim, additional length of the ureter of a few centimeters can be obtained by mobilization of the kidney, allowing spatulated ureteroureterostomy. Other options to foreshorten the ureteric course include calicoureterostomy, transureterostomy, and autotransplantation [39–41]. If all else fails, nephrectomy is a final resort.

A number of nonbiological ureteral substitutes have been investigated with limited and generally short-lived success. The ileal ureter has proved the most reliable ureteric replacement to date [42,43]. The main drawbacks to the use of the bowel, as in other bowel replacement surgery, relates to the production of mucus (which can cause obstruction), inadequate peristalsis, anastomotic stricture, and reabsorption of excretory waste products. Consequently, contraindications to ileoureteric substitution include uncorrected bladder outlet obstruction and impaired renal function. Recurrent urinary tract infection and subsequent renal impairment are potential complications [38]. The appendix is an alternative biologic substitute but is of limited length [44]. The fallopian tube has been employed but is limited by its relatively small caliber.

Postoperative Care and Follow-Up

Postoperative care following surgery for ureteric injuries requires close monitoring of renal function with appropriate fluid and electrolyte replacement, especially in the presence of postobstruction diuresis. Adequate antibiotic cover, wound care, and prophylaxis against deep vein thrombosis follow standard surgical practice. Meticulous care of catheters and drains is critical, given the dependence of renal function and uneventful postoperative recovery on these devices.

Common complications include urinary leakage, infection, and hematoma and complications related to drains and catheters. Percutaneous nephrostomy tubes may kink or become displaced due to their awkward locations in the flank. Proper anchoring techniques and aftercare are therefore essential. Chronic and recurrent infections can also result from the use of long-term nephrostomy drainage. Alternatively, the use of internal stents may avoid such complications but often causes storage LUT symptoms and, in the long term, may become encrusted if not changed every 4–6 months. Vesicoureteric reflux may occur following reimplantation and may present with loin pain, recurrent infection, and dilation of the pelvicalyceal system.

Monitoring of wound drainage and contrast radiography immediately after placement of stents or drains is essential. Tube nephrostograms are useful for diagnostic purposes. A repeat imaging study by an appropriate modality such as an IVU or CT urogram following stent removal and long-term follow-up (including IVU at 6 weeks and possibly longer) are recommended.

Conclusions

It is evident that it is important to diagnose ureteral injury as soon as possible and, if identified at the time of surgery, to carry out ureteral stenting (if possible) during endoscopic surgery or direct repair during open surgery. Failing this, a number of open surgical options to foreshorten the course of the ureter are available. If this is not possible, either ureteral substitution or autotransplantation should be considered.

Definitive management of ureteric injury diagnosed postoperatively depends on the level and the extent of ureteric loss, its etiology, associated injuries or complications, and time to discovery. The functional status of the kidneys and the age, condition, and prognosis of the patient are similarly important. Most injuries below the pelvic brim can be treated with a neoureterocystostomy employing a bladder elongation procedure. Mid and upper ureteric injuries above the pelvic brim, however, are more challenging. Small defects above the pelvic brim can be repaired with a spatulated ureteroureterostomy. In cases of extensive ureteral loss, measures such as mobilizing the kidney, transureteroureterostomy, renal autotransplantation, and ureteral substitution using small bowel may be required.

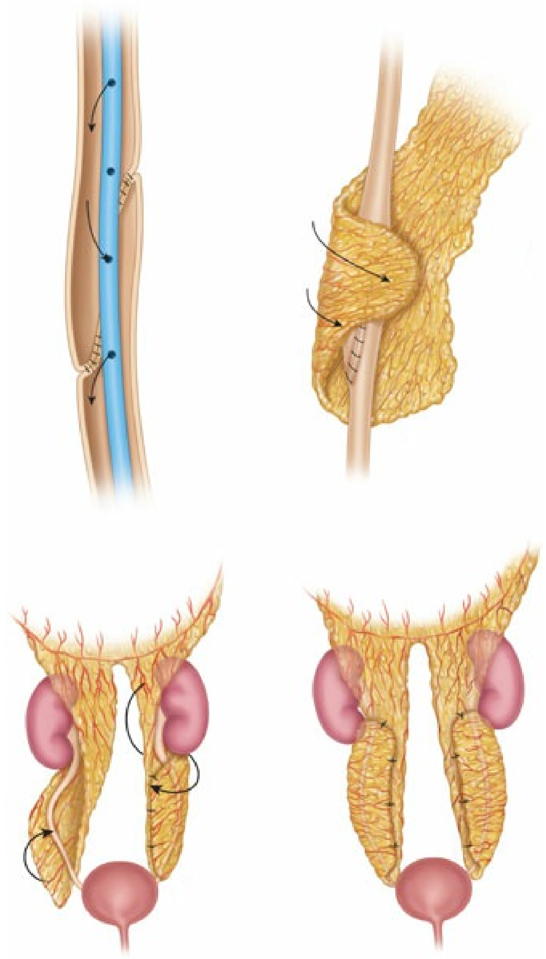

Figure 112.1 The principle of end-to-end spatulated anastomosis of the ureter with omental wrap around to provide support to the repair.

Although reconstruction should be attempted whenever possible, in rare situations, based on the general condition of the patient, the function of both kidneys, and the degree of damage to the ureter, nephrectomy may represent the most appropriate management.

BLADDER RECONSTRUCTIVE SURGERY

Bladder reconstruction and urinary diversion may be preformed for refractory cases of defunctionalized bladder (e.g., from radiation [45]), nonreconstructable fistulae [46], destroyed bladder outlet and refractory bladder overactivity, and impaired compliance.

Overactive bladder (OAB) syndrome and neurogenic bladder can lead to considerable morbidity in patients. Idiopathic DO (IDO) is a urodynamic finding that is demonstrated in approximately 69% of men and 44% of women with OAB-dry and 90% of men and 58% of women with OAB-wet symptoms [47]. Neurogenic DO (NDO) may also lead to renal impairment that may result from voiding dysfunction and back pressure on the upper tracts in association with high-pressure phasic detrusor contractions and detrusor sphincter dyssynergia. In both conditions, first-line pharmacotherapy is still anticholinergic agents, often combined with bladder retraining. More recently, B3 agonists have been shown to be beneficial in patients with OAB [48] with or without IDO. However, their role in NDO still requires further exploration. In the context of neurogenic bladder dysfunction, the clinical picture is complicated by an admixture of other functional problems associated with uncoordinated detrusor contractions, poor bladder compliance, and varying degrees of sphincteric obstruction.

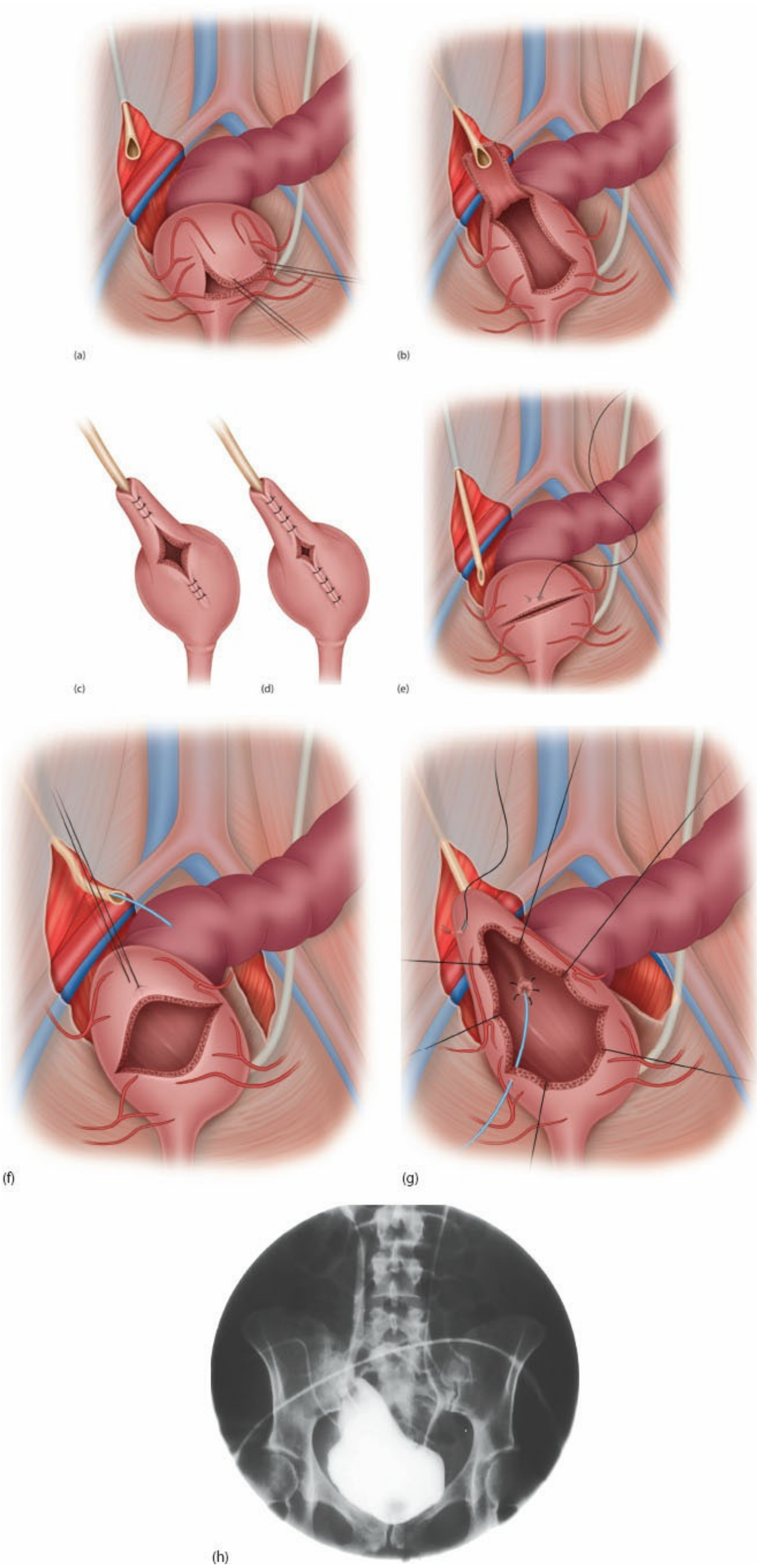
(a)
(b)
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Figure 112.2 (a) With the formation of a Boari flap, a flap of bladder is raised; note the ischemic nature of the apex. (b) The ureter is anastomosed. (c, d) The flap is completed. (e) Forming a bladder elongation flap. (f) Mobilizing the flap. (g) The bladder elongation flap easily reaches the pelvic brim, allowing ureteric reimplantation and is well vascularized. It is secured to the psoas muscle. (h) Postoperative cystogram.

In the past decade, the treatment of pharmacologic refractory OAB and NDO has changed. In previous years, the mainstay of therapy for bladder overactivity was augmentation cystoplasty, mostly using the *clam* technique [49]. Four further options have also been explored: bladder autoaugmentation [50], sacral neuromodulation [51], posterior tibial nerve stimulation [52], and intravesical botulinum neurotoxin injection therapy [53]. In cases of OAB, both neuromodulation and intradetrusor botulinum injections (discussed elsewhere in the book) are used prior to major reconstructive surgery. In addition, botulinum toxin has been found to be effective for NDO. The efficacy of these two treatments for decreased bladder compliance is not well documented. Bladder reconstruction and urinary diversion is often reserved for patients that have failed or are not candidates for neuromodulation and botulinum toxin. These will be discussed here; while a number of surgical techniques for the treatment of DO have been described, it is now widely accepted that procedures such as detrusor transection and transtrigonal phenol injection produce unpredictable and temporary improvement with potentially serious side effects. Their routine use can therefore no longer be supported. We will focus our discussion on surgical procedures that preserve the bladder and increase its functional capacity and reduce storage pressures and those that create a new storage reservoir.

Augmentation Cystoplasty

The principle underlying augmentation cystoplasty is that by bivalving a functionally OAB or high-pressure bladder in neurogenic patients and introducing a segment of detubularized intestine, a low-pressure bladder with an increased functional capacity will result.

The two commonly used intestinal segments are ileum and sigmoid colon. The sigmoid is usually used in patients where a short small bowel mesentery renders the use of ileum difficult. Ileum is preferred as it produces lower reservoir pressures and better compliance. The original technique described for clam cystoplasty is still widely used, but modifications to this include opening the bladder in the sagittal plane that appears to be equally effective or opening the bladder as a *star* [54]. This specific modification can be particularly useful in patients with NDO where the bladder is small and thick walled. An alternative surgical technique popularized by McGuire is his modification of the hemi-Koch procedure. This utilizes a transverse *smile* incision (looking posteriorly), which is fashioned 3 cm above the ureteral orifices, creating an anteriorly based detrusor flap [55]. Most surgeons find coronal or sagittal bivalving of the bladder to be effective and acceptable, provided that adequate opening of the bladder is performed right down to the ureteral orifices, both to adequately open the bladder and to prevent *diverticulation* of the cystoplasty segment. The ileal segment should also be detubularized as this will greatly increase bladder capacity (law of Laplace) and reduce the effect of peristaltic activity [56]. In addition, it is advisable that bladder capacity is increased to in excess of 500 mL especially in the neuropathic population.

Although the majority of bladder augmentation procedures are performed via an open technique, laparoscopic and robot-assisted techniques have been described [57,58]. The aim of minimally invasive surgery is to minimize the trauma of surgery, allow earlier recovery, and return to activities without compromising the surgical outcomes. Whether this is achieved with current laparoscopic or robotic procedures is still debatable.

A number of studies attest to the efficacy of augmentation cystoplasty in children, adolescents, and adults with DO and NDO [59–62]. Mundy and Stephenson reported a series of 40 cases in whom 90% were cured at a mean follow-up of 1 year [54]. Mean functional bladder capacity was increased from 280 to 440 mL, reduced compliance was improved in 70% of patients, and DO abolished in 50%, the remainder having low-pressure DO. In a series of 26 adolescents undergoing enterocystoplasty, 19 of whom had a *clam* cystoplasty, the results were satisfactory in all 3 males but poor in 5 out of the 16 females. In three patients, difficulty was experienced with clean intermittent self catheterization (CISC) [60].

- In a series of 39 children with spina bifida, bladder capacity at safe storage pressures of <29 cm of saline was achieved in all patients with a reduction in upper tract dilatation in 91.7% of the kidneys [61]. A satisfactory result was achieved in all but one patient.
- Singh and Thomas [63] reviewed 67 patients who underwent augmentation cystoplasty. Of these, 47 had an ileal segment and 20 had a sigmoid segment. These data are presented in combination with a further 11 patients who had an ileocecal cystoplasty. Fifty-two patients had an artificial sphincter, nine had a colposuspension, and one had both. Acceptable continence was achieved in 93.6% of patients.
- Hasan et al. [62] reported on 48 patients who underwent augmentation cystoplasty for IDO (n = 35) or NDO (n = 13). Mean follow-up was 38 months, with 83% achieving a good outcome, 15% a moderate outcome, and 2% an unsatisfactory result.
- Flood et al. [64] reported on 122 augmentation cystoplasties. It must, however, be borne in mind that the “McGuire” technique used was different from the standard clam procedure reported for all the other series described earlier, and this was a very mixed group of patients: 67% had an ileal augmentation, 30% a detubularized cecocystoplasty, and 3% sigmoid. In 19 patients, this procedure was related to undiversion and 17% had IC, 7% radiation cystitis, 13% miscellaneous conditions, and the remainder was either NDO or DO. Mean follow-up was 37 months. Bladder capacity was increased from a preoperative mean of 108–438 mL, and, of 106 successful patients, 75% had an excellent result, 20% were improved, and 5% had major, persistent problems.

The earlier literature supports augmentation cystoplasty as being an effective therapy with a low operative morbidity and satisfactory long-term results, although most of the reported series have a follow-up of less than 5 years. It must be remembered that this is major surgery, and despite adequate preoperative counseling, many patients take some months to adapt to their new bladder and to learn to void effectively by abdominal straining. It is important to monitor postoperative residual urine volumes. CISC is necessary for a number of these patients, particularly those with NDO. Interestingly, the reported incidence of CISC varies from 15% up to 85% of cases [58]. It is evident that a number of factors contribute to the need for CISC. These include the level of residual deemed acceptable by the supervising urologist and the concomitant use of procedures directed at the bladder outflow either urethral dilation (rebalancing) or treatments for stress incontinence. A particular debate centers on the treatment of coexisting stress incontinence at the time of clam cystoplasty; contemporary opinion remains divided on this matter since measures designed to treat stress incontinence will generally increase the need for CISC.

Other problems encountered with augmentation cystoplasty include persistent mucus production, recurrent or persistent urinary tract infections, and metabolic disorders, which are usually mild and subclinical. The metabolic picture is usually of a hyperchloremic metabolic acidosis. This should be managed with 2–6 g sodium bicarbonate therapy. Provided that patients are counseled preoperatively, this is rarely a problem. Persistent urinary infection can be troublesome, particularly in female patients, and has been reported in up to 30% of cases, often requiring long-term antibiotic therapy. Long-term bowel dysfunction occurs in up to a third of patients and is thought to be related to the interruption of the normal enterohepatic circulation [65]. Bladder perforations have been reported in up to 10% of patients [61]. At present, a lifelong follow-up of these patients is recommended, not only because of the aforementioned complications but also in view of the suggestion that augmentation cystoplasty predisposes to the subsequent development of malignancy. However, there remains no convincing evidence to support an association with tumor in the absence of other predisposing factors such as previous tuberculosis or chronic urinary stasis such as that associated with paraplegia [66].

Augmentation cystoplasty is an effective management option in contemporary practice in patients with intractable DO or NDO resistant to conventional therapy. In addition, cystoplasty can be used as part of an undiversion procedure. Although a proportion of patients are not significantly improved by this procedure, one series found a *good to moderate* outcome in only 58% of patients with DO [62]. It must be borne in mind that up to 30% of patients experience increased frequency and looseness of bowel motions and a tendency to incontinent episodes, with a significant number of patients requiring long-term CISC.

Bladder Autoaugmentation/Detrusor Myectomy

In 1989, Snow and Cartwright initially reported a technique that they named bladder autoaugmentation [68]. This procedure involves the excision of the detrusor muscle over the entire dome of the bladder, leaving the underlying bladder urothelium intact. A large epithelial *bulge* is created, which functions by augmenting the storage capacity of the bladder, and this is referred to as autoaugmentation.

Following initial studies in six dogs, this technique was extended to seven patients aged 4–17 years, all of whom had poorly compliant bladders documented on pressure flow urodynamics. Following excision of the dome detrusor muscle, the lateral margins of the detrusor were fixed bilaterally to the psoas muscles. Patient follow-up was short. A subsequent report by these workers after studying a total of 19 patients concluded that, with a follow-up of between 3 months and 4 years, 80% of patients were continent and another 10% were significantly improved. A significant increase in bladder capacity of >50 cc occurred in only 40% of patients, with minimal change in 35%; 25% actually had a decrease in capacity. The procedure was, however, accompanied by improved continence and reduced rates of hydronephrosis [68].

In 12 pediatric patients with low-capacity bladders and demonstrable DO (aged 4–14 years, 10 with NDO), 6 months following autoaugmentation, the mean increase in bladder capacity was 40% with a 33% decrease in mean leak-point pressure [68]. Postoperative complications were minor. A modification of the previous technique was used whereby a vesicomyotomy was performed rather than vesicomyectomy with no fixation of the bladder laterally to the psoas muscles. A subsequent preliminary report in five adult patients, with the follow-up ranging from 12 to 82 weeks, reported an increase in bladder capacity, which varied from 40% up to 310%; this was measured at an intravesical pressure of 40 cm H_2O.

Stohrer et al. reported a series of 29 patients aged 14–64 years with an average age of 35 years. Of these patients, 24 were felt likely to have NDO. All patients underwent preoperative urodynamic evaluation. The technique reported by these authors is based on the original one described by Snow and Cartwright with an extraperitoneal approach filling the bladder to 200–250 mL [67]. A 7–8 cm diameter section of the detrusor around the urachus is dissected completely and removed leaving the mucosa intact. The detrusor is not fixed to the psoas muscle and all bands of detrusor overlying the urothelium are removed. The authors now have follow-up to 7 years and while they find that 50% of patients can void without significant residuals, up to half require ISC. They found an improved compliance and increasing capacity of 130–600 mL [69].

An alternative surgical approach that has been explored in case reports is laparoscopic-assisted autoaugmentation, but comment on this cannot be made in the absence of adequate numbers of patients and no significant follow-up [70]. It is recognized that spontaneous perforation of an augmentation cystoplasty bladder is a potential risk, occurring in up to 10% of cases. This may be due to high intravesical pressure [71] and can usually be managed successfully by conservative measures [72]. Patients may be at even greater risk of perforation following autoaugmentation because of the thinness of the mucosa in the bulging *diverticulum* produced by the operation. Evidence in support of this is provided by animal studies where autoaugmentation resulted in higher risk of perforation at lower pressures than augmentation cystoplasty [73]. To date, this complication has yet to be reported in clinical series, possibly because of ingrowth of fibrous tissue around the mucosal diverticulum with time, which may also account for the limited increase in capacity seen following the procedure. This phenomenon, if progressive, may limit the durability of this operation.

At present, while autoaugmentation has a number of attractive features, it is clear that the resultant increase in bladder capacity and reduction in DO are far less pronounced than following augmentation cystoplasty. The number of cases reported in the literature is small with relatively short follow-up. However, Abrams has reported good results with reference to symptoms and urodynamic parameters in an IDO population. In 24 cases followed up for a minimum of 2 years and median (range) follow-up of 79 (28–142) months, autoaugmentation was successful in 80% of patients with IDO but only in 2/6 with NDO [74]. The positive results reported by this group have not been reproduced elsewhere. It is questionable whether the associated benefits adequately compensate for the limited long-term efficacy of the procedure, and this procedure has been largely abandoned. The search for less invasive techniques therefore continues.

Urinary Diversion

Urinary diversion may be either temporary or permanent. All surface diversions are simple surgical endeavors to correct the urinary waste disposal problems of patients who are unfortunate enough to have either lost or never actually achieved normal bladder function.

While clearly *diversion is diversion* and *cystoplasty is cystoplasty*, the development of the so-called continent diversion has confused this distinction. The surgical principles and the procedures that are used to create the urinary reservoir of this diversion are identical to those for a total cystoplasty. Because the only difference between these is the mechanism of their emptying, we would suggest a more rational terminological distinction, that is, *stoma-cystoplasty* and *sphincter-cystoplasty*.

The two key components of the creation, or re-creation, of a naturally functioning bladder are bladder-base sensation and a sufficiency of functional sphincter muscle. These are irreplaceable, but, all too often, one or both are sacrificed at the time of a urinary diversion.

Even a small area of urothelium that has normal sensation can make all the difference when it is available for inclusion in a functional reconstruction because the sensation of bladder fullness avoids the need to time its emptying. Similarly, the remnants of an incompetent sphincter mechanism can sometimes be made to function satisfactorily. Thus, it is important to preserve every bit of the functional tissue that might be important to a future reconstruction even if one cannot envisage either the possibility of an undiversion or that it could subserve a useful purpose. The opportunity of restoration of sphincteric function *today* has often been denied by the excisions of *yesterday*.

Similar considerations apply to the rectal sensation and the sphincteric control of defecation. An anal mechanism, or even its apparently useless remnants, should never be excised needlessly as many patients have lost their chance of anorectal continence as a result of an unnecessarily extensive routine abdominoperineal resection.

Options for Urinary Tract Diversion and Reconstruction

A consideration of the range of procedure options available for urinary diversion, some of which are no longer advocated, summarizes the practical experience upon which the evolution of current preferences are based. These options can be conveniently considered in four distinct categories:

1. *Free-draining surface diversion of the upper urinary tract*: This naturally requires the collection of continuously draining urine. The need for this may be temporary; however, it may be permanent if the surgical retrieval of the reservoir function of the LUT is not possible.
2. *Incontinence surface diversion of the lower tract*: This is often required for the management of voiding difficulties; when these are irremediable, this may be a long-term arrangement. An indwelling urethral catheter may be either drained continuously into a bag or intermittently released. Intermittent emptying of the natural bladder reservoir can also be achieved by intermittent catheterization of the urethra or a leak-proof suprapubic conduit (Figure 112.3).
3. *Cystoplastic reconstruction of a urinary reservoir that is emptied either by sphincter control or by stomal catheterization*: A total substitution cystoplasty may be appropriate when the whole bladder has to be removed; however, many bladder abnormalities require only a readjustment or a partial cystoplastic substitution. A reconstructed cystoplastic reservoir, partial or total, may be controlled by the sphincter mechanism *sphincter-cystoplasty* or it may be emptied by intermittent catheterization of a leak-proof conduit *stoma-cystoplasty* (Figure 112.4).
4. *Internal urinary diversion controlled by the anal sphincter—ureterosigmoidostomy*: For some patients, a rectosigmoid urinary diversion is a preferable alternative to surface diversion when the circumstances are appropriate. For nephrological and carcinogenic reasons, this procedure fell into disrepute for a number of years but procedural developments have addressed some of the potential problems: these include the limitation of renal damage and the early detection of malignant change [75] (Figure 112.5).

When satisfactory sphincteric control of a cystoplasty is irretrievable, many alternative procedures such as catheterizable stoma-cystoplasty reservoirs enable patients to achieve a reasonably acceptable quality of life.

The surgical procedures of *cystoplasty* and of *continent diversion* have evolved as a result of the great endeavors and contributions of numerous colleagues over the years—whole textbooks have been written about them. However, the value of the terminological distinction between *cystoplasty* and *continent diversion* is questionable because the functional requirements and the surgical principles of creating their reservoirs are essentially similar.

Cystoplasty is a generic term for a reconstructive procedure (plasty) to recreate the functional capacity of a bladder reservoir (cysto). Like the term *urodynamics*, *cystoplasty* is commonly used, understood, and misunderstood to mean different things. This adds additional confusion to the already complex field of the retrieval and the construction of functional urinary reservoirs.

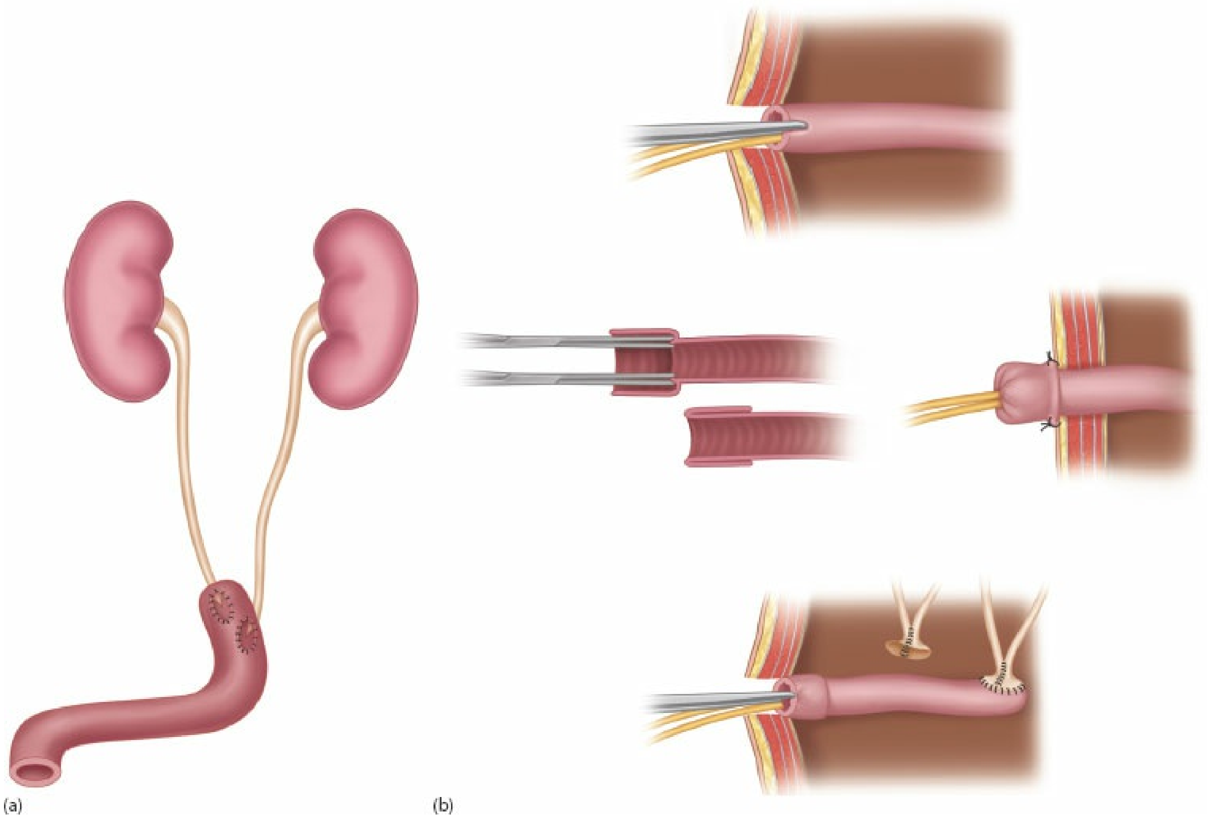

Figure 112.3 (a) An ileal conduit. (b) Formation of the ileal conduit.

Some *simple* cystoplasty operations restore the natural functional reservoir capacity of the bladder without involving any substitution procedure and not all substitution procedures involve the use of bowel. Other tissues used in substitution include the stomach [76] and dilated ureter [77]. Attempts at using tissue-engineered substitutes are still at early stages and require considerable development [78,79]. However, the term *cystoplasty* is commonly used somewhat loosely, as a *semispecific shorthand* to denote the substitution of the bladder reservoir, partial or total, generally with the tacit assumption that bowel is used for the substitution and also that the functional control of the outlet is the natural urethral sphincter mechanism.

Developments in the surgical retrieval of the natural bodily function of *intermittent urinary waste disposal* often involve the creation of catheterizable leak-proof abdominal stoma conduits that are used for the intermittent emptying, either of normal bladders when the urethra is irremediably dysfunctional or of substitution urinary reservoirs that are either partially or totally reconstructed. Thus, an integrated reconsideration of the practical principles of cystoplasty and diversion seems appropriate, together with an integrated reconsideration of terminology. In this section, we use simple descriptive terminological exactitudes.

A *urethra-cystoplasty* is a reconstructed urinary reservoir, the outlet of which is the urethra. When this is controlled by the sphincter, it is a *sphincter-cystoplasty;* if it is emptied by self-catheterization, it is a simple *urethra-cystoplasty*. The reservoir of a sphincter-cystoplasty may be either a partial or a total substitution of the bladder. If bowel is used for the substitution, it can be optionally identified as an *ileal sphincter-cystoplasty* or a *colonic sphincter-cystoplasty*—as opposed to an *omental urethra-cystoplasty*.

A urethro-cystoplasty is a different entity because it denotes reconstruction of both the bladder and the urethra.

A *stoma-cystoplasty* is a urinary reservoir with an abdominal stoma-conduit outlet. Its *continence* is usually maintained by a valved leak-proof conduit that can be catheterized intermittently. The reservoir may be the native bladder—a partial substitution in situ or a total substitution that is either in situ or ex situ. Alternatively, a stoma-cystoplasty can be less precisely described as a *continent diversion*.

The functional characteristics and the principles involved in the construction of the bowel substitution urinary reservoirs of both a stoma-cystoplasty and a sphincter-cystoplasty are essentially similar; the difference is simply the mechanism of their evacuation.

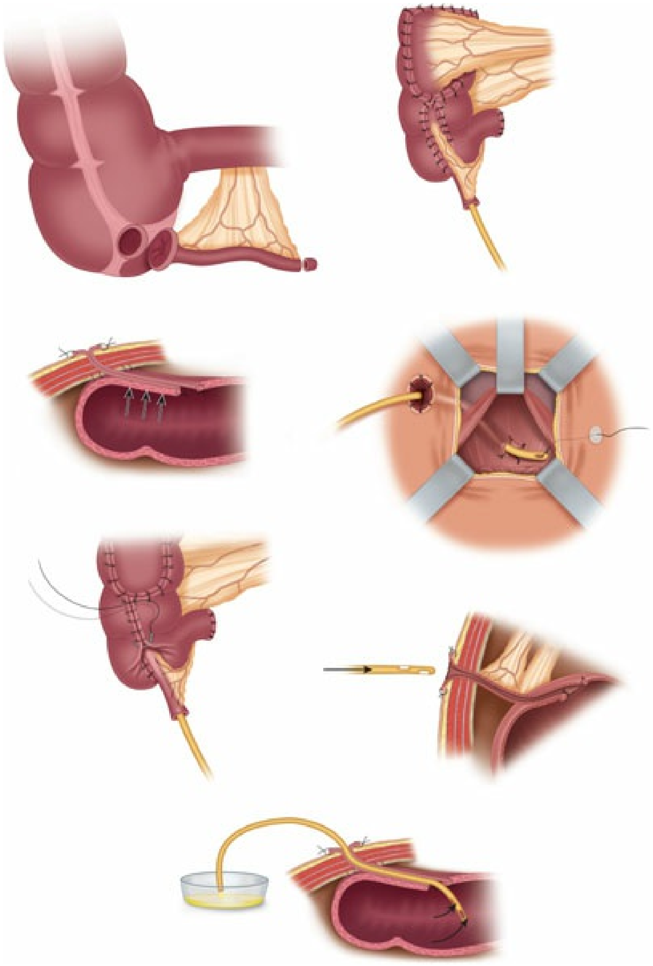

Figure 112.4 Formation of a pouch with a catheterizable stoma.

A leak-proof stoma conduit is a mechanistic construction specifically designed for emptying the reservoir by catheterization. The reliable sphincteric control of a sphincter-cystoplasty is often dependent upon a careful urodynamic assessment and appropriate surgical adjustment and management: this requires quite separate consideration.

Whether or not this terminology will be generally adopted, time will tell; it seems preferable to the ill-defined *continent diversion*. A particular advantage is that it facilitates an independent analytical consideration of the three separate component procedure principles of cystoplastic reconstruction:

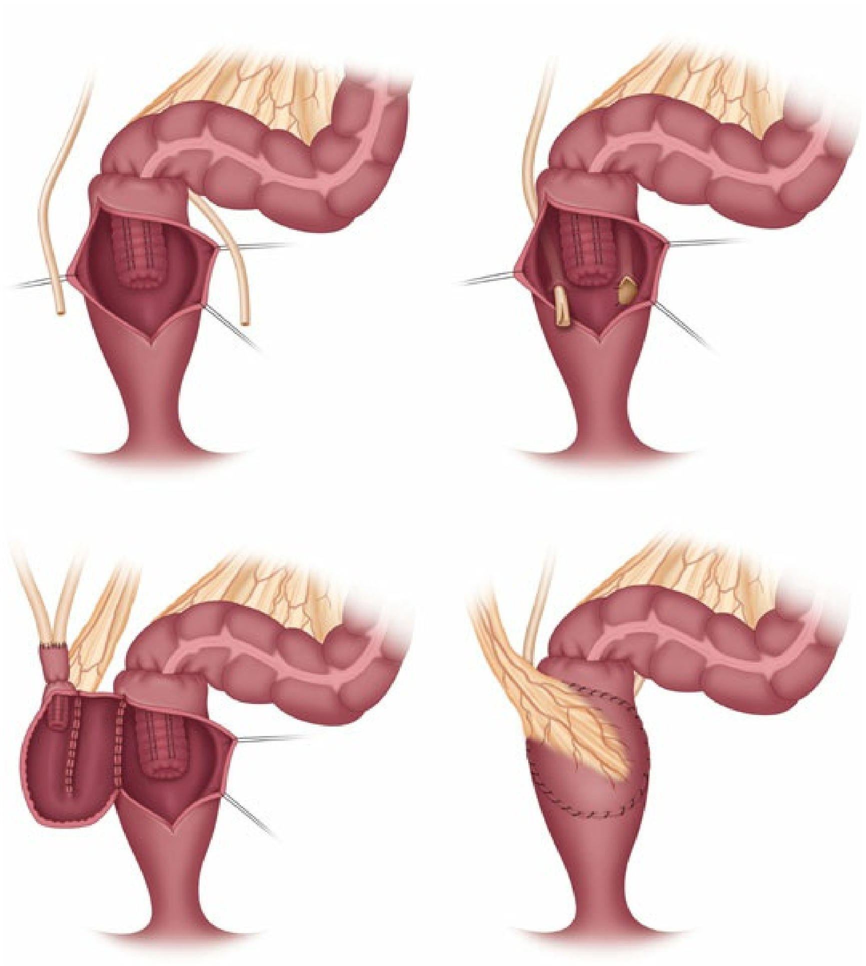

Figure 112.5 Formation of a ureterosigmoid pouch of the Mainz II type. Cystoplasty, stoma-cystoplasty, and sphincter-cystoplasty—a perspective of urinary reservoirs that are emptied intermittently.

1. The creation of a urinary reservoir that has low-pressure and reflux-proof ureteric implantations (these requirements are common to the reservoirs of both a sphincter-cystoplasty and a stoma-cystoplasty).
2. The intricate mechanistic construction of a valved leak-proof stoma conduit that is required for the evacuation of the reservoir of a stoma-cystoplasty by self-catheterization.
3. A functionally orientated urodynamically controlled adjustment is often required to ensure the voiding efficiency and sphincteric control of a sphincter-cystoplasty.

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113 Gynecological Developmental Abnormalities

Melissa C. Davies and Sarah M. Creighton

The Müllerian system develops from the sixth week of life and it is estimated that the prevalence of congenital abnormalities is approximately 5% [1–3]. These anomalies may be major or minor and may occur in isolation or in conjunction with other congenital malformations or as part of a syndrome. Many patients with simple anomalies will remain asymptomatic and may be diagnosed incidentally while being investigated for other problems or undergoing routine gynecological/obstetric procedures. The others present in a variety of ways depending upon the abnormality present. The commonest means of presentation are primary amenorrhea, obstructed uterus or vagina, dyspareunia, and on investigation for infertility or recurrent miscarriage. Those diagnosed, such as neonates, will usually be patients in whom there are associated major anomalies of the genitourinary and alimentary tracts such as persistent cloacal anomalies and anorectal malformations.

DEVELOPMENT OF THE MÜLLERIAN TRACT

An understanding of the embryological development of the urogenital system is essential to the diagnosis and management of developmental abnormalities. This subject is covered in more detail in Chapter 22.

Primordial gonads (genital ridges) appear during the sixth week of embryogenesis. The associated Müllerian and Wolffian ducts also develop. The fate of these undifferentiated ducts depends upon the genetic sex of the embryo. In XY embryos, the SRY gene (sex-determining region of the Y chromosome) stimulates testicular differentiation. The developing testes produce androgens and anti-Müllerian hormone (AMH), which cause virilization and regression of Müllerian structures. In XX individuals, absence of the SRY gene allows the gonads to develop into ovaries, and the subsequent lack of AMH allows the Müllerian ducts to develop into a uterus, fallopian tubes, and vagina.

The Müllerian ducts grow in a caudal and medial direction and fuse in the midline to form the primitive uterus. These ducts form the right and left fallopian tubes and midline fusion of these structures produces the uterus, cervix, and proximal two-thirds of the vagina. This rudimentary vagina fuses with the posterior urethra at week 7 to form the urogenital sinus. Fusion of the Müllerian ducts also brings together the lateral peritoneal folds that form the broad ligaments. The vagina develops from a combination of the Müllerian tubercles and the urogenital sinus. Cells proliferate from the upper portion of the urogenital sinus to form structures called the sinovaginal bulbs. These fuse to form the vaginal plate that extends from the Müllerian ducts to the urogenital sinus. This plate begins to canalize, starting at the hymen and proceeds upward to the cervix (see Figure 113.1). This process is not complete until 21 weeks of gestation [4].

The external genitalia in females consist of the genital tubercle, the urogenital sinus, and the urethral and labioscrotal folds [5]. The genital tubercle becomes the clitoris and the urethral folds develop into the labia minora, and the labioscrotal folds become the labia majora. By week 12 of development, these structures are recognizably female. These structures are sensitive to androgens and form the penis and scrotum in normal male development.

IMAGING

Accurate imaging is pivotal to the diagnosis of many of the conditions described later. Ultrasound is routinely used as the primary mode of investigation. Recent developments in this field have allowed better assessment of uterine anomalies, particularly with the introduction of high-resolution transvaginal ultrasound probes. This may not be appropriate in children or young teenagers or in those whose primary diagnosis is vaginal absence. In addition, ultrasound is more technically difficult to perform in those people who have had multiple surgical procedures and extensive abdominal scarring. More recently, 3D ultrasound has been employed in the diagnosis of uterine anomalies; its benefits include the fact that it is noninvasive and allows for more accurate diagnosis compared with conventional ultrasound [6]. Recent advances in 3D ultrasound technology have improved the sensitivity and specificity of this imaging modality [7], and in experienced hands, it is reported to be more sensitive than other imaging modalities. Ultrasound has the benefit of being safe in pregnancy, which is useful given the subjects are nearly all young fertile women; it also allows concomitant assessment of neighboring structures such as the urinary tract. Renal dysplasia and renal agenesis are associated with Müllerian anomalies and must not be overlooked [8].

Magnetic resonance imaging (MRI) is still considered the gold standard of imaging in this patient group [9]. It is an extremely useful tool in assessing these complex malformations [10,11], particularly where there is no vaginal cavity in which to put an ultrasound probe, or in children or adolescents who have not engaged in sexual activity (see Figure 113.2). There are limited data comparing the accuracy of MRI with 3D ultrasound; however, it appears that the two imaging modalities are comparable in terms of sensitivity and specificity [12].

Other imaging modalities may give useful information. Hysterosalpingography (HSG) gives information about the internal contour of the uterus and allows an assessment of the size and extent of uterine septa. However, it does not provide enough information to allow one to discern between a septate uterus and bicornuate uterus. It has two main drawbacks: first, many patients consider it to be an uncomfortable procedure, and it may be complicated by pelvic inflammatory disease. Also, it is not appropriate for the investigation of the adolescent patient and its main use is in the evaluation of subfertility.

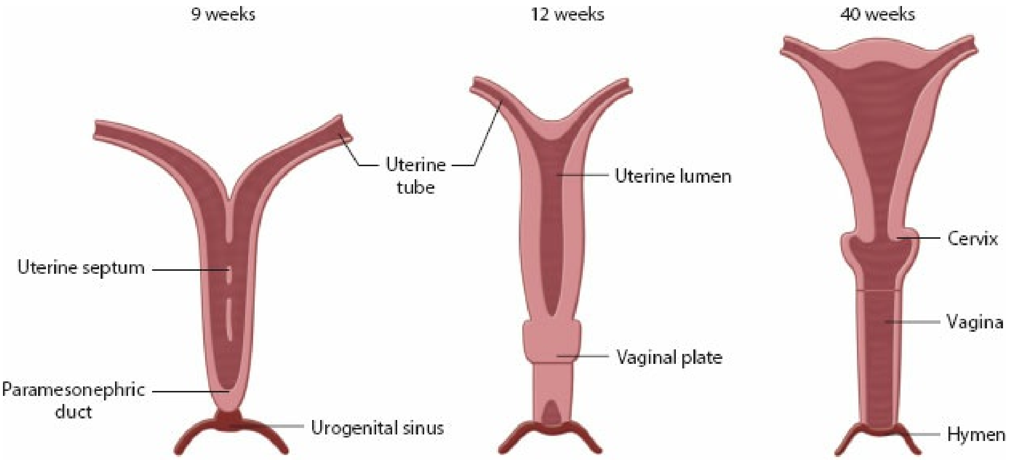

Figure 113.1 Embryological development of the Müllerian system.

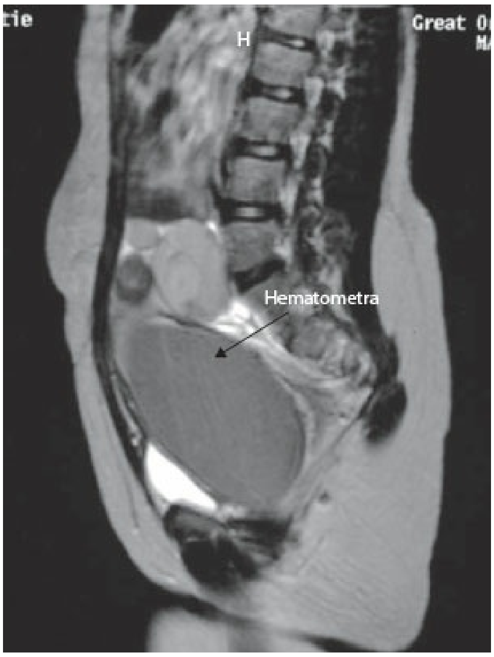

Figure 113.2 Magnetic resonance imaging of an obstructed uterus in a young girl with cloaca.

Hysteroscopy can be useful in the diagnosis of uterine anomalies and has the benefit of allowing treatment in some cases, particularly in septa and arcuate uterus [13]. As hysteroscopy does not provide any information on the outer surface of the uterus, it may be difficult to distinguish between a septate and bicornuate uterus.

Diagnostic laparoscopy should be undertaken only in cases where all other imagining modalities have failed, and the potential for combining this with laparoscopic treatment should also be considered [14].

SIMPLE/ISOLATED ANOMALIES

Imperforate Hymen

The hymen is the embryological septum between the sinovaginal bulbs above and the urogenital sinuses below. The incidence of imperforate hymen is estimated to be 1 in 1000 live female births [14]. Hymen malformations are not usually associated with other Müllerian or uterine anomalies. Failure of this septum to perforate in embryo or early childhood may present at adolescence with obstructed menstrual flow. The diagnosis may be made prenatally [15] or rarely in the neonatal period with obstruction of the urinary tract [16]. However, the history is usually of several months of cyclical abdominal pain in an adolescent without menstruation. A pelvic mass may be palpated or found on ultrasound scan. On inspection of the vulva, it is usually possible to see a bulging vaginal membrane. The treatment for these patients is a simple incision with excision of a quadrate of hymenal tissue to allow drainage of the vagina and uterus. Wide excision of the hymen too close to the vaginal epithelium may result in stenosis at the introitus [17].

There have been case reports of familial cases of imperforate hymen usually between siblings, suggesting a recessive mode of inheritance [18]. There has also been a report of imperforate hymen in two generations of the same family [19], which suggests a possible dominant mode of transmission.

Transverse Vaginal Septa

This uncommon condition occurs in approximately 1 in 70,000 females [20]. It occurs due to a failure of the Müllerian ducts and urogenital sinus to canalize. These septa are most commonly found at the junction of the middle to upper two-thirds of the vagina. In cases of a complete transverse septum, associated uterine anomalies are common; one series reports the rate to be as high as 95% [21]. Most presentations of this condition are in young girls after the menarche with cyclical pelvic pain as a result of hematocolpos, which may be complicated by hematometra, bilateral hematosalpinges, and possibly endometriosis. It can usually be easily distinguished clinically from an imperforate hymen as there is no bulging membrane seen at the introitus. It can rarely occur before puberty when the presentation is with pelvic pain; the obstruction in this case is thought to be due to a buildup of mucous secretions from the cervical glands.

In one interesting case, expectant management was employed, where the thickness of the septum and volume of the dilated vagina were monitored regularly using ultrasonography. The thickness of the vaginal septum decreased from 26 to 8 mm over a period of 5 years, thus allowing a less complicated surgical procedure in a more mature patient [22]. The thinning of the septum was felt to be due to a pressure effect of the hematocolpos. The use of vaginal dilators (see Figure 113.5) to achieve a similar thinning effect has also been described in a single case report [23].

However, in the majority of cases, the treatment is surgical excision without delay. Accurate imaging usually with MRI is essential to determine the operative approach. Menstruation can be suppressed with luteinizing hormone releasing hormone (LHRH) analogues while planning surgery. If the septa are thin and low, it may be possible to remove using a vaginal approach [24]. Care must be taken to ensure the septum is entirely removed as vaginal stenosis may result if the procedure is incomplete. Thick transverse septa or those located higher up in the vagina will require an abdominoperineal approach, which may be open or laparoscopic [25]. In those cases where the distance between the margins is too great, then some form of graft, either with skin or intestine, will be required.

Longitudinal Vaginal Septa

Longitudinal septa are often asymptomatic and may not present until the patient is sexually active with dyspareunia, or in some cases during labor where there may be a delay in the second stage [26]. They result as a failure of reabsorption of the vaginal septum during embryogenesis. It may be complete, and extend from the cervix to the introitus, or partial, which may be of any length along the course of the vagina. The management for the majority of these is usually surgical resection if symptomatic. Care must be taken to resect the septum right up to the cervix or dyspareunia will continue.

Rarely, one hemivagina is obstructed, with the other functioning normally. This may cause an unusual clinical picture of apparently normal menstruation, from the unaffected side associated with pelvic pain. Vaginal examination may reveal a unilateral swelling due to hematocolpos. As menstruation appears initially normal, this results in delayed diagnosis of obstruction that would normally be made much quicker in the absence of any menstrual flow. Also, as this is an uncommon condition presenting in young females, the patient may present to a pediatrician rather than a gynecologist, especially as the patients are having what appears to be normal periods. Further investigation of these patients may demonstrate uterine anomalies. The imaging modality of choice in these cases would normally be MRI [11]. Over 80% are thought to have an associated uterine malformation, the commonest of which is a complete uterine septum [21].

Surgical treatment of simple vaginal longitudinal septa is generally uncomplicated and is approached vaginally. As the vagina is a vascular structure, care should be taken with hemostasis. As with transverse septa and imperforate hymen, postoperative vaginal stenosis should be looked for and treated if necessary.

Uterine Anomalies

Traditionally, it has been reported that uterine anomalies are present in 0.5%–2.0% of women [27,28]. However, a recent cross-sectional study undertaken in Denmark has demonstrated an anomaly rate of 9.8% [29]. Anomalies were associated with oligomenorrhea and being nulliparous. However, there was no association with miscarriage and Müllerian anomalies reported, which is contrary to previous reports in the literature [27]. Attempts have been made to classify uterine anomalies. The most widely accepted classification system for uterine anomalies is from the American Society for Reproductive Medicine [30]. This classification organizes the anomalies into six major uterine anatomic types (see Figure 113.3).

The resulting anomalies can be considered to be due to one of four events [31]:

1. Failure of one or more of the Müllerian ducts to develop: *Agenesis, unicornuate uterus without rudimentary horn*
2. Failure of the ducts to canalize: *Unicornuate uterus with rudimentary horn*

3. Failure of or abnormal fusion of the ducts: *Uterus didelphys, bicornuate uterus*
4. Failure of the reabsorption of the midline uterine septum: *Septate uterus, arcuate uterus*

The most common of these appears to be septate uterus, which accounts for approximately 35% of all uterine anomalies [31]. The extent of the septum varies and may be partial or complete. It is known to result in early pregnancy loss and infertility, and this is how the majority of these patients present. However, septa can also be found by chance in women with an uncomplicated obstetric history and so the decision on treatment can be complex. If treatment is recommended, then the most appropriate treatment for septate and arcuate uterus is resection of the septum, which can be achieved via hysteroscopic metroplasty, thus avoiding the need for a laparotomy and an incision in the uterus. There is some evidence that metroplasty may improve reproductive outcomes in these women [32].

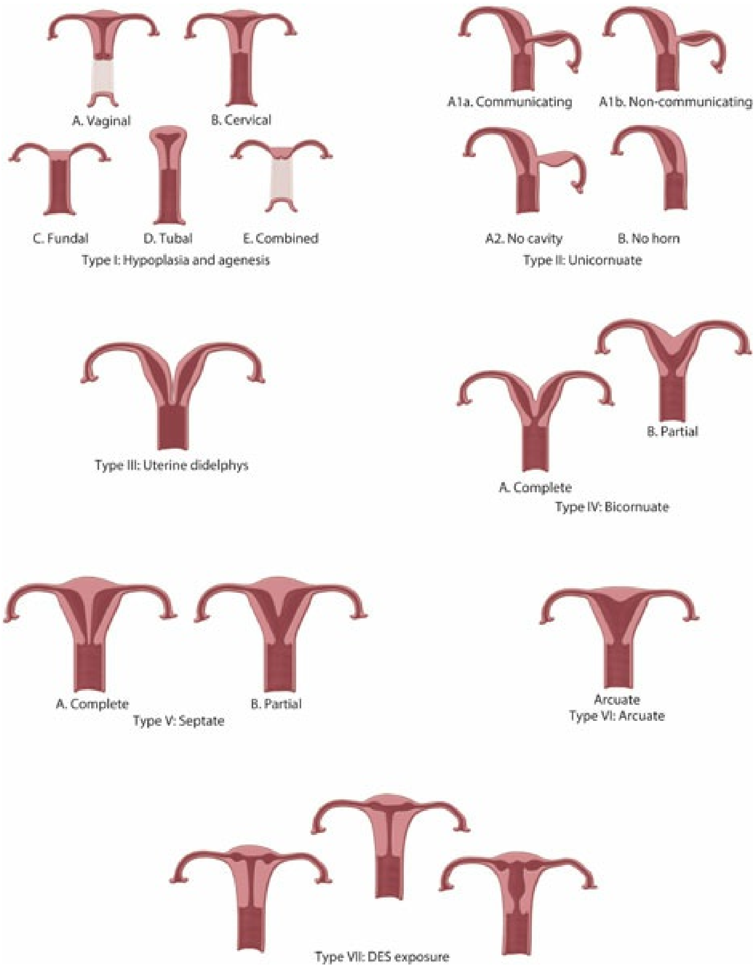

Figure 113.3 The American Fertility Society Classification of Müllerian Anomalies.

Bicornuate uterus accounts for 25% of uterine anomalies [31]. These patients also have recurrent miscarriage, premature delivery, and infertility. There have also been reported neonatal risks, and these include low Apgar scores and small-for-date infants. Surgical options for these patients are limited. Pregnancies do occur in these women and they should be carefully monitored throughout. This is complicated further if there are multiple pregnancies, and twin pregnancies in bicornuate uterus have been reported [33,34].

Unicornuate uterus results from the normal differentiation of only one Müllerian duct. This may present with miscarriage or preterm delivery. One study demonstrated a preterm delivery rate of 25% and early miscarriage rate of 37.5% [35]. Noncommunicating rudimentary horns with functional endometrium usually present with pain; this necessitates the removal of the horn, which may be carried out laparoscopically (see Figure 113.4) [36]. Presentation as an adolescent can be delayed as the presence of normal menstruation from the unobstructed side leads to a low index of suspicion. Removal of the horn is essential to treat pain but also as pregnancy may occur within the horn [37]. There have been reports of removal of pregnant uterine horns, and in this situation the risks are greater as the pregnant uterus is a more vascular structure. It is essential to obtain renal imaging such as preoperative intravenous pyelogram (IVP) as up to 30% will have associated renal tract anomalies [38]. Furthermore, it is suggested that the standard treatment of cases such as these should include fetocide and methotrexate; this in addition to gonadotropin-releasing hormone would allow a safer approach to the laparoscopic removal of the uterine horn. The obstetric outcomes in subsequent pregnancies of this group of patients are better than expected. In a large cohort of 120 consecutive females with a diagnosis of unicornuate uterus having a total of 341 pregnancies, the live birth rate was reported as 72.1% (227/315), with a preterm birth rate of 18.5% [39].

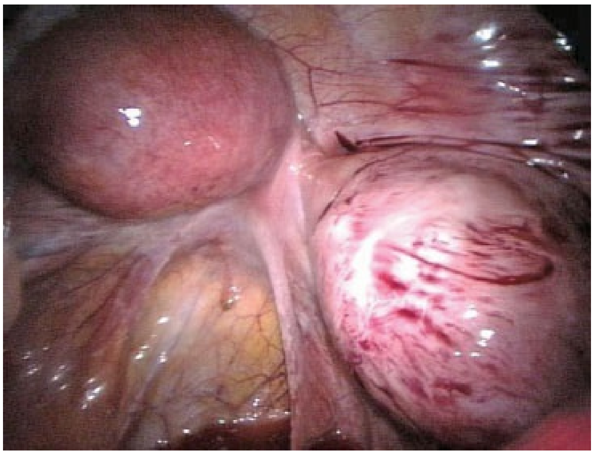

Figure 113.4 Laparoscopic view of an obstructed uterine horn.

Didelphic uterus is often associated with a hemivagina, or a vaginal septum of varying degree, and possible duplicated kidneys or renal agenesis. It is thought to account for 10% of all uterine anomalies.

Absent Cervix

Congenital absence of the cervix is a rare condition and occurs in 1 in 80,000–100,000 births [40]. It is known to be associated with vaginal aplasia, both partial and complete, and renal anomalies. In a recent retrospective review of 18 patients, 39% had associated vaginal aplasia. [41]. Presentation is usually with primary amenorrhea and cyclical lower abdominal pain. Endometriosis or pelvic infection may result from the chronic hematometra. The differential diagnosis includes high transverse vaginal septum, and in some cases, the actual diagnosis may not be clear until surgery.

The management of this condition has changed in recent years with the advances of reproductive technology. Previously, patients with cervical atresia were offered a total hysterectomy as complications of recanalizing the cervix were common and a viable pregnancy was unlikely [26,42]. Now the recommended treatment options consist of either suppression of menses with preservation of the uterus for pregnancy with reproductive assistance or uterovaginal anastomosis, which can now be performed laparoscopically [40]. There are very little data on fertility outcomes following uterovaginal anastomosis; the largest study published stated that the postoperative complication rate was low with only 22% requiring further surgery. Furthermore, they report six spontaneous pregnancies in four of their patients [41]. Despite these encouraging results, it is important to realize that the possibility of serious complications exists and postoperative sepsis after uterovaginal anastomosis has resulted in septic shock and death [43].

Reproductive technology has advanced to allow these patients an opportunity to become pregnant and in vitro fertilization techniques have assisted these patients to become pregnant. There have been case reports of implanting embryos transmyometrially, which have resulted in a viable pregnancy [44,45]. In the latter case report, the patient underwent uterovaginal canalization using amniotic membrane at the time of cesarean section [45]. One of the difficulties of these techniques is the management of miscarriage should it occur. Cervical dilation and curettage is often not an option as there may be no obvious cervix, or a small scarred stenosis. Therefore, most cases would require a laparoscopic or open removal of the remnants of pregnancy. One case report has used a conservative approach of observation where the patient's B-hCG level was monitored with ultrasound examination of the uterus [40].

COMPLEX ANOMALIES

Complex anomalies can be considered in two groups: anatomical or endocrine. This allows us to distinguish between them based upon the underlying cause rather than the system affected. Complex anatomical anomalies include the Mayer–Rokitansky–Kuster–Hauser (MRKH) syndrome.

Congenital Absence of the Vagina

Agenesis of the vagina occurs in approximately 1 in 5,000–30,000 live female births [46,47]. It is commonly referred to as MRKH syndrome. In the majority of suffers, there is no discernable vagina present, while approximately 25% will have a short blind-ending pouch. This is almost always associated with an absent or rudimentary uterus. The karyotype is XX and the ovaries are normal. Anomalies of the urinary tract are present in an estimated 34% of patients, and spinal anomalies are found in 12% [48]. Although the etiology of this condition is unknown, there has been speculation as to a genetic cause and currently possible implicated genes include HNF1b and members of the Wnt gene family [49–51].

Treatment usually involves formation of a vagina. The preferred method for this is nonsurgical with the use of pressure dilation therapy [52]. This involves the use of graded dilators applied to the perineum at the point where the vagina would normally be sited (see Figure 113.5). In most patients while there is no vagina, there is often a vaginal dimple that acts as a guide for patients to apply pressure on the site. Success of this treatment is high [49] but is limited to motivated patients, and it is recommended that they are seen regularly during this treatment and offered psychological support to improve outcomes.

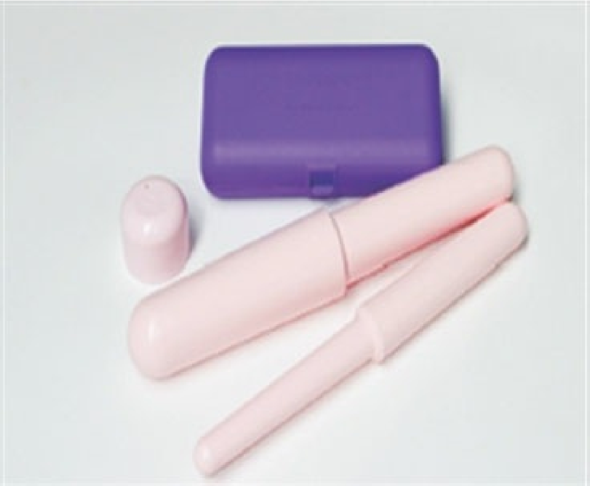

Figure 113.5 Femmax dilators.

For those in whom dilation has not worked or is not possible, then surgical construction is necessary. The timing of this procedure should be carefully considered, as many of those who have surgery will need to use some form of pressure dilation subsequently to maintain the vagina. Numerous forms of vaginoplasty have been employed in the treatment of these patients. They range from simple skin grafting to more complex intestinal vaginoplasties. The use of bowel segments for vaginoplasty has been reported in the literature as early as 1907 [53]; segments of the rectum, ileum, and sigmoid colon may be employed. Stenosis (apart from at the introitus) is rare and the vagina remains moist and of appropriate caliber. However, a vagina constructed from the intestine will be relatively insensitive and may have excess mucus production requiring the patient to wear pads permanently. There have been reports of diversion colitis with colovaginoplasty and this can be difficult to treat [54]. This seems to be less common with ileal vaginoplasty. Vaginal malignancy has also been reported following both intestinal and skin graft vaginoplasty [55] with a mean length of time to diagnosis of carcinoma of approximately 17 years [56]. More recent reports of laparoscopic techniques that have become available have been presented, including laparoscopic Davidov, Vecchietti, and balloon vaginoplasty procedures [57–59]. Of these, the laparoscopic Vecchietti procedure is the most widely performed (Figure 113.6). An olive-sized Perspex bead is inserted into the vaginal dimple. Nylon threads are passed through a small hole in the olive and passed up through the vaginal vault under laparoscopic vision. The threads are brought out onto the abdominal wall and attached to a traction device. Traction is applied to the device daily to stretch the vagina. The procedure is painful requiring hospital admission but a vagina suitable for intercourse can be created in a few days [57].

Tissue engineering technological advances have allowed the formation of autologous vaginal tissue in the research setting. Raya-Rivera et al. [60] have presented their findings from four patients who underwent vaginal reconstruction using tissue-engineered graft from cells obtained following a vulvar biopsy. A follow-up of these patients at 81 months demonstrated a viable vagina; furthermore, Female Sexual Function Index scores were reported to be in the normal range.

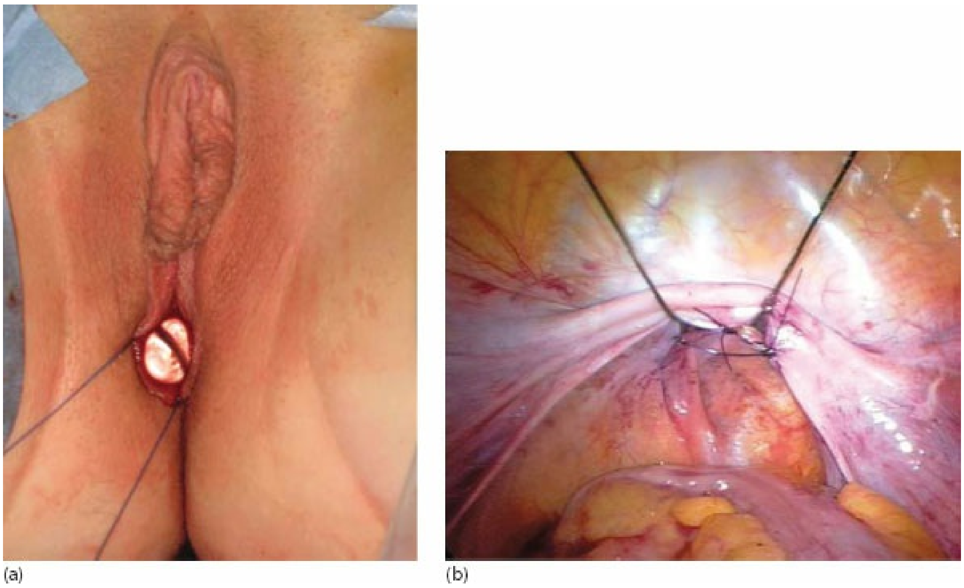

Figure 113.6 Laparoscopic Vecchietti. (a) The Vecchietti “olive” positioned at the vaginal introitus, (b) laparoscopic view after introduction of threads from vaginal dimple through peritoneal cavity.

Psychological preparation is essential both before and after any surgery. The maintenance of the neovagina postoperatively often requires regular dilatation until regular sexual intercourse occurs. This is of particular importance in skin graft vaginas. The patient should be emotionally well adjusted and mature [61].

Fertility options for these patients are limited, but as they have normal functioning ovaries, then surrogacy is an option. There have been reports of successful surrogacy treatment in patients with Rokitansky syndrome [62–64].

Congenital Adrenal Hyperplasia

Congenital adrenal hyperplasia (CAH) is the most common cause of ambiguous genitalia and occurs in approximately 1 in 14,000 births in the United Kingdom. The pathogenesis in the majority of cases is 21-hydroxylase deficiency. The lack of this enzyme leads to a decrease in the level of cortisol, which in turn causes an increase in adrenocorticotrophic hormone (ACTH) secretion. This causes an increase in the levels of cortisol precursors that are forced along the androgen pathway. In its most severe form, aldosterone levels will also be low, which may lead to salt wasting, volume depletion, hypotension, reduced renal blood flow, and raised renin activity. The aim of treatment in these patients is to replace the aldosterone with fludrocortisone and replace glucocorticoid to suppress the ACTH overactivity.

The presentation differs depending upon the form of disease and ranges from neonatal salt wasting crisis and ambiguous genitalia to precocious puberty or virilization at puberty. The majority of cases however are diagnosed in neonates who are noted to have ambiguous or masculinized genitalia at birth. Virilization of the female genitalia occurs to a varying degree, causing labial fusion, clitoromegaly, and a confluence of the vagina and distal urethra (see Figure 113.7) [65]. While fertility rates are lower than normal in these females, pregnancy rates appear unchanged [66].

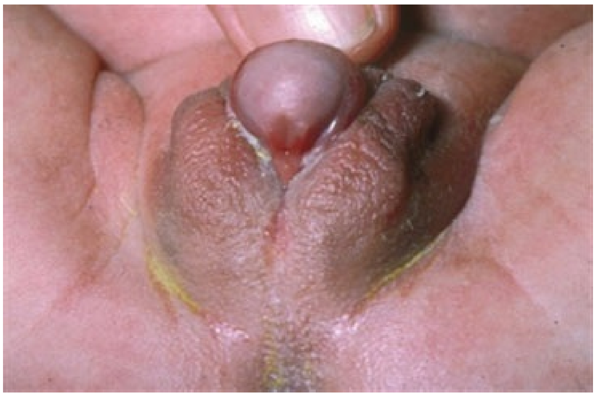

Figure 113.7 Newborn with congenital adrenal hyperplasia.

Current standard practice includes corrective genital surgery to separate the labia, reduce the size of the clitoris, and separate the vagina and urethra [67]. The aims of this are to create a feminine appearance, allow passage of menses, preserve sexual function, and prevent subsequent urinary tract complications [68]. This is usually performed as a *one-stage* procedure in infancy, although many patients require further surgery in adolescence to facilitate menstrual flow and allow penetrative sexual intercourse. There has been increasing recent controversy among clinicians and patient peer support groups as to the need for and timing of feminizing genital surgery. Genital surgery is associated with damage to the sensory innervation of the clitoris and is associated with loss of sexual sensation and an increased risk of sexual dysfunction [69]. Long-term data are however scanty and at present no consensus has been reached.

Androgen Insensitivity: Complete and Partial

Androgen insensitivity syndrome has an incidence thought to be somewhere in the region of 1 in 13,000–40,000 live births [47,70]. The condition is known to be due to a defect in the androgen receptor (AR) gene. It is an X-linked recessive disorder where affected individuals have an XY karyotype with a spectrum of clinical manifestations and is generally subdivided into complete and partial. All patients have testes and normal testosterone production and metabolism with either a female or ambiguous phenotype. There are usually no Müllerian structures present.

Patients with partial androgen insensitivity are diagnosed at birth, as there is ambiguity of the genitalia, and a decision regarding the sex of rearing needs to be made. This is a difficult and sensitive issue and should be handled in a specialist center with a full multidisciplinary team of experts available, including psychologist, pediatric urologists, and endocrinologist. Those with complete androgen insensitivity may present later in life with primary amenorrhea or in some cases with inguinal hernia containing testes. Of those girls diagnosed in childhood with Androgen Insensitivity Syndrome (AIS), over half presented with inguinal hernia and Complete Androgen Insensitivity Syndrome (CAIS) should be considered in all girls presenting with inguinal hernia [71].

Recommended treatment for these patients includes removal of gonads as there is a potential for malignant change and lengthening of the vagina if necessary. Gonadectomy may be delayed until after puberty, which allows the young woman to undergo puberty spontaneously and minimizes disruption to schooling for hospital appointments and surgery. The gonadectomy should ideally be carried out laparoscopically, and preoperative imaging is required to accurately locate the gonads. After removal of the gonads, patients will require hormone replacement, typically until 50 years of age, when most women would experience a natural decline in hormone levels. Patients should also undergo regular monitoring of bone mineral density. Vaginal lengthening may be undertaken at any time, and the patient should be counseled appropriately before. The treatment options for vaginal lengthening are as for MRKH with dilation therapy as the first-line choice of treatment.

ASSOCIATED WITH OTHER ANOMALIES OR AS PART OF A SYNDROME

Anorectal Malformation and Cloaca

Many patients with gynecological developmental abnormalities may have other anomalies and the converse is also true. Females born with a persistent common cloaca channel will not only require reconstruction to separate the common cavity into three distinct structures—vagina, urethra, and rectum—but there are also a significant percentage of these patients with associated gynecological anomalies. The commonest of these is a duplicate vagina [72]. In patients with a persistent cloaca, the rate is quoted as being as high as 50% [73]. Yet many of these patients are not routinely investigated for gynecological developmental anomalies. In one recent study, 36% of female patients born with a cloacal anomaly presented with an obstructed uterus in puberty; all of whom required surgery [74]. Any surgery required is more difficult in these patients as they have often undergone multiple surgical procedures as young children. Furthermore, fertility issues are also complicated by the fact that these women once pregnant will need to deliver via cesarean section with an experienced surgeon present.

Traditionally, patients have undergone vaginal substitution with usually some form of bowel graft. More recently, there have been attempts to reconstruct the vagina using native vaginal tissue in those individuals with duplicate vagina [75].

Turner Syndrome

Turner syndrome (TS) is the most common sex chromosome disorder in females and occurs in 1 in 2000 live female births [76]. It is the result of a complete or partial X chromosome monosomy. The syndrome is phenotypically characterized by short stature, webbed neck, wide carrying angle, and low posterior hairline.

Ovarian dysgenesis is documented as occurring in 95% of TS sufferers [77]. Ovarian failure occurs in the first few months or years of life. Therefore, these patients are not able to undergo a spontaneous puberty, and amenorrhea and minimal breast development are the norm, though not inevitable. One study has shown that 16% of its Turner's population have undergone spontaneous puberty [78]. However, few patients with TS are fertile and spontaneous pregnancy occurs in approximately 5% [78], usually in patients who have mosaicism [79]. Furthermore, those who mange to become pregnant have documented poor outcomes, with a 29% miscarriage rate, 7% perinatal death rate, and a 20% chance of having offspring with a chromosomal abnormality, e.g., Down syndrome and TS [80].

Initial management of these patients includes an echocardiogram and renal tract ultrasound as there are a significant percentage of associated cardiac and renal anomalies. Growth hormone therapy should be considered in childhood to try and increase final height. Estrogen replacement is also necessary to induce a normal puberty. After puberty, nearly all TS patients will require long-term hormone replacement to prevent the onset of osteoporosis and atherosclerosis [81]. Due to the complex nature of this disease, it is best managed by a multidisciplinary team where appropriate advice and counseling can be given.

CONCLUSION

As these conditions are rare, the diagnosis is often missed or delayed causing much anxiety for both the patients and her family. The key to managing these patients is thoroughness and attention to detail and it is imperative to provide as accurate a diagnosis as possible.

Many of these conditions have adverse implications for fertility or sexual function. Psychological input is crucial and should be offered to the family as a whole. Support will need to be ongoing, in many cases through childhood and adolescence. Full information about the diagnosis and its implications must be made available to the family and should be explained clearly so that the patients and their parents can fully appreciate what the problem is and what future holds for them. Other helpful resources that are available to these patients include patient support groups and written literature. Such complex and rare conditions need the input of a multidisciplinary team comprising at the very least a psychological, surgical, and endocrinological component. Specialized backup services such as imaging, biochemistry, and genetics are also essential. Patients with complex developmental anomalies should be referred to specialized clinics that can provide the services required and optimize future sexual and reproductive potential.

Currently, the main areas of research in the field of Müllerian anomalies are related to improved diagnosis through imaging and genetic studies and improved surgical outcomes with the utilization of tissue-engineered graft materials. It is likely that reliance upon MRI will decrease with the advance of 3D ultrasound improving the possibility of accurate office assessment and diagnosis. Tissue engineering has the ability to change the surgical landscape of vaginal reconstruction, and it is likely that as technology improves, the concept of growing replacement body parts will become feasible and preferable to the use of intestine or cutaneous flaps in the reconstruction of the genital tract.

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114 Pediatric Urogynecology

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INTRODUCTION

Anomalies of female embryogenesis may result in a wide spectrum of problems related to the development of the urinary and genital tracts. Many of the clinical abnormalities seen in girls and young women that appear to involve the genitalia alone may be the harbinger of related urinary tract disorders. Abnormalities presenting in infancy may be easy to recognize secondary to abnormal antenatal ultrasonographic or physical examination in the newborn period. Many urogenital malformations, however, are elusive and may become evident only after a clinical problem arises.

The most common urogynecological disorders prompting childhood evaluation focus on problems of urinary continence and introital abnormalities. Interlabial masses, often included in the differential diagnosis of urinary incontinence, as well as difficulties with appropriate gender identification in genetic and phenotypic females, are discussed in this chapter. As congenital abnormalities result from abnormal embryogenesis, it is appropriate to begin with a brief overview of normal female embryology.

FEMALE EMBRYOLOGY

Congenital abnormalities commonly involve both the urinary and genital tracts. An understanding of normal embryogenesis is imperative for understanding congenital abnormalities. A detailed discussion of the embryology of the lower urinary tract is provided by Marshall [1] and Stephens et al. [2].

The divergence of normal sexual differential into male and female phenotypes begins in week 9 of gestation. If no Y chromosome is present, the ovaries develop, whereas the testes and Sertoli cells do not. As a result, the Wolffian system regresses (absence of androgen production) and the Müllerian ducts form the fallopian tubes, uterus, and proximal part of the vagina (absence of Müllerian inhibiting factor). The embryologic origins and adult counterparts of the female genital tract are shown in Figure 114.1 and described in Table 114.1.

URINARY INCONTINENCE IN GIRLS

Etiology

Female urinary incontinence may have a functional or neurogenic etiology or may be secondary to congenital abnormalities of the lower urinary tract. The most common cause of severe urinary incontinence in children is related to a neurologic deficit. The leading causes of neurogenic incontinence include myelomeningocele (spina bifida), sacral agenesis, and vertebral or spinal cord lesions. In these conditions, changes within the spinal cord may occur over time, making careful evaluation and close follow-up essential.

In all children presenting with urinary incontinence, urinalysis should be performed to assess the presence of infection, hematuria, proteinuria, glucosuria, or renal concentrating defect (early morning specific gravity < 1.008). Chronic nighttime wetting, polyuria, or nocturia may indicate renal failure or diabetes and requires thorough medical evaluation.

Incontinence can be broadly divided between that requiring surgical intervention and that requiring medical or behavioral therapies. In general, incontinence related to primary nocturnal enuresis or infrequent voiding tends to resolve with time and does not require surgery. The following sections address the clinical presentation, evaluation, and treatment of lower urinary tract abnormalities associated with urinary incontinence in girls.

FUNCTIONAL CAUSES OF URINARY INCONTINENCE

Functional causes of urinary incontinence include primary nocturnal enuresis, dysfunctional voiding, and pseudoincontinence (i.e., vaginal voiding).

Nocturnal Enuresis

Primary nocturnal enuresis is defined as persistent nighttime wetting past the age of 5 years. Nocturnal enuresis occurs in approximately 20% of 5-year-old children and is more common in boys than girls [3]. Daytime wetting, urinary urgency, and frequency are more common in girls. Diagnosis and treatment of nocturnal enuresis is multifactorial, relying on both the pathophysiology and psychological analysis of the child. Simple behavioral strategies to help children gain control include star charts and other reward systems, fluid restriction, bladder training (including retention control training), and wakening. These are often used as a first attempt to control bedwetting and can be undertaken by families with less professional involvement [4]. Treatment using desmopressin, bedwetting alarm, or combination therapy is often successful in children that do not respond to behavioral modification alone [5–7]. Daytime and nighttime symptoms such as wetting, urgency, and frequency may be treated with anticholinergic medications as well as biofeedback [8,9].

Dysfunctional Voiding and Voiding Dysfunction

Although the terms “dysfunctional voiding” and “voiding dysfunction” are often used interchangeably, such usage is incorrect. According to the Standardization Committee of the International Children’s Continence Society, children with dysfunctional voiding void against a tightened or contracted external urethral sphincter [10]. The term describes malfunction during the voiding phase only. These children have difficulty relaxing their pelvic floor musculature and habitually contract the urethral sphincter during voiding. The rectum and urethra both traverse the pelvic floor. As a result, day- and nighttime wetting, urinary frequency, urgency, hesitancy, urinary tract infections, constipation, and/or encopresis is common. These children respond well to biofeedback [8]. Botulinum toxin A (Botox®) can be injected into the external sphincter in severe cases that are refractory to more conservative management options [11].

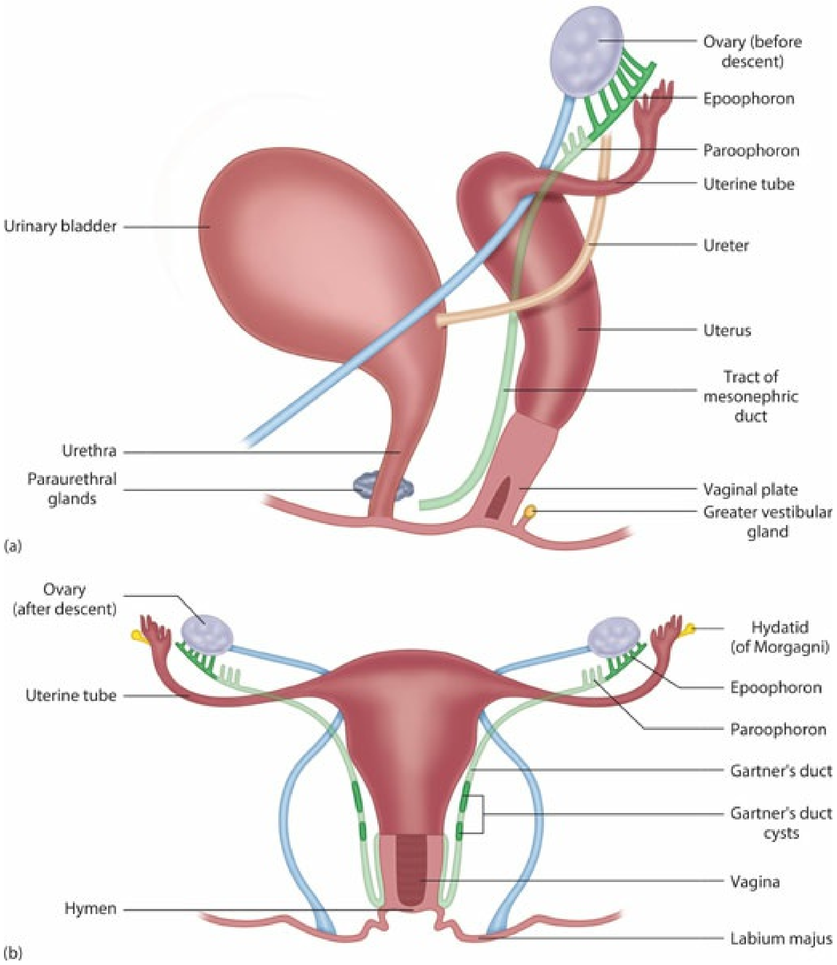

Figure 114.1 Embryology and development of the female genital tracts: (a) a 12-week fetus and (b) a newborn female (urogenital sinus, mesonephric duct, paramesonephric duct).

Table 114.1 Female Embryology

Weeks of gestation	**Embryonic structure/event**	**Adult counterpart**
7–8	Genital ridge transformed	Ovary
9–10	Müllerian ducts fuse distally	Fallopian tubes, uterus, cervix, proximal vagina
12–20	Sinovaginal bulbs elongate and form vaginal plate; canalization of plate at urogenital sinus	Distal vagina
	Genital tubercle elongates	Clitoris, hymen
	Urethral folds do not fuse	Labia minora
	Labial swellings enlarge	Labia majora
	Urogenital groove remains	Introitus
	Mesonephric ducts	Ureters
	Vestigial structures: Mesonephric duct	
	Proximal end	Appendix vesiculosa, paroöphoron, and epoöphoron
	Distal end	Gartner's duct/cysts

Voiding dysfunction, on the other hand, is a much broader term that encompasses all disorders of urinary elimination and storage. These problems can significantly affect a child's quality of life. A thorough history, physical exam, and noninvasive evaluation are essential to ruling out organic causes and to establish an etiology [12]. It is helpful for patients and their families to keep an elimination diary to ascertain the child's specific toileting habits. For example, many parents are not aware that their child has constipation unless specifically queried as to the frequency and caliber of the stool. Simple treatment of constipation with stool softeners (i.e., mineral oil, Kondremul) or laxatives (i.e., milk of magnesia, Dulcolax, or polyethylene glycol 3350) permit better overall toileting behavior. Voiding dysfunction may be treated by behavior modification or pharmacological agents and rarely requires surgical intervention. A rare consequence of dysfunctional elimination is *phantom* urinary incontinence—an entity whereby children sense wetness when they are, in fact, dry. This phenomenon is strongly associated with obsessive compulsive disorder and responds completely to effective treatment of constipation [13]. A list of common pharmacotherapeutic agents for bladder dysfunction is provided in Table 114.2.

Vaginal Voiding

Vaginal voiding is often confused with true urinary incontinence. Micturition into the vagina results in leakage when the child stands upright, allowing efflux of urine from the vaginal vault. Clinical findings consistent with vaginal voiding include postvoid dribbling, labial fusion, and leaning forward at an extreme angle during micturition [14]. Simple maneuvers to direct the urinary stream more accurately by separating the legs further during voiding, and waiting a few minutes after micturition to allow efflux into the toilet, usually solve the problem (Figure 114.2).

Table 114.2 Pharmacotherapy for Neurovesical Dysfunction

Drug	Action	Dose/frequency
Bethanechol	Cholinergic	0.6 mg/kg/day 3–4 times daily
Dicyclomine	Anticholinergic	5–10 mg 3–4 times daily
Oxybutynin	Anticholinergic	0.2 mg/kg 2–4 times daily
Propantheline	Anticholinergic	1.5 mg/kg/day 3–4 times daily

CONGENITAL ABNORMALITIES CAUSING INCONTINENCE

Congenital anomalies may cause incontinence by interfering with the function of the sphincter mechanisms or the storage capacity of the bladder, or by anatomically bypassing normal sphincter mechanisms (Table 114.3).

Imaging studies are essential to define the anatomic abnormalities causing the incontinence. The first studies obtained are usually renal and bladder ultrasonography and voiding cystourethrogram (VCUG). The plain abdominal scout film of the VCUG assesses bony abnormalities and the presence or absence of fecal impaction. Magnetic resonance urography and intravenous pyelogram are useful to identify ectopic ureters, duplication anomalies, and ureteroceles, as well as providing useful information regarding renal function. Urodynamic studies are often useful in detecting sphincteric, storage, and urinary flow abnormalities and are essential in all patients with neurogenic incontinence. The goals of treatment for congenital abnormalities of the female urogenital tract are restoration of physical appearance and function, preservation of renal function, and achievement of manageable urine storage and continence.

Abnormal Storage

Bladder Exstrophy

Bladder exstrophy (Figure 114.3) is a rare congenital malformation, resulting in a lower abdominal wall defect exposing an open bladder and urethra, a wide diastasis of the pubic symphysis, and an epispadic urethral opening. It has an incidence between 1 in 10,000 and 50,000 live births and is less common in females than in males [15,16]. Debate continues about the development of the bladder wall and matrix proteins. Why some children develop normal bladder capacities while others go on to develop small and poorly compliant bladders is incompletely understood.

A range of surgical techniques (complete versus staged repairs) have been employed to achieve successful primary bladder closure with or without pelvic osteotomies. Early bladder closure within 72 hours was advocated in the past; more recently, delayed primary closure has demonstrated comparable outcomes [17,18]. Bladder augmentation or diversion are surgical options later in life, although some patients require no such intervention [19]. Bladder neck reconstruction may be performed at the time of bladder closure or afterward. Continence rates vary greatly depending upon the strictness of definition as well as length of follow-up. Stress incontinence has been managed successfully with injections of dextranomer/hyaluronic acid (Deflux®) into the bladder neck [20,21]. In a survey of women who underwent closure of bladder exstrophy as infants, most experienced normal menses, the majority were sexually active and satisfied with their social lives, and some had borne children (all via cesarean section). Unfortunately, almost half reported some degree of psychological distress resulting from their malformation [22].

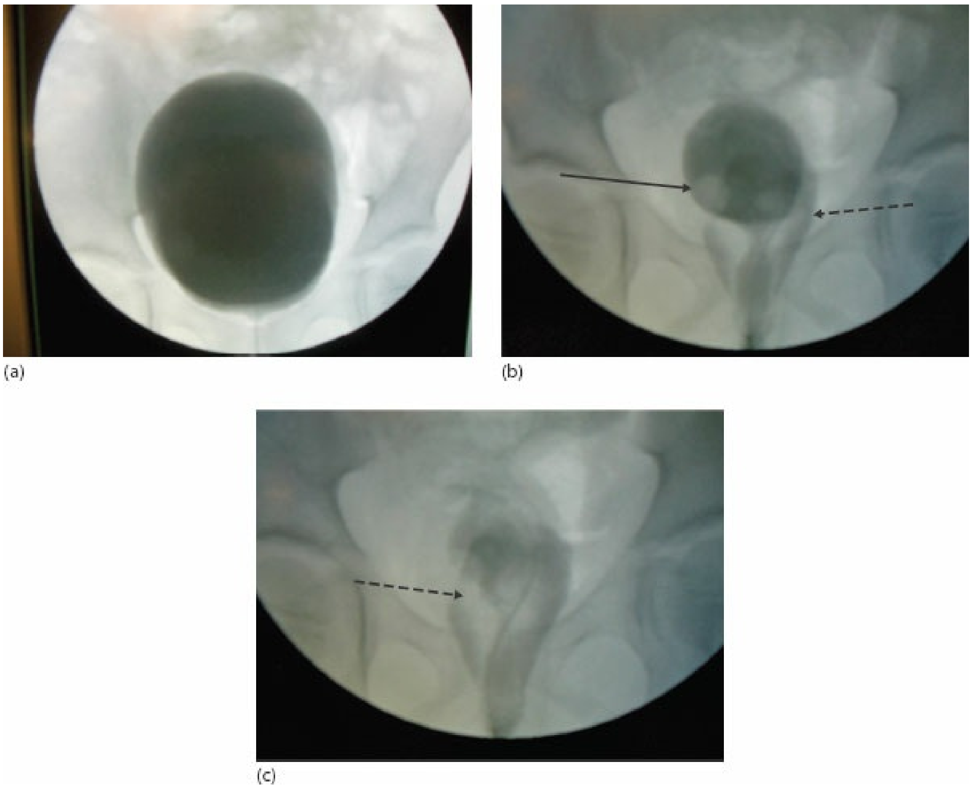

Figure 114.2 A 4-year-old girl with bilateral vesicoureteral reflux and daytime dampness was treated with endoscopic implantation of Deflux. A voiding cystourethrogram 3 months later shows cure of reflux, but the presence of vaginal voiding. (a) Bladder filling; (b) voiding phase showing absence of reflux, the presence of filling defects in bladder base (Deflux implants, solid arrow), and beginning of vaginally voided contrast (dashed arrow); (c) postmicturition film showing the presence of dense contrast within the vagina (dashed arrow) and nearly empty bladder.

Table 114.3 Mechanisms of Incontinence in Congenital Genitourinary Anomaliesa[a]

Abnormal storage	Abnormal sphincter	Bypass sphincter
Bladder exstrophy	Epispadias	Ectopic ureters
Cloacal exstrophy	Urogenital sinus	Vesicovaginal fistulae
Bladder agenesis	Ectopic ureteroceles	
Bladder duplication	Neurogenic[b]	
Neurogenic[b]		

[a] Multiple mechanisms for incontinence often coexist in a given patient.

[b] Abnormalities of storage or sphincteric function may be seen with neurogenic bladders (e.g., spina bifida) and may be related to detrusor hypo- or hyperactivity, or from secondary changes within the detrusor muscle, resulting in stiff (noncompliant) or floppy (very compliant) bladders.

Cloacal Exstrophy

Cloacal exstrophy (Figure 114.4) has an incidence of 1 in 200,000–400,000 and is much less common in females. Cloacal exstrophy is much more complex than bladder exstrophy and is commonly referred to as the omphalocele, exstrophy of the bladder, imperforate anus, and spinal abnormalities (OEIS) complex [15].

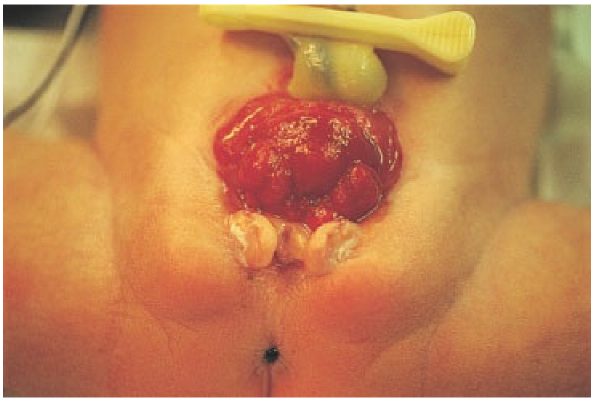

Figure 114.3 A newborn girl with bladder exstrophy. Note separation of the labia and clitoris, and the normal vagina.

Management of cloacal exstrophy requires a multidisciplinary team–based approach, with the principal goals of treatment focusing on patient function, psychosocial development, and overall quality of life. The treatment of storage abnormalities of the bladder resulting from this anomaly usually involves bladder augmentation with intestinal segments. Clean intermittent catheterization (CIC) may also be required to maintain urinary continence.

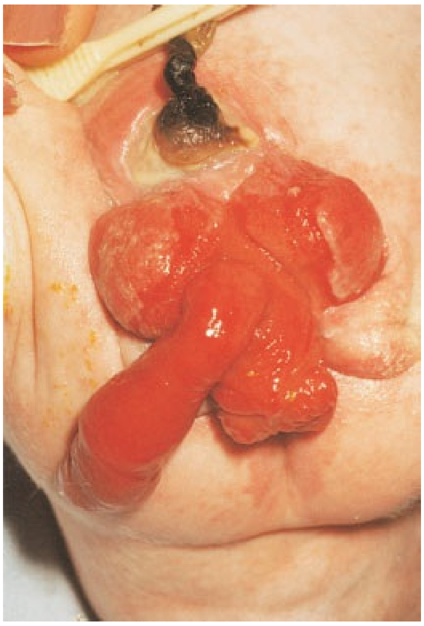

Figure 114.4 Newborn with cloacal exstrophy illustrating separation of bladder halves, herniation of the hindgut, and prolapse of the ileocecal segment.

Myelomeningocele

In the pediatric population, myelomeningocele (Figure 114.5) is the most common cause of neurogenic bladder leading to problems with urinary storage, sphincteric function, and elimination. In the United States, the prevalence is approximately 1 in 1000 live births. The goals of management of pediatric neurogenic bladder include achieving low-pressure urinary storage and providing urinary continence while preserving upper tract function. CIC in conjunction with anticholinergic medication has brought about a dramatic improvement in the management of patients with myelomeningocele. The use of CIC has been shown to promote continence, preserve renal function, and decrease the incidence of symptomatic pyelonephritis [23]. McGuire et al. [24] determined that leak-point pressure > 40 cm H_2O was predictive of renal deterioration over time. CIC serves to keep bladder pressure low, thereby decreasing significantly the risk of upper tract deterioration. Bladder augmentation, with creation of a cutaneous continent catheterizable channel and/or bladder neck procedures, is a frequent component in attaining management goals in a substantial number of children who fail medical management.

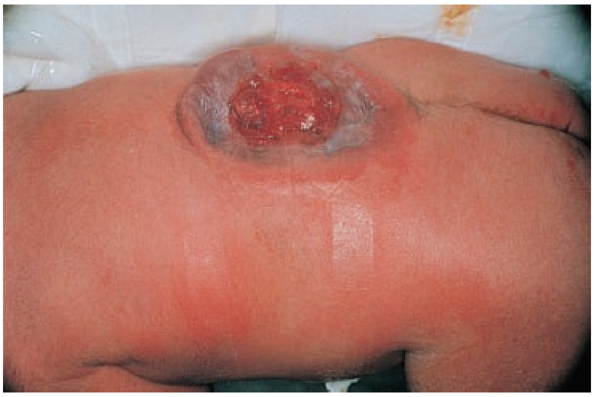

Figure 114.5 A newborn with characteristic appearance of myelomeningocele protruding from the lower back.

Abnormal Sphincter

Anatomic abnormalities may impede normal development of the bladder neck. Incompetence of the bladder neck may result in primary urinary incontinence and is seen in conditions such as female epispadias, urogenital sinus, bilateral ureteral ectopia, and ectopic ureteroceles. Conservative measures to improve sphincteric function are limited and surgical intervention is warranted. Surgical options focus on the creation of an increase in bladder outlet resistance or a new sphincter mechanism.

Female Epispadias

Female epispadias (Figure 114.6) occurs in 1:480,000 female births [25] and may result in variable presentations, depending on the severity of the urethral defect. In mild cases, the diagnosis may not be apparent until the child remains wet into childhood. In complete epispadias, incontinence results secondary to (1) a foreshortened and widened urethra, (2) a partially absent external urethral sphincter, and (3) a poorly developed bladder neck. Treatment is directed at the reconstruction of these deficient structures and ureteral reimplantation proximal to the reconstructed bladder neck [26,27]. Persistent incontinence may be treated with urethral bulking agent injection at the bladder neck.

Urogenital Sinus Anomalies

Persistence of a urogenital sinus may result in the urethra emptying into the vaginal vault. This may not be readily apparent unless the urethra is not visualized during attempt at catheterization. Infants may present with a dilated vagina, possibly resulting in an abdominal mass, if the posterior lip of the hymen causes partial obstruction at the orifice of the urogenital sinus (Figure 114.7). Retained urine in the vagina (urocolpos) and uterine canal may increase to enormous volumes. Drainage of urine with vaginal catheterization followed by a vaginogram showing contrast within the cervical canal and uterus, and possibly into the peritoneal cavity, is diagnostic. Treatment involves endoscopic division of the posterior hymenal lip. Further reconstructive surgery is often required (see discussion of congenital adrenal hyperplasia in the “Disorders of Sexual Differentiation” section).

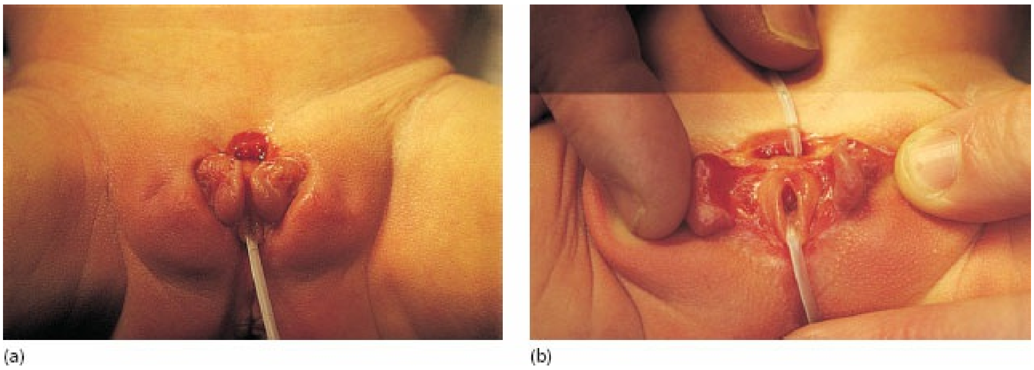

Figure 114.6 (a) Appearance of a newborn girl with epispadias and (b) note the open bladder neck with a catheter introduced superior to a normal catheterized vagina and separation of the labia and clitoris.

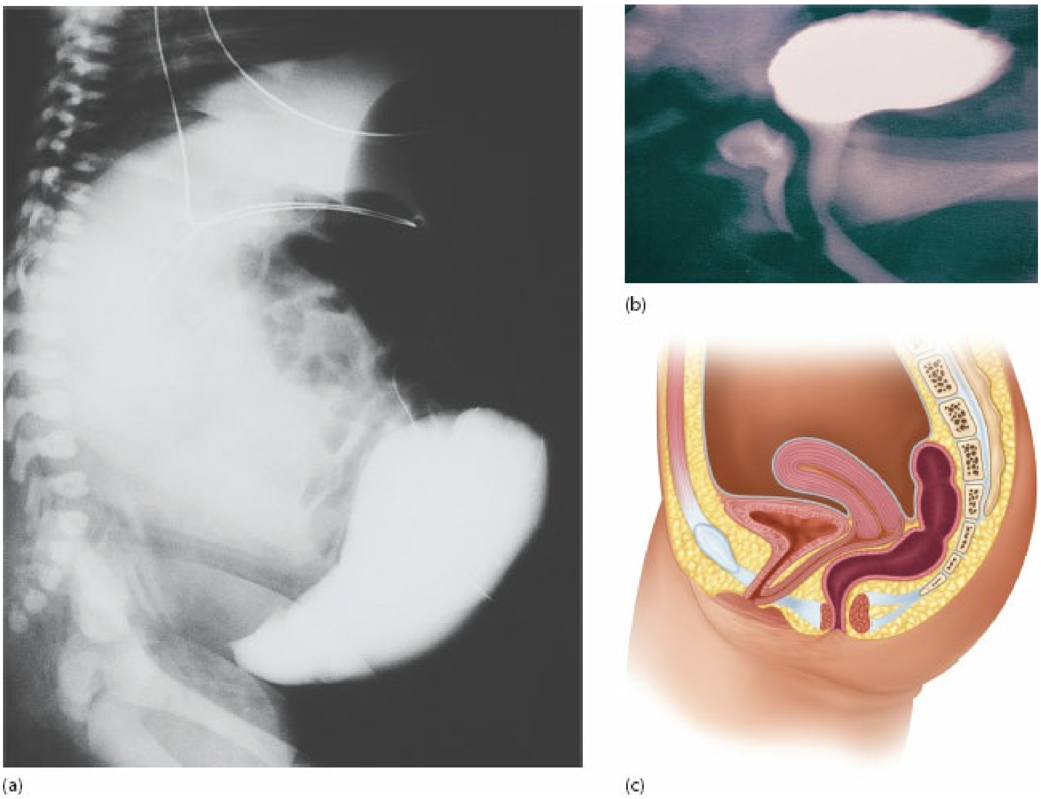

Figure 114.7 (a) This contrast vaginogram in a newborn girl with an abdominal mass shows retained fluid and an obstructed vagina (urocolpos) secondary to a urogenital sinus abnormality. (b) A flush genitogram in another patient reveals a urogenital sinus with contrast seen within the bladder and vagina. (c) Line drawing showing the relationship between the urethra, narrow distal vagina, and urogenital sinus.

Duplicated Ectopic Ureters

An ectopic upper pole ureter may join the lower end of the remnant mesonephric duct system comprising Gartner's ducts. These ureters are associated with nonfunction of the associated renal moiety and may result in cystic dilation of Gartner's duct with eventual rupture of the cyst and drainage into the vaginal opening. Drainage of fluid or pus into the vagina prompts further investigation. Renal and pelvic ultrasound may demonstrate a dilated or abnormal upper pole renal moiety, and a cystic structure may be seen in the pelvis or vaginal area. Computerized tomography scanning or magnetic resonance imaging are helpful in further delineating the anatomy, while retrograde fluoroscopic studies are diagnostic if the often-elusive ectopic orifice can be identified (Figure 114.8).

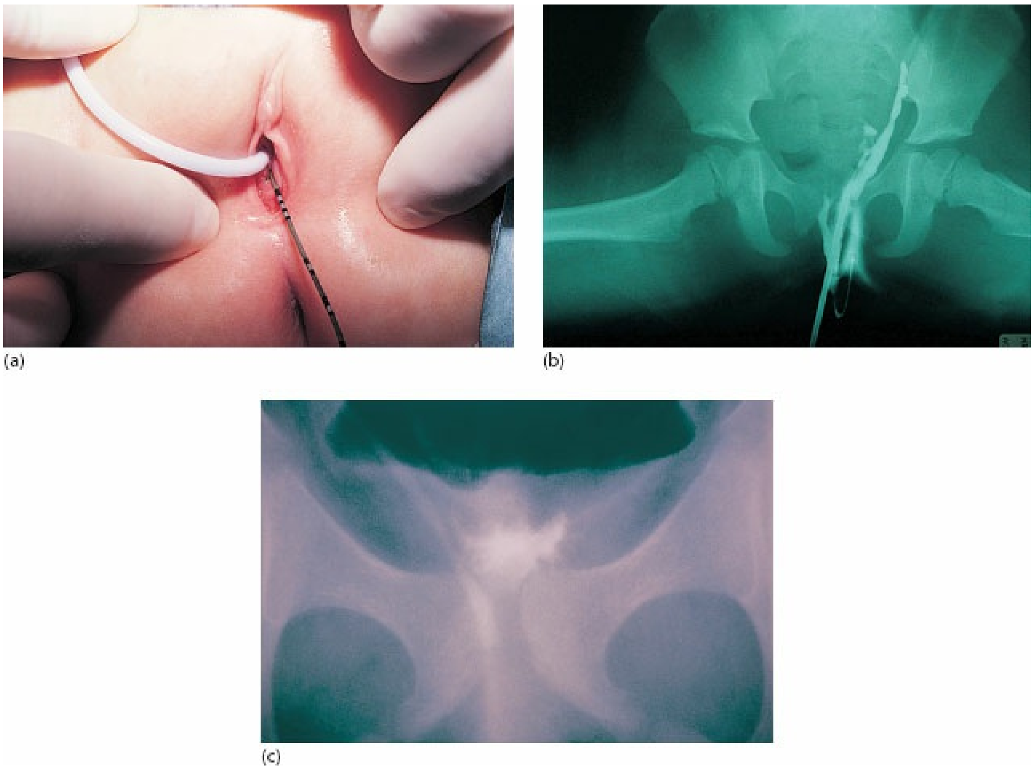

Figure 114.8 A young girl with continuously damp underpants was found to have ureteral ectopia to her vagina: (a) the vagina showing a ureteral stent placed within the ectopic ureter and a Foley catheter within the urethra; (b) retrograde pyelogram showing contrast within the ectopic ureter; and (c) an intravenous urogram in another patient revealing an ectopic ureter of an upper pole moiety terminating beyond the bladder neck and into the vaginal introitus.

Appropriate treatment of ureteral ectopia is dependent upon whether or not there is ureteral duplication and whether the ectopic ureter drains into the genital or urinary tract. Ectopic ureters to the genital tracts may be treated by simple upper pole nephrectomy; ectopia to the urinary tract usually involves ureterectomy in addition to heminephrectomy in order to prevent postoperative urinary reflux and infection (Figure 114.9).

Bypass of Sphincter Mechanism

In instances where the bladder neck and sphincter mechanism have developed normally, urinary incontinence may develop as a result of ureteral ectopia distal to the continence mechanism. The most common cause of this abnormality is ectopic ureters. Incontinence may not be purely secondary to a bypass mechanism, as abnormal urethral development may also contribute to poor urinary control.

Bilateral Single Ectopic Ureters

Ectopic ureters result when a ureteric bud develops more cranially than usual from the mesonephric duct. In females, ectopic ureters usually open into the urethra, vestibule, or vagina. Incontinence is a common complaint in girls with ectopic ureter(s). Bilateral ectopic ureters may enter the urethra just distal to the bladder neck. Because of inadequacy of urethral length associated with this condition, incontinence may result. In single ectopic ureters, a cyclic VCUG may demonstrate vesicoureteral reflux when the bladder neck relaxes upon micturition; reflux is often not demonstrated during bladder filling when the bladder neck is in a contracted state. Treatment involves ureteral reimplantation and bladder neck reconstruction for bilateral single ectopic ureters and upper pole partial nephrectomy and lower pole reimplantation for duplicated ectopic ureters. In unsuccessful cases, a continent catheterizable channel (i.e., appendicovesicostomy) or continent urinary diversion may be considered [28].

INTERLABIAL MASSES

Vaginal masses in infants and young girls are generally referred to as interlabial masses. Although many of these lesions arise within the introitus, those arising in the urethra or bladder must be recognized to afford proper management. Many patients with masses within the vaginal area complain of leakage of fluid (i.e., urine, pus, transudate). Thorough physical examination of the introitus is mandatory in the complete evaluation of urinary incontinence.

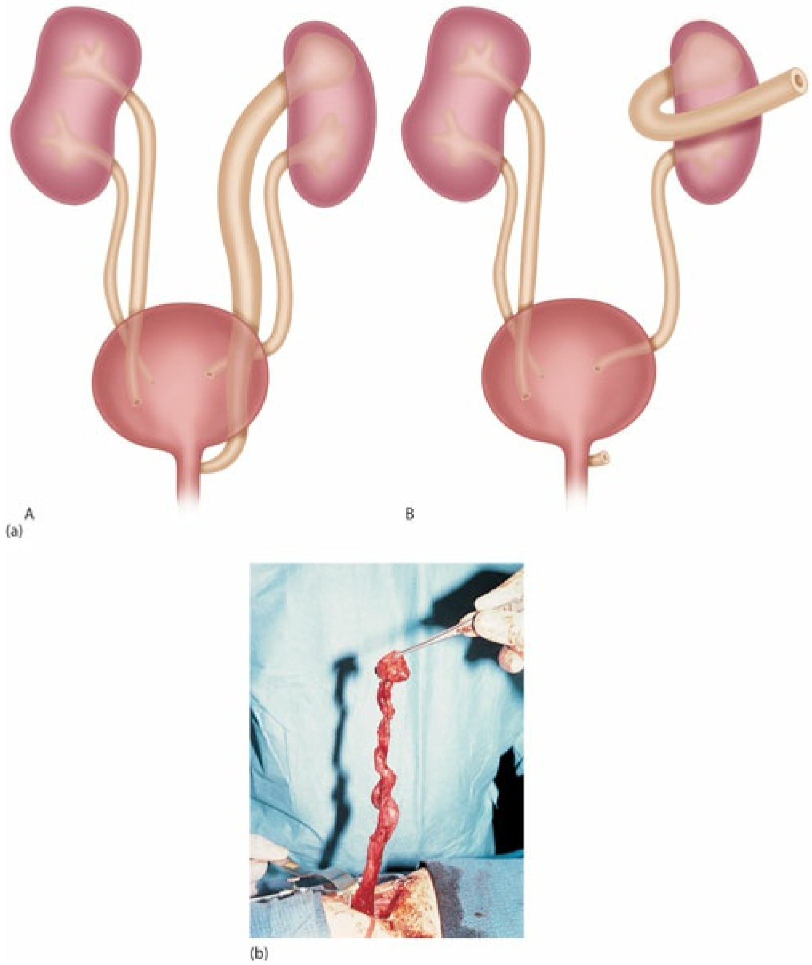

Figure 114.9 (a) Illustration of nephroureterectomy: (A) preoperatively and (B) postoperatively. (b) Nephroureterectomy specimen from the patient in Figure 114.7.

Skene’s Glands (Paraurethral Glands)

The tubular Skene’s glands (Figure 114.10) arise from the urethral epithelium and are the counterparts to the male prostate gland. In females, these glands may be present at the urethral meatus and hymen. Cysts (tense, yellow, thin-walled) partially arising within the urethral meatus but mostly external to it may resemble a bulging hymen associated with hydrometrocolpos, or a prolapsing ureterocele (fleshy, compressible, protruding through the urethra).

Bartholin’s Glands

The major vestibular glands of Bartholin arise from the urogenital sinus and open into the vestibule on either side of the hymen. The main glands lie against the ischiopubic ramus deep to the bulbospongiosus muscle and cavernous tissue. Blockage of the main ducts of Bartholin’s glands may lead to cystic dilation at any age but rarely become infected prior to puberty.

Prolapsed Ureterocele

Ureterocele is a dilated distal ureter within the detrusor muscle that may extend beyond the bladder neck (cecoureterocele). Ureteroceles are often associated with an upper pole renal moiety of a duplicated collecting system [29]. They may be ectopic or orthotopic. An interlabial or vulvar mass may be identified if the ectopic ureterocele extends through the urethral meatus (Figure 114.11). Treatment is directed at ureterocele excision, bladder neck reconstruction, and ureteral reimplantation [30].

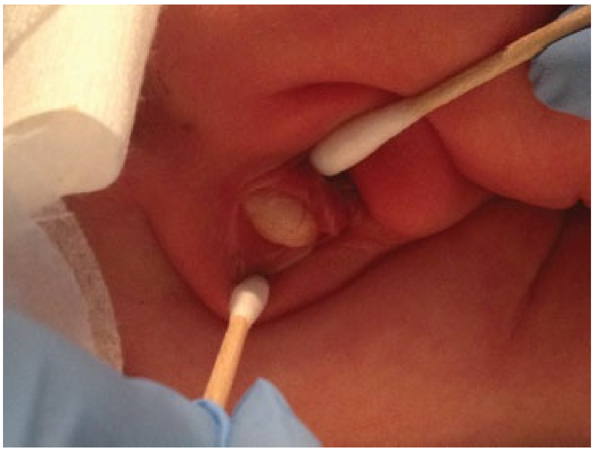

Figure 114.10 Skene's glands in a newborn girl.

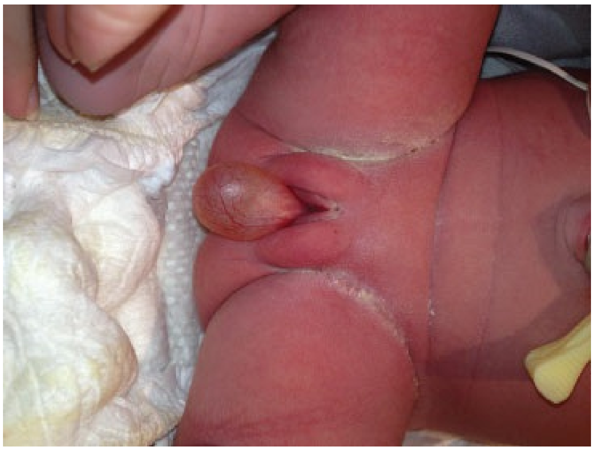

Figure 114.11 A newborn girl with urinary obstruction: external appearance of a prolapsing ectopic ureterocele.

Hydro(metro)colpos

Circulating maternal estrogen in the female neonate may result in an increased production of cervical mucus. Hydrocolpos and hydrometrocolpos result when mucus collects in the vaginal vault and uterus, respectively. The vaginal orifice may be blocked secondary to imperforate hymen, urogenital sinus, anatretic rectocloacal canal, or vaginal/uterine atresia. Hydrometrocolpos, by virtue of its abdominal extension, may compress the urethra, rectum, and ureters.

Treatment of hydro(metro)colpos secondary to a normally located imperforate hymen may involve simple perforation of the hymen when the infant is in the newborn nursery. If the hymen appears thickened, incision under general anesthesia may be required. Higher obstruction involves a more formal approach to treat the associated urogenital abnormalities (i.e., urogenital sinus, atresia, rectocloacal canal).

Urethral Prolapse

Eversion of the distal urethral mucosa through the meatus results in a circumferential interlabial lesion (Figure 114.12). Urethral prolapse may be painful or may bleed or weep serosanguinous fluid, prompting medical attention; however, such lesions do not lead to urinary incontinence. On examination, urethral prolapse appears edematous or necrotic, with the urethral meatus seen within its center. This lesion should be distinguished from neoplasms of the vagina or bladder (see Figure 114.14). A prolapsed urethra associated with mild edema without necrosis or significant pain may reasonably be treated conservatively with sitz baths and estrogen cream over a 2 to 3-week period. More significant lesions should be excised [31].

Rhabdomyosarcoma

Rhabdomyosarcoma of the vagina and bladder (Figure 114.13) most commonly presents with vaginal bleeding and a palpable cervical or vaginal mass [32]. Classically, a cluster-of-grape-like lesion is visualized as an interlabial mass [33]. Because of the propensity of these lesions to spread, a complete endoscopic and radiographic evaluation is indicated to confirm the diagnosis and rule out local extension and metastatic disease. Primary chemotherapy has resulted in improved bladder salvage and is often curative in the setting of metastatic disease. Surgical excision, with or without radiation therapy, is reserved for postchemotherapy biopsy-proven residual masses [34]. In recent years, a multimodal approach to genitourinary rhabdomyosarcoma has led to increased survival as well as pelvic organ preservation [35].

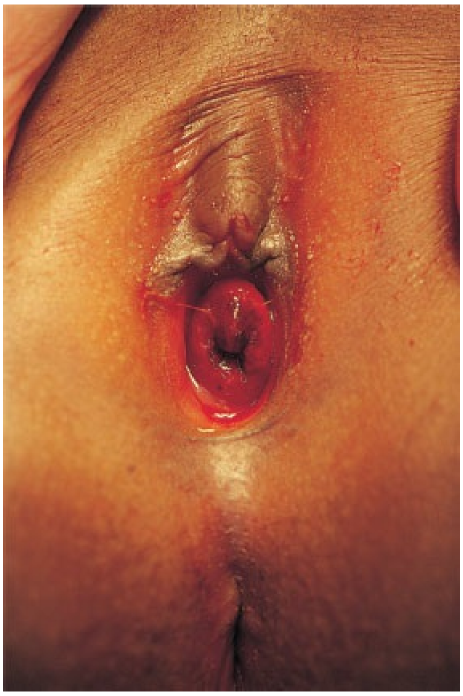

Figure 114.12 An 8-year-old African-American girl with urethral prolapse presented with *vaginal* pain and blood spotting.

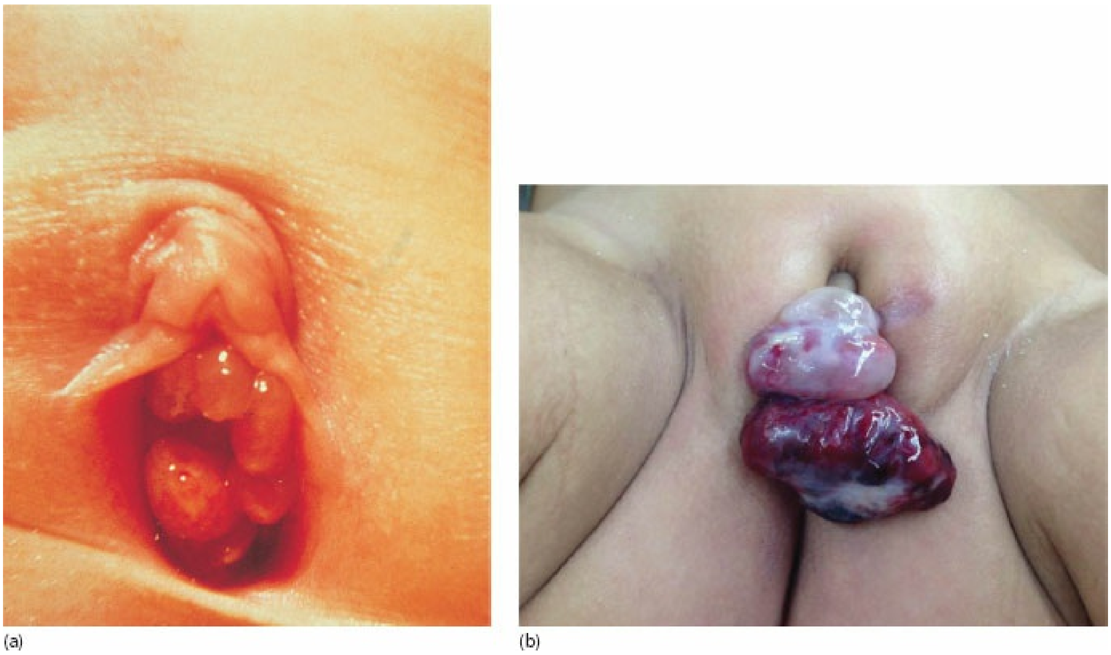

Figure 114.13 (a) A 5-year-old girl with rhabdomyosarcoma of the vagina (sarcoma botryoides) presented with blood spotting and dysuria. (b) An 18-month-old little girl with embryonal rhabdomyosarcoma who initially presented with urinary retention and prolapsed bladder tumor.

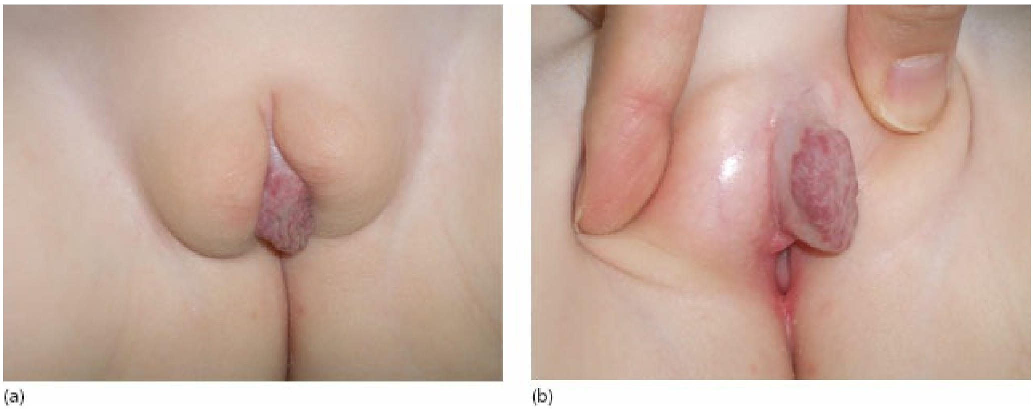

Figure 114.14 (a, b) A 1-year-old girl presenting with an enlarging introital mass revealing a large cavernous hemangioma of the clitoris.

Introital Hemangiomas

Hemangiomas of the female genitalia are rare. In most cases, hemangiomas are congenital and can involve any part of the genitalia. Cavernous hemangiomas (angioma cavernosum, cavernoma) are similar to strawberry hemangiomas but are more deeply situated. They may appear as a red-blue spongy mass of tissue filled with blood. Some of these lesions spontaneously involute, usually as a child approaches school age. Hemangiomas can be quite large and may be confused with tumors, or—if involving the clitoris—may appear as clitoromegaly similar to that seen in cases of congenital adrenal hyperplasia (Figure 114.14). Treatment options include steroid injection, potassium-titanyl-phosphate laser ablation and/or excision, depending on the size and location.

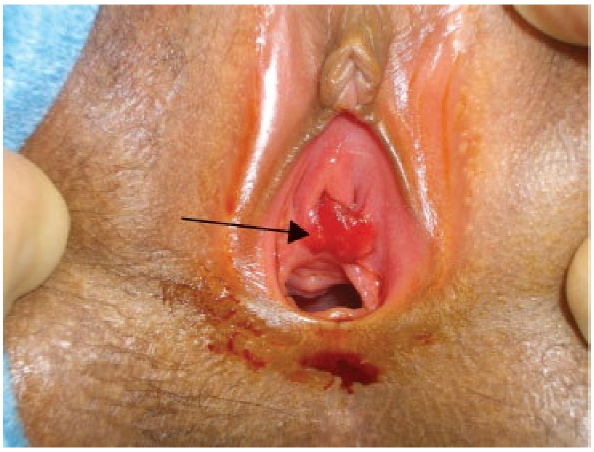

Figure 114.15 A 6-year-old girl presenting with blood spotting in underwear and dysuria. Arrow shows urethral polyp.

Urethral Polyps

Urethral polyps are rare anomalies, characterized as benign urothelial-lined masses attached to a fibrovascular stalk, and may lead to symptoms by obstructing the ureter or bladder neck by a ball–valve mechanism. Some of these polyps, diagnosed later in life, may represent acquired lesions. Polyps may occur anywhere along the urinary tract. Primarily they are composed of connective tissue covered by epithelium. Additionally, smooth muscles and islands of glandular cells and even nerve tissue have been found. Treatment is by endoscopic ablation or excision, depending on origin. Fibroepithelial polyps may present as interlabial masses and may lead to bleeding or dysuria when located in the urethral meatus (Figure 114.15).

DISORDERS OF THE FEMALE GENITALIA

Disorders of Sexual Differentiation

A complete description of the array of intersex disorders is beyond the scope of this chapter. However, urologists and gynecologists must be familiar with the more common disorders of sexual differentiation whereby gender assignment and rearing is along female lines. These conditions include girls of normal appearance who are genetically male (46,XY DSD; previously referred to as male pseudohermaphrodite) and genetic females appearing as males (46,XX DSD; previously female pseudohermaphrodite) [36].

46,XX DSD (Female Pseudohermaphroditism)

Females with 46,XX DSD may appear as males with nonpalpable testes (Figure 114.16). The most common etiology is congenital adrenal hyperplasia (21-hydroxylase deficiency in >90%). This autosomal-recessive disorder is among the most common heritable metabolic disorders [37]. The absence of 21-hydroxylase leads to the overproduction of androgens and results in a wide spectrum of genital abnormalities, ranging from mild masculinization of the clitoris (clitoromegaly) to complete masculinization. The labioscrotal folds are often rugated and hyperpigmented, giving the physical appearance of severe hypospadias with cryptorchidism. In virtually all cases, however, the internal female anatomy is normal. After the diagnosis is established, surgical treatment is individually tailored; feminizing genitoplasty entails reduction clitoroplasty, vaginoplasty, and urogenital mobilization [38,39]. These patients generally require lifelong glucocorticoid (hydrocortisone) and mineralocorticoid (9-alpha-fludrocortisone) supplementation [40].

46,XY DSD (Male Pseudohermaphroditism)

46,XY DSD patients are genetic males but may appear as phenotypic females. Testicular feminization is the most common cause of 46,XY and results from the lack of androgen receptors at the cell surface of all tissues. This diagnosis should be suspected in all girls with inguinal hernias; the hernia sacs may contain testes. The diagnosis should also be considered in adolescent girls with normal development and primary amenorrhea [36]. Development and sexual identity is female. Treatment involves bilateral orchiectomy. The availability of estrogen-replacement therapy allows for the option of early gonad removal at the time of diagnosis that also takes care of the associated hernia, psychological problems with the presence of testes, and the malignancy risk. Estrogen must be replaced at puberty in girls who have undergone prepubertal orchiectomy, which is the standard of care due to risk of malignancy.

Vaginal Agenesis and the Mayer–Rokitansky Syndrome

Agenesis of the vagina in genetic females (Figure 114.17a) may be associated with various other defects of the genitourinary tract. Most patients present in adolescence with amenorrhea or pain, but this condition may also present in young girls with urinary tract infection or hydrocolpos. Genital defects range from vaginal agenesis alone to agenesis of the uterus and fallopian tubes. These genital anomalies are associated with (ipsilateral) renal agenesis [41]. In some patients, stress urinary incontinence may result after having urethral intercourse.

Treatment of the Mayer–Rokitansky syndrome (vaginal agenesis and solitary kidney) may include progressive vaginal dilation, vaginoplasty, or neovaginal reconstruction with bowel. Many iterations and modifications of vaginal dilation exist. Most simply, the patient can self-dilate with progressively larger vaginal dilators. Alternatively, an olive-shaped dilator or balloon can be (laparoscopically) placed into the vaginal dimple through the retropubic space. Upward traction is progressively applied via a pulley mechanism attached to the abdominal wall [42,43]. Alternatively, skin can be grafted into the vaginal space [44], or sigmoid colon can be used in vaginal replacement [45] (Figure 114.17b). Longterm outcomes of patients undergoing creation of bowel neovagina indicate it is a durable and functionally desirable reconstructive option [46].

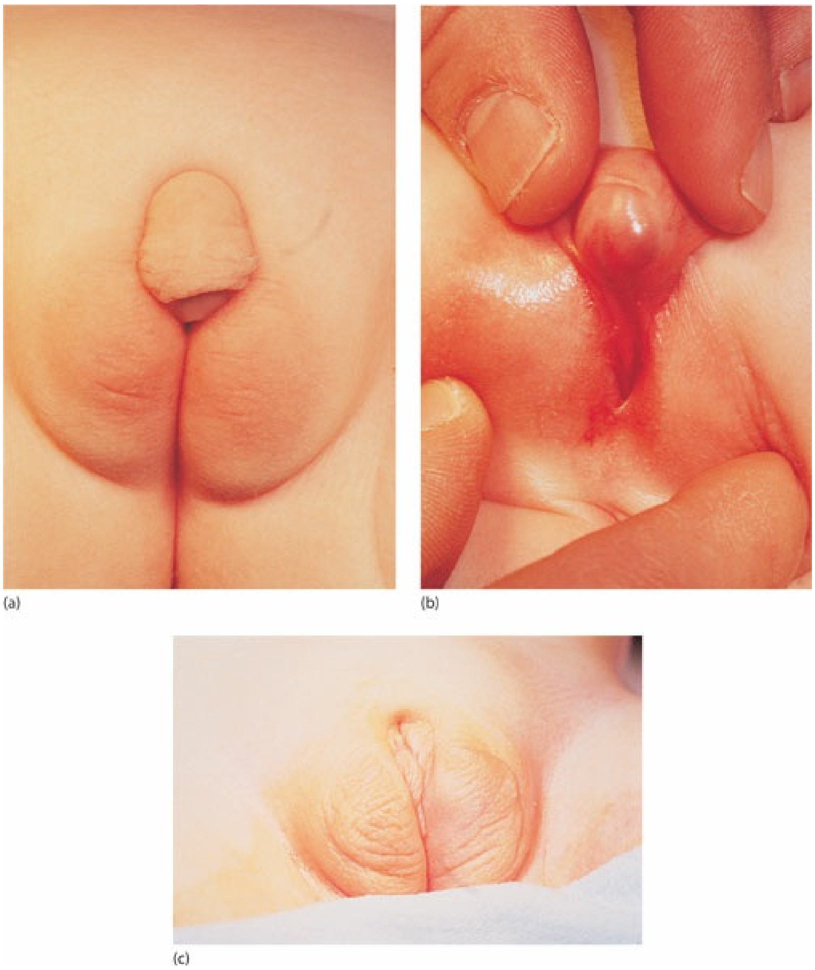

Figure 114.16 This newborn with ambiguous genitalia, elevated 17-hydro-oxyprogesterone and XX chromosomes was diagnosed with congenital adrenal hyperplasia (21-hydroxylase deficiency): (a)

preoperative appearance showing phallic structure and nonpalpable gonads; (b) prominent scrotal folds and clitoromegaly; and (c) appearance 6 months after reduction clitoroplasty and scrotoplasty.

URINARY TRACT RECONSTRUCTION

Lower Urinary Tract Reconstruction

Since 1950, bowel segments have been used to replace a diseased or severely dysfunctional bladder. The current success in reconstruction of the lower urinary tract reflects improved understanding of the physiological principles involved in bladder and urethral function [47–52]. Spontaneous voiding can occasionally be achieved with an abnormal lower urinary tract, provided that the pressure gradient between the bladder and distal urethra is low. It follows, then, that even in cases where the bladder is replaced in part (intestinal cystoplasty) or entirely (neobladder), patients may still be able to empty their bladders satisfactorily. Many patients require bladder neck reconstruction [53] or a sling procedure to achieve continence and most will require CIC [54]. Since the advent of injectable urethral bulking agents, many patients with sphincteric incontinence owing to various causes have benefitted from antegrade and retrograde bladder neck bulking [55].

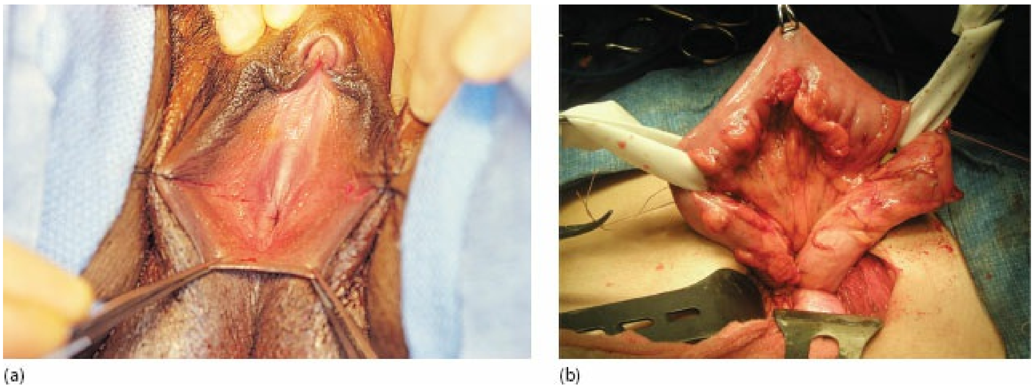

Figure 114.17 (a) Vaginal agenesis in a 16-year-old with Mayer–Rokitansky syndrome. The sexually active patient engaged in urethral coitus. (b) The sigmoid colon (8–10 cm) is isolated on its mesentery and will be mobilized to the vaginal introitus to create a neovagina. The colonic mucus allows for natural lubrication during coitus.

Continent reconstruction of the lower urinary tract is often desired in the face of congenital or acquired anomalies of both the outlet and bladder. The early work of Hendren, Mitrofanoff, and others has led to surgical approaches that produce both better reservoir function and a continent outlet [56]. Continent urinary diversion encompasses three interrelated but independently functioning components. These include a channel by which urine is conducted to the skin, a reservoir or pouch, and a mechanism by which continence is achieved [57]. A host of tissues are available to the reconstructive surgeon (Table 114.4).

The flap valve principle for continence dictates that a portion of the continence channel be fixed on the inner wall of the reservoir. This is the same principle by which ureteral tunneling in the bladder muscle prevents reflux during voiding. In general, a 5:1 length-to-diameter ratio of the continence structure is required.

Table 114.4 Tissues Available for Lower Urinary Tract Reconstruction[a]

External conduit	Urinary reservoir	Continence mechanism
Appendix	Bladder	Anal sphincter
Fallopian tube	Cecum	Artificial urinary sphincter
Ileum	Colon	Benchekroun (hydraulic valve)
Skin tube	Rectum	Koch (nipple valve)
Stomach	Stomach	Mitrofanoff (flap valve)
Urethra		Urethral sphincter

Ureter

[a] In general, three components are required for continent diversion: (1) conduit from the reservoir to the skin, (2) a pouch or reservoir, and (3) a mechanism by which continence is attained.

The Mitrofanoff principle of continent reconstruction describes a supple catheterizable structure (ureter, appendix, etc.) implanted into the inner wall of the reservoir to create a flap valve continence mechanism [58]. The most popular form of flap valve construction for urinary continence is the use of appendix implanted into the bladder or reservoir (appendicovesicostomy). The small stoma may be concealed within the umbilicus (Figure 114.18). Assurance of complete bladder emptying is essential, as this type of continence channel is very effective in its ability to withstand elevated intraluminal pressures. In the noncompliant patient, pouch rupture, or upper tract injury may result from failure to empty the reservoir regularly.

Urinary Tract Reconstruction and Pregnancy

Future pregnancy must be kept in mind when reconstructing the genitourinary tract. Pregnancy may be complicated and requires care by both the obstetrician and urologist. Renal obstruction and incontinence may result as the uterus enlarges. Neobladder reconstruction has a good outcome, but chronic bacteriuria is frequent and occasionally requires an indwelling catheter in the third trimester [59]. Similarly, when suprapubic catheterizable continent stomas have been constructed, indwelling catheterization through the stoma during the third trimester may be required to avoid recurrent urinary tract infections from status [60].

Successful pregnancies and deliveries have been reported after both continent and loop urinary diversions [61–64]. The mode of delivery should be guided by obstetric indications, although vaginal delivery has been successful in the majority of cases. Alternatively, if the bladder neck has been reconstructed, it is usually advisable for delivery to be by cesarean section to avoid damage to the bladder neck reconstruction. The urologist should be available to the obstetric team for consultation if cesarean section is deemed necessary, especially if a bladder augmentation with bowel has been carried out, in order to avoid injury to the vascular pedicle to the bowel segment.

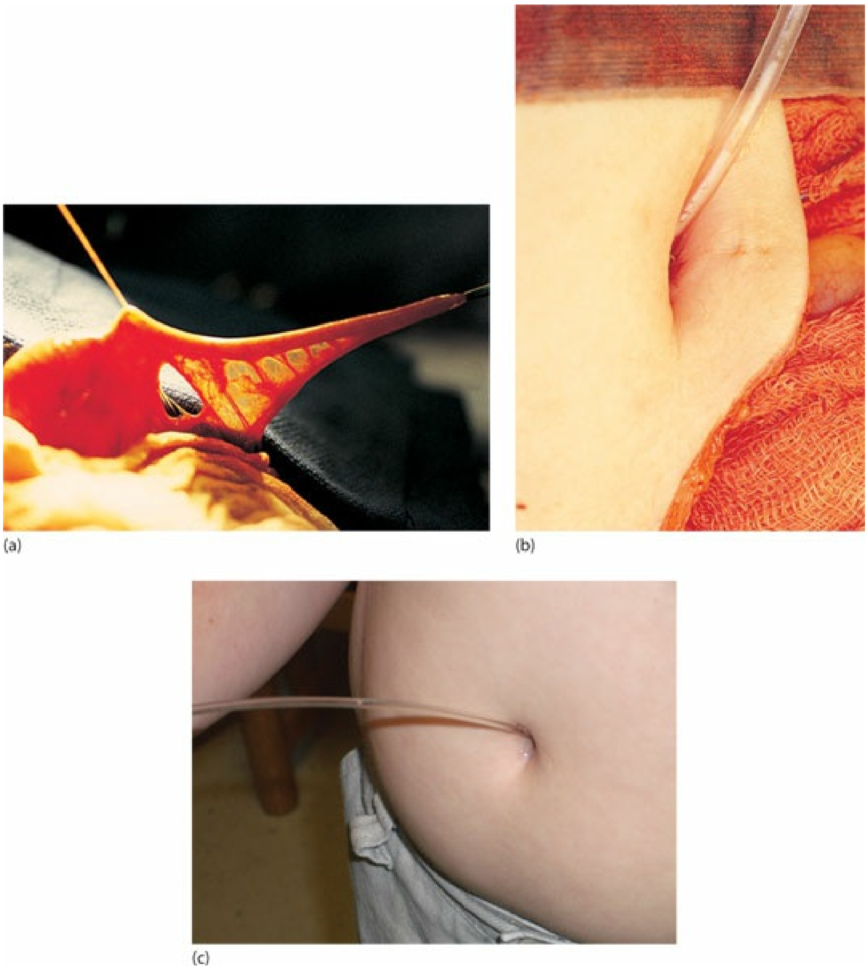

Figure 114.18 In the Mitrofanoff procedure, the appendix is mobilized with its blood supply as illustrated in (a) and reimplanted into the bladder in a tunneled nonrefluxing fashion. The proximal appendix may be brought out to the umbilicus for clean intermittent catheterization (b). Same patient 2 years after appendicovesicostomy performing self-catheterization (c).

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115 Female Genital Cosmetic Surgery: From Female Genital Cutting to Vaginal Rejuvenation

Lauri J. Romanzi

OVERVIEW

Genital modification spans the course of recorded history. Mounting attention focused on traditional female genital cutting (FGC) parallels the modern phenomenon of *female genital cosmetic surgery* (FGCS), a.k.a. *vaginal rejuvenation*. Vaginal rejuvenation is a marketing term with no formal medical definition. In its December 2013 policy statement, the Society of Obstetricians and Gynaecologists of Canada (SOGC) recommends that "Non-medical terms, including but not restricted to vaginal rejuvenation, clitoral resurfacing, and G-spot enhancement, should be recognized as marketing terms only, with no medical origin; therefore they cannot be scientifically evaluated" [1,2].

Adopted in response to unprecedented health-care market demands in the industrialized Americas, Europe, Australia, and Asia, the term *vaginal rejuvenation* includes procedures done for (oft overlapping) functional, cosmetic and sexual enhancement client goals. The alternate terms *female genital plastic surgery, cosmetic genital surgery, aesthetic gynecology*, and *genital beautification* are used by plastic surgeons, urologists, gynecologists, and urogynecologists providing these services, which include the most common procedures of labiaplasty in the form of labia minora reduction, labia majora reduction and augmentation, clitoral unhooding, Grafenberg (G)-spot injection, periclitoral injection, perineoplasty, Laser Vaginal Rejuvenation® (LVR), Designer Laser Vaginoplasty® (DLV), *revirgination* through hymenoplasty or hymenorrhaphy, and wrinkle reduction surface radiofrequency therapy applied to labial, vulvar, and groin skin. Arguably, the most widely used marketing term is female genital cosmetic surgery (FGCS). Overall FGCs satisfaction ranges from 89%–100% with complication rates (wound dehiscence, hematoma, dyspareunia) to 5%–9.3% [3,4].

The American College of Obstetrics and Gynecology (ACOG) included vaginal rejuvenation, designer vaginoplasty, revirgination, labiaplasty, and G-spot amplification in the 2007 Committee Opinion 378 "Vaginal rejuvenation and cosmetic vaginal procedures" stating that "Medically indicated surgical procedures may include reversal or repair of female genital cutting (FGC, a.k.a. female genital mutilation, or FGM) and treatment for labial or asymmetrical labial growth secondary to congenital conditions, chronic irritation or excessive androgenic hormones." This committee opinion goes on to list vaginal rejuvenation, designer vaginoplasty, revirgination, and G-spot augmentation as procedures with no medical indication, the safety and efficacy of which have yet to be proved. It ends stating "Women should be informed about the lack of data supporting the efficacy of these procedures and their potential complications, including infection, altered sensation, dyspareunia, adhesions, and scarring" [5].

In response to growing FGCS demand, the International Society for the Study of Women's Sexual Medicine (ISSWSH) sponsored a medical ethics roundtable of six American reproductive health experts in 2007, the results of which were published in the Controversies section of the *Journal of Sexual Medicine*. Conclusions ranged from "FGCS is within the purview of all women, since it is substantively no different than any other cosmetic operation, all of which, by definition, have no purpose other than to alter the appearance of the intended body part without any medical indication" to "women must be informed that normal labial architecture includes a wide variety of labial contours, including asymmetry," thereby deducing that no FGCS is ever indicated for cosmetic purposes.

Another ISSWSH roundtable contributor presciently reminds readers that today's *vaginal rejuvenation* is substantively no different from the centuries-old practice of FGC carried out in traditional societies for "cultural, religious, or nontherapeutic reasons" by a reported 140 million women worldwide, with an estimated incidence of 3 million women and girls per year. Declared a human rights violation in 2012 by the World Health Organization (WHO), FGC has been rendered illegal by almost all governments of the same countries where FGCS services are in demand and readily available. The ISSWSH contributor who included this discrepancy in the debate paradoxically concluded that the answer to this conundrum lies in progressive classification to further distinguish FGC from FGCS [6].

The principles of medical ethics set forth by Beauchamp and Childress (autonomy, nonmaleficence, beneficence, and justice) were applied by three other ISSWSH contributors, two of which chose one of the FGCS target procedures, labiaplasty, as a philosophical exercise pertaining to the entire FGCS phenomenon. They conclude "… the performance of these procedures is not always ethical, nor is it always unethical. Therefore it is the surgeon's burden to …practice well within the boundaries of ethical conduct," ending with an extrapolation to "…other vulvovaginal cosmetic procedures, such as 'vaginal rejuvenation' and 'hymenoplasty.'" Another contributor applied the same medical ethics instrument, deducing "… patient autonomy and technological advancement have been linked together in a business proposition. Does this reflect the true nature of the practice of medicine and… the physician-patient relationship? I would argue no" [6,7]. Others posit the concept of FGCS as none other than genital mutilation, equally deserving of prosecution under antifemale genital mutilation statutes [8].

On these paradoxical conclusions, we endeavor, in this chapter, to review afresh the current state of affairs regarding the traditional practice of FGC and its modern cousin, FGCS.

TRADITIONAL FEMALE GENITAL RITUALS: CUTTING AND ELONGATION

One finds ancient precedents of the modern quest for surgical modification of female genitalia in the traditional practices of FGC in and labial elongation in various African, Arab, and Asian cultures. Both FGC and labial elongation are categorically eschewed by international reproductive health stakeholders and human rights advocates. Both phenomena are in use as asylum-seeking justifications presented on behalf of immigrant and refugee women in the same countries where FGCS is on the rise and where FGC has been rendered illegal. And yet, *many* women of all ages in FGC-practicing cultures readily express pride in their FGC-based traditions, denying oppression or negative sexual or general quality of life impact related to their personal FGC, their voices rising in stark contrast to women with compelling, tragic FGC stories who have achieved international acclaim through the film and book versions of their traumatizing histories [9–11].

The role of enculturation cannot be underestimated. On the other end of the traditional vulvar alteration spectrum comes the regionally popular central African practice of labial elongation, believed to enhance female orgasm, facilitate female ejaculation, and augment sexual satisfaction for both male and female sides of the coital equation [12].

TRADITIONAL FEMALE GENITAL RITUALS: CUTTING OR MUTILATION?

Reflecting ancient traditions often integral to weeklong rites of passage, FGC occurs with variable rates in some countries, such as Senegal, where it is required by a minority of ethnic groups and not ever done in others and at universally high rates (>88%) in Somaliland, Somalia, Egypt, Guinea, Sierra Leone, Djibouti, Mali, and Eritrea and in approximately half of women in Egypt and Ethiopia [13].

Excision of parts of the female vulva dates back to ancient Egypt, where "Phaeronic" circumcision excised the entire clitoris, labia minora, and labia majora with the resulting wound sewn robustly closed in the midline, leaving a 1–2 cm opening anterior to the forchette to permit passage of urine and menses. Upon returning from Egypt (25 BC) a Greek geographer wrote: "One of the customs most zealously observed among the Egyptians is this, that they rear every child that is born, and circumcise the males, and excise the females" [14].

Motivations for this most extreme version of FGC include assuring virginity at marriage and fidelity thereafter, improving the cosmetic appearance of female genitalia, and practice of the female counterpart to male coming-of-age circumcision rituals. Few would debate the mutilating aspect of Phaeronic excision, the results of which may be witnessed in menopausal Somali women even today. One sees an age-related difference, however, among premenopausal teen and adult Somali women who have undergone far lesser excisions, little to no vagina-blocking midline fixation, and minimal to no excision of the clitoral glans, the results of which do indeed appear similar to labiaplasty and clitoral unhooding FGCS results [15].

Now in the well-publicized focus of global efforts to improve the status, health, and well-being of women and girls in developing nations, anti-FGC campaigning first gained momentum in the United States with *The Hosken Report: Genital and Sexual Mutilation of Females* (1979) by Fran Hosken, founder of the Women's International Network and the daughter of a physician [16]. Over the decades, this cultural expose has grown into an international outcry against the forced excision of the genitalia of girls and women. International reproductive health stakeholders united in the effort to abolish this practice range from the WHO and the United Nations (UN) to a growing number of nongovernmental organizations dedicated to the eradication of FGC, further echoed in the laws of numerous industrialized nations alarmed at the genital traditions of FGC-practicing immigrant communities [17–24].

The WHO classifies FGC into four clinical categories [25,26]:

1. *Clitoridectomy*: Partial or total, including instances where only the prepuce (fold of skin over the clitoris) is removed. (NB: This "excision of the prepuce" is the traditional equivalent of "clitoral unhooding" FGCS procedures.)
2. *Excision*: Partial or total removal of the clitoris and labia minora, with or without excision of the labia majora. (*NB*: Partial excision of labia minora is equivalent to FGCS labiaplasty options.)
3. *Infibulation*: Narrowing of the vaginal opening to the creation of a covering seal, formed by cutting and repositioning the inner, or outer, labia, with or without removal of the clitoris. *(NB*: Narrowing of the vaginal opening, albeit involving different genital structures, forms a substantial portion of today's *vaginal rejuvenation* industry.)
4. *Other*: All other harmful procedures to the female genitalia for nonmedical purposes, e.g., pricking, piercing, incising, scraping, or cauterizing the genital area. The WHO includes traditional labial elongation in this category. *(NB*: Genital tattoos and piercings fit these criteria.)

This WHO condemnation is supported by federal laws banning FGC, such as the UK Female Genital Mutilation Act of 2003, the London Safeguarding Children Board's handbook entitled "Safeguarding children at risk of abuse through female genital mutilation," and the U.S. federal legislation involving similar language [27–29].

ANTI-FGC BACKLASH

While modern concerns hinge on the concept of informed consent and realistic concerns about mortality and acute and chronic morbidities related to FGC, this unifaceted, politicized interpretation of the role and (il)legitimacy of FGC is now coming under fire from circumcised African women both proud and pleased to have undergone their culture's FGC process. The apparent leader of this fledgling movement is Fuambai Sia Ahmadu, a medical anthropologist who has served under the UK's medical research council, the U.S. National Institutes of Health, and the office of the vice president of Sierra Leone. She is a cosignatory to the Public Policy Advisory Network on African Female Genital Surgeries (PPAN) published in The Hastings Center Report November/December 2012 issue, the publisher of *SiA*, "a magazine for empowered circumcised women," and founder of *African Women Are Free to Choose*, an organization challenging the notion that FGC is a human rights violation. Her autobiographical synopsis presents cogent counterarguments to the efforts to eradicate genital cutting traditions in developing nations at the same time that FGCS-demanding women in industrialized nations are suffering no such lack of access to all manner of genital cosmetic renovations [30–32]:

> Some 20 odd years ago, when I was just finishing university in the US, I chose to travel to my country of heritage – Sierra Leone – to undergo female initiation. This included female circumcision.
>
> My aunt, mother and grandmother approached me and said they wanted to take me, along with a slightly older aunt, my younger sister and cousin, to "join Bondo". I was excited, recalling memories of my childhood in Africa, watching exuberant women dancing and singing during adolescent girls' initiation ceremonies, called Bondo. These women would take over the town, while men and uninitiated children had to stay in the houses. The women flanked the awesome Bondo masquerade, a powerful representation of our female ancestors, dancing and entertaining the crowds.
>
> We underwent several rites as part of our transition from girlhood to womanhood, the most significant being our excision operation – the reduction of the exposed clitoral hood, glans and labia minorae. My immediate experience was of pain and culture shock, while my eight-year-old sister felt nothing and was

> soon up and about with other young girls playing in the Bondo encampment.
>
> My initial fear – that I would never enjoy sex again and be scarred forever – turned into pride and amazement when I first held a mirror "down there", saw a clean, smooth look, and experienced my first post-operation sexual orgasm with my then boyfriend back in the US.
>
> In December 2012, this practice – now condemned as Female Genital Mutilation – came under an official ban by a UN Resolution, at the same time that the Hastings Centre Report, a leading bioethics journal, published an advisory statement dispelling many of the popular myths about female genital surgeries. Yet, in recent years, all over the internet and in Western women's magazines I see glossy advertisements of white women who have undergone what is now popularised as Female Genital Cosmetic Surgery (FGCS).

With permission from http://www.fuambaisiaahmadu.com/ and http://www.stuff.co.nz.

LABIAL ELONGATION

A ritual counterpart to FGC is the practice of labial elongation, a tradition found widely in central Africa, particularly Rwanda, Malawi, Uganda, and Zambia [12,34–36]. Labial elongation has been labeled a "WHO type 4 FGM" by some watchdog organizations. In reality, communities practicing labial elongation do so to enhance the sexual pleasure of the man and the woman. In personal, direct conversations with gynecological colleagues, both male and female, from elongating cultures, one is assured that elongation is neither painful, humiliating, nor a tool of oppression. According to female colleagues who have elongated their own labia, they describe it as a rite of passage that acknowledged their own sexual awakening and fostered expectations of sexual pleasure within marriage. To date, the only woman who has ever claimed traumatic memories associated with labial elongation in my experience has been one chronically ill, illegal immigrant undergoing medical evaluation pursuant to an asylum seeking application to the U.S. government.

Labial elongation has its own "Fuambai Sia Ahmadu" in Dr. Sylvia Tamale, feminist, human rights activist, and law professor in Uganda, who argues that elongation enhances female sexual pleasure and is *not* a human rights violation. In 2005, Dr. Tamale published Eroticism, Sensuality, and "Women's Secrets" among the Baganda: A Critical Analysis [37].

In this analysis, Tamale decries the labeling of Okukyalira Ensiko—the practice of labial elongation among Baganda women in Uganda—as a type 4 female genital mutilation by the WHO, a declaration that "completely disregards the ways in which Okukyalira Ensiko enhances women's sexual pleasure." She further points out that cosmetic procedures such as clitoral piercing performed in industrial, Westernized countries are not listed in WHO's type 4 FGM procedures despite meeting criteria. Such double standards in global health turn this African practice of sexual enhancement into a misinterpreted, inaccurate illustration of traditional cultural practices claimed to violate the rights of women and children, when, far from suffering WHO's FGM symptoms of "incompleteness, anxiety, and depression," Baganda women undergoing labial elongation experience none of these symptoms, contradicting this negative characterization. Western researchers lent further academic credibility to the female empowerment and reported benefits of labial elongation in a 2008 peer-reviewed community survey of Rwandan women [38].

MOTIVATIONS FOR CONTEMPORARY FEMALE GENITAL COSMETIC SURGERY

Normal vulvar anatomy varies widely. Waxing of pubic hair and Internet access to genital images appear to have contributed to the rise in numbers of women in industrialized nations seeking modification of their own genitalia to match what they subsequently believe to be "normal" [39]. Grassroots movement to address this genital conundrum exist in online galleries of vulvar images such as "The Labia Library"; Kotex® online platform for teens that reinforces "Well, there is no 'normal' looking vagina; just like your face is different to almost everyone in the world so is your vagina"; and the U.K.'s National Health Service website that explains "Labia vary from woman to woman, so don't judge yours by anyone else's standards" [40–42].

Regardless of the wide range of normal genital anatomy, women continue to seek modification. Physicians addressing such concerns have no meaningful resources in standard medical texts with which to create a reference point for the patient, and for themselves, as most anatomy illustrations of genitalia offer just one morphological image, lacking any acknowledgment or illustration of the wide variations in normal genital architecture [43]. What data exist on genital morphology variability show that normal clitoral size, labial measurements, vaginal, perineal, and clitoral–urethra length vary widely, with no association to age, parity, ethnicity, hormone, or sexual activity status [44]. In addition to cosmetic appearance and body image concerns, client/patient motivations also include chafing, interference with sexual and sporting activities, discomfort in clothing, and improvement in sexual friction and sexual satisfaction. Results show 90%–95% satisfaction overall and 80%–85% sexual satisfaction specifically in one review of FGCS published by a stateside group of FGCS clinicians [4,45].

Further reports of FGCS motivations show a nuanced interplay between body image, genital physical discomfort, and sexuality. In one recent cohort study, 1/3 of women seeking labiaplasty reported being teased about the appearance of their genitals compared to 3% in the control group. The labiaplasty group did not have higher rates of childhood abuse nor any difference on validated measurements of disgust or general appearance compared to controls not seeking labiaplasty [46]. They did not rate higher for anxiety or depression but were more likely to report poor sexual and body image satisfaction and to demonstrate avoidance behaviors regarding these concerns [47]. In a recent prospective comparative trial of women undergoing labiaplasty compared to controls, 91% showed postoperative improvement in long-term follow-up of 11–42 months, and four meeting preoperative criteria for body dysmorphic disorder related to their labia no longer met criteria for this diagnosis post-op (although one did continue to meet criteria, but for her nose, as her vulvar dysmorphia was ameliorated by the labiaplasty operation) [48]. Among peripubertal girls, motivation for labiaplasty is often related to marked asymmetry of the labia minora, anatomic comparison to other girls, normal genital changes associated with puberty, and images on the Internet and in anatomy books [49].

FGCS MARKETING

A multidisciplinary realm inhabited by urologists, gynecologists, urogynecologists, and cosmetic plastic surgeons, FGCS is singular among cosmetic specialties for the practitioners' tendency to publicly seek out "botched" cases for "expert revision," a phenomenon heretofore unknown in the history of cosmetic therapies and surgeries. Online search for "botched *rhinoplasty* or *breast augmentation* or *tummy tuck*, etc.." yields almost exclusively lay-press articles, with no plastic surgeon publicly claiming to be the savior of bad outcomes. When searching "botched labiaplasty," however, one is met with the claims of urological, gynecological, and urogynecological FGCS clinicians exhorting the perils of undergoing FGCS operations at the hands of the grossly unqualified, promising cosmetic rescue for women botched by incompetents, such as "There are only a handful of surgeons who perform these surgeries in adequate volumes to be proficient and adept. Technical skill is of paramount importance but having an artist's eye is of equal value" [50]. Others literally own websites containing the phrases "labiaplasty revision" and "botched labia" in the website domain names, which contain web pages titled "Labiaplasties gone wrong" and "Labiaplasty nightmares," an unprecedented predatory medical marketing phenomenon [51–53].

FGCS: THE MENU

Procedures sought by clients and marketed by FGCS practitioners occur in three overlapping categories: functional, cosmetic, and sexual enhancement.

FGCS for Function

These procedures address discomfort or other morbidity involving congenital or acquired changes in the architecture of the genitalia, perceived as anomalous to the client, often but not always in relation to activities of daily living, sexual activity, or wardrobe discomforts.

Labiaplasty

While labiaplasty is most notorious for associated cosmetic goals, many teen and adult women seeking the operation do so for function reasons, particularly if there is *catching and pinching* of labia during vigorous sporting activities and/or if there is marked asymmetry of the labia minora, or robust, redundant or hypertrophied labia minora that distort body contour in tight clothing or beachwear [4,44,45,54].

Prolapse

Most often marketed as vaginoplasty options, especially in urogynecological FGCS clinics, standard prolapse operations are presented as methods of vaginal rejuvenation. Arguably the most accurate application of this marketing phrase, it has attracted the most criticism from ACOG in the area of medical marketing ethics [5]. The most commonly illustrated of these are anterior and posterior colporrhaphy and perineorrhaphy. Women undergoing anterior and posterior compartment repairs undergone for vaginoplasty to rejuvenate the vagina report 90%–100% satisfaction rates, with 0%–4% regret, and a low rate of complications including wound dehiscence, dyspareunia, rectoperineal fistula, post-op bleeding, and surgical site infection [54].

Hymen Restoration

Hymenoplasty involves careful reconnection of the hymen remnants to recreate a pseudo-virginal state, most commonly requested by women from cultures that place high social significance on virginity and gaining popularity in Europe and the United States from women seeking virginity certificates or hymen restoration surgery [55]. This procedure is under scrutiny due to the inherent cross-cultural and socioethical issues involved. Domestic violence was found with high prevalence in 1 Swiss study of 80 women seeking "revirgination." Of the 19 women who went through with hymen restoration in this series, only 2 of them experienced the desired "virginal bleeding" at first coital episode after surgery [56]. A second Swiss survey of 100 public hospitals addressed this issue present in Switzerland's immigrant communities, most frequently Turkey and Arab nations. Most of the clinics responding revealed that they usually or always provide revirgination hymenoplasty to immigrant women [57]. Another crosssectional survey of Lebanese university students revealed that physical harm and death are considered strongest justification for undergoing hymen restoration, although the majority of students did not endorse revirgination on ethical grounds of honesty between married couples, with no difference in this opinion related to the participants' gender or religious background [58]. A Swedish survey of clinicians showed that while a majority of clinicians would provide virginity certificates or hymen reconstruction to young women undergoing honor-related threat, the remainder have engaged the international zero tolerance policy toward such requests [59]. One Indian website offers a revirgination that guarantees bleeding at first coitus by including prerequisite vaginal tightening, because with hymen reconstruction only "… most patients do not bleed and their husbands complained that vagina was loose. Many … ended up with divorce. One should go for vaginal tightening of muscles (in addition to hymenoplasty)" [60].

A 2010 British Broadcasting Company article investigated hymen reconstruction services available in Paris, performed most often for Arab immigrant women facing ostracism, death, or suicide as the price paid for entering marriage without intact virgin status. The profiled French physician, who performs two to three hymen restorations per week, states "I believe we as doctors have no right to decide for her or judge her" [61].

In the United States, revirgination motives include a desire to improve one's sex life and "the ultimate wedding anniversary gift" for clients' husbands. In one online article, a woman from New York City explains "If a woman isn't a virgin when she gets married, a man can always put her down for that" [62].

Nonsurgical revirgination options may be found at www.hymenshop.com, in the form of an artificial hymen kit guaranteed to give the male partner the sensation of breaking through a membrane. Containing a red dye, it further promises the appearance of virginal blood on the sheets, "… not too much but just the right amount. Add in a few moans and groans and you will pass through undetectable!" Free delivery to any world destination is to be had for the bargain price of $29.95 [63].

FGCS for Cosmetics

These procedures address client desires to alter the cosmetic appearance of external genitalia.

Labia

The goal is to preserve/create symmetry while reducing dependent labial length.

Labia Minora

1. *Linear excision labiaplasty* (Figure 115.1): Linear reduction involves full thickness, full contour, gently sculpted excision of the labia minora. The simplest of all labia minora reduction surgeries, it is marketed under the name “linear reduction” on FGCS websites, though it is often called “amputation” by these same FGCS surgeons who claim to be “botched labiaplasty” experts. This technique completely excises the entire labial edge [54].
2. *Z-plasty wedge labiaplasty* (Figure 115.2): This technique follows plastic surgery Z-plasty principles that facilitate maintenance of the labial edge, a flat excision interface that avoids concave or convex deformation of the revised labia, and low-tension closure of the labial skin, both reducing labial bulk and dependent length [64].
3. *V-wedge labiaplasty*: Central or posterior (Figures 115.3 and 115.4)
   This simple full-thickness wedge also permits maintenance of the labial edge without the complicated staggered excision of a Z-plasty wedge resection. No comparative data exist between wedge resection techniques [53]. Wedge technique involve both central (pie slice) and posterior (anterior edge sewn to incised perineal surface) options [54]. Between various V-wedge and linear excision techniques, cosmetic and sexual satisfaction was similar in one multicenter trial of various FGCS operations [4].
4. *Deepithelialization labiaplasty* (Figures 115.5 and 115.6): An ellipse of dermis is excised from either the lateral or medial aspect of the labum, avoiding fullthickness excision, preserving the labial edge [54].

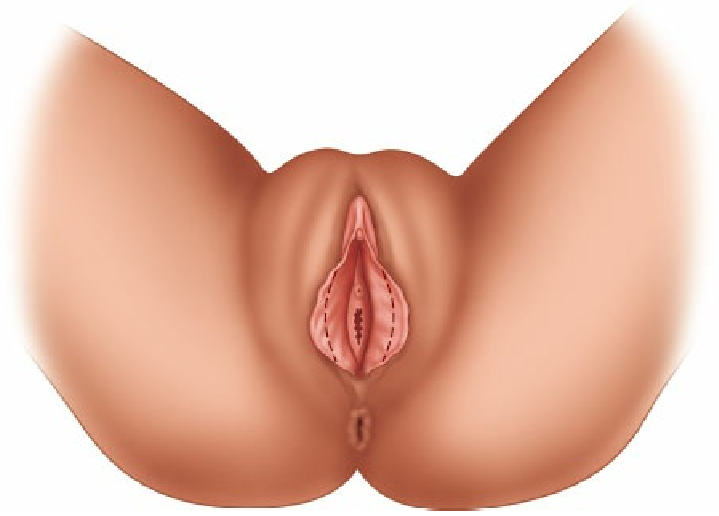

Figure 115.1 Labiaplasty: linear resection. (From Iglesia CB et al., *Int Urogynecol J*, 24, 1997, 2013.)

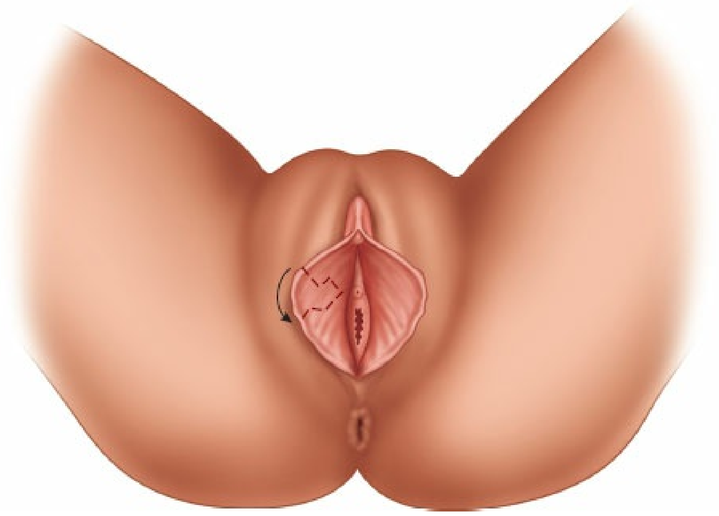

Figure 115.2 Z-wedge labiaplasty. (From Goldstein AT and Romanzi LJ, *J Sex Med*, 4, 550, 2007.)

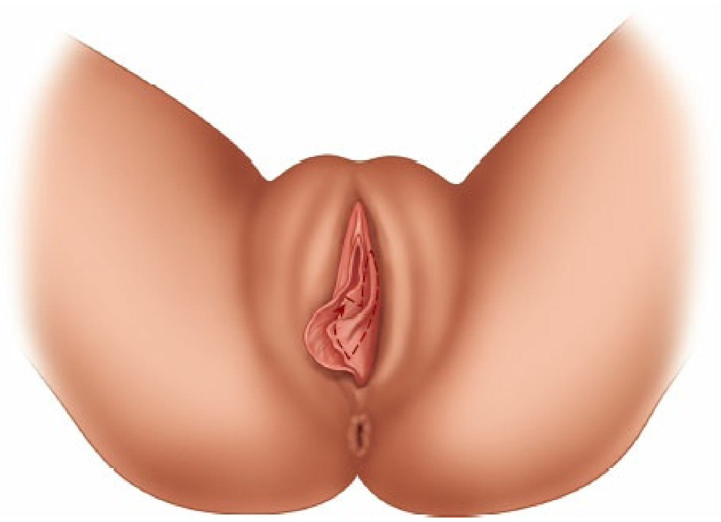

Figure 115.3 V-wedge labiaplasty: central. (From Goodman MP et al., *J Sex Med*, 7(4 Pt 1), 1565, April 2010; Courtesy of Miklos/Moore.)

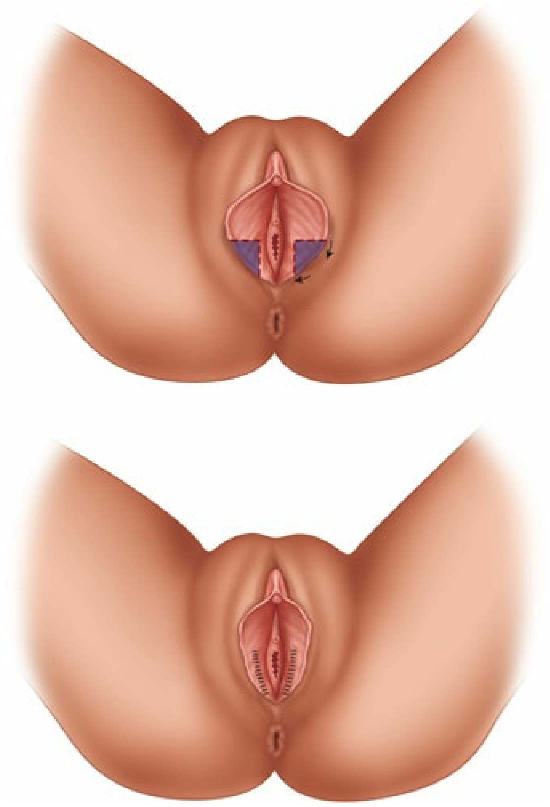

Figure 115.4 V-wedge labiaplasty: posterior.

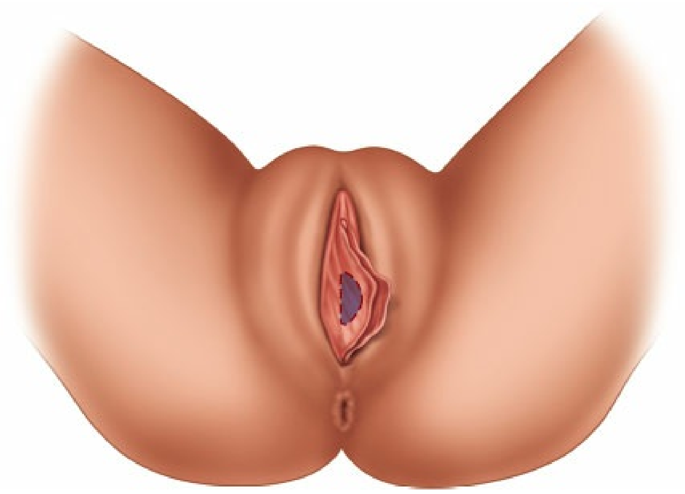

Figure 115.5 Lateral deepithelialization.

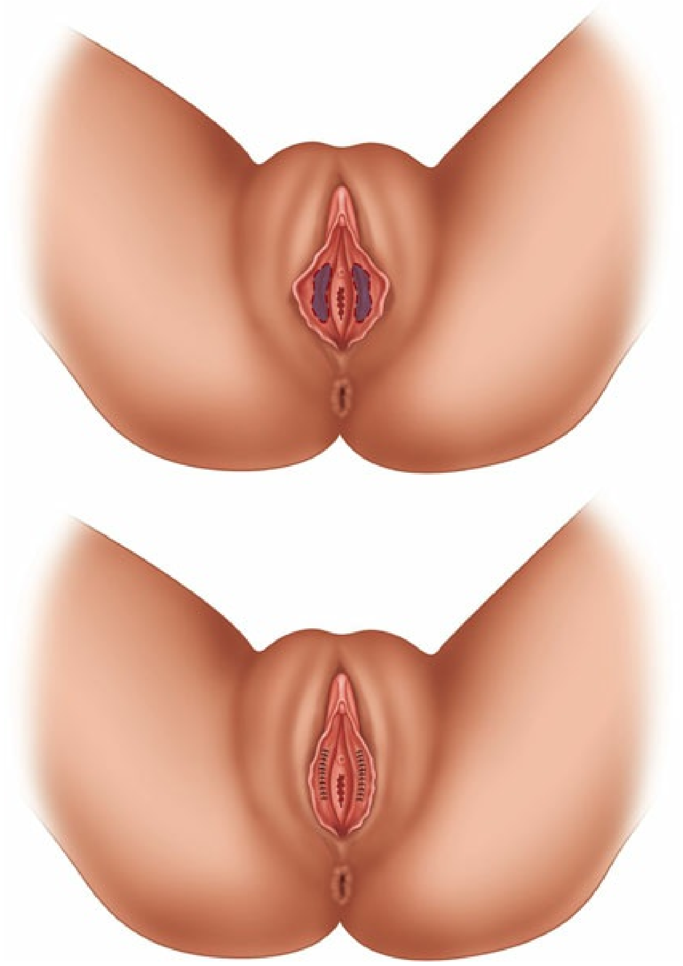

Figure 115.6 Medial deepithelialization.

Labia Majora

1. *Deepithelialization labiaplasty*: The skin overlying the majora is excised in an elliptical dissection, without removing underlying fibromuscular or fat pad structures. The skin edges are reapproximated vertically to achieve smoother labia majora skin, less dependent bulk when standing, and increased dermal turgor [65].
2. *Labial augmentation with injectable filler*: Cosmetic fillers include autologous fat and

synthetics, including hydroxyapatite, polyacrylamide gel, hyaluronic acid, and bovine collagen. Similar to oral labial bulking through injected filler material, cosmetic surgeons now offer injection of filler to restore a youthful fullness and turgor to wrinkled, deflated labia majora. Marketing claims include statements such as "Sagging labia majora can impact your confidence and hinder your sense of youthfulness. This procedure can help you take back the control over your body" [65].

   Cosmetic fillers may be complicated by injection site bruising, temporary swelling, uneven lumpiness of injected material, bacterial wound infection with symptomatic lesions at 5 years (most commonly due to *Staphylococcus epidermidis* and *Propionibacterium acnes),* migratory nodules, granulation, and chronic inflammation [66–68].

3. *Radiofrequency*: Skin tightening using surface application of dermatologic radiofrequency technology is offered in some FGCS centers as a method to reduce wrinkling of labia majora and surrounding skin of the groin and buttocks [65].

Vagina

DLV: "…designer laser vaginoplasty is for (vulvar) aesthetic enhancement" [69]. Patented DLV® has never been described in any gynecological text, surgical atlas, peer review journal, or other publications. DLV and its sexual enhancement cohort LVR are not taught in any surgical or gynecological residency training program, nor in any urogynecology, female urology, female pelvic medicine and reconstructive surgery, plastic surgery, or other reconstructive surgical subspecialty fellowship training programs. Patient choice for LVR® and DLV procedures is confined to doctors who have paid for the LVR DLV franchise, which includes training; certification; participation in an exclusive, robust web marketing network; and contractual obligation forbidding disclosure of the patented techniques. As such, and despite patient satisfaction testimonials on the franchise physician websites, there are no scientific data in any peer-reviewed medical journal for LVR or DLV. Technique details in published interviews in the lay-press disclose that the laser is used to make all incisions and that recovery takes 4–6 weeks [70].

FGCS for Sexual Enhancement (These Procedures Allegedly Increase Sexual Gratification)

1. *Perineoplasty* (Figure 115.7): The majority of websites offering illustrations of FGCS for sexual enhancement commonly include illustrations or descriptions consistent with standard perineoplasty operations, including dissection, suturing, and recuperation estimates found in gynecologic surgery atlases for perineorrhaphy and perineoplasty. The marketing language emphasizes restoration of *coital friction* to improve both female and male sexual satisfaction.
2. *Clitoral unhooding* (Figure 115.8): Amenable to inclusion in the WHO Type 1 FGM category that includes *excision of the clitoral prepuce*, clitoral unhooding is most commonly promoted in the sexual gratification arena of FGCS but does own some territory in the cosmetic FGCS marketplace as well [4,54].
3. *LVR*: LVR is marketed as a method of sexual enhancement by the patent and franchise holders. Descriptions state that incisions are made with the laser with recuperation lasting 4–6 weeks. Website claims state that LVR "help(s) alleviate symptoms of stress urinary incontinence" and "…can enhance vaginal muscle tone, strength and control" [69,70].
4. *G-spot amplification*®: Another patented technique, G-spot enhancement is based on the theory of the Grafenberg spot, an alleged erogenous zone on the anterior vaginal wall in the suburethral area, and the possibility that vaginal orgasm might occur more readily and with greater intensity if this area is made larger/more prominent through temporary filler injection of hyaluronic acid into the urethrovaginal space [71–74]. The founder's research data of "… a pilot study (in which) 87% of women surveyed after receiving the G-shot® reported enhanced sexual arousal/gratification" cannot be verified on literature search of peer-reviewed journals [75]. Results are reportedly temporary, lasting 3–5 months [75,76].

   The existence and function of the G-spot as an anatomic entity continues to spur debate since first described by Grafenberg in 1950. In a 2004 study of genital and sexual function in women, the anterior vaginal wall was not described as an area of erogenous stimulation, though other vaginal parameters, such as depth, did correlate to sexual sensitivity and orgasm intensity [73].

On the G-shot website, the client consent form includes over 50 complications, including dyspareunia, fistula, sexual dysfunction, and permanent numbness [75].

5. O-shot®: O(rgasm)-shot utilizes autologous platelet-rich plasma (PRP) injection therapy to stimulate clitoral function. PRP therapy is derived from patient plasma and allows *release of growth factors from activated platelets in areas where PRP is either injected or applied to the surface in gel form. PRP has many applications in orthopedics for tendon, muscle, and bone injuries, in addition to dermatologic efficacy in optimizing autologous free fat graft uptake, complex wound healing, melasma, alopecia, and depressed facial scars [77–83]. With the O-shot, PRP is harvested and reinjected periclitoral using patented techniques known only to those clinicians trained and certified by the physician who developed and patented the procedure, with alleged significant improvement in female sexual response, orgasm achievement, and orgasm intensity. The O-shot website contains further claims of cure of coincident urinary incontinence.*

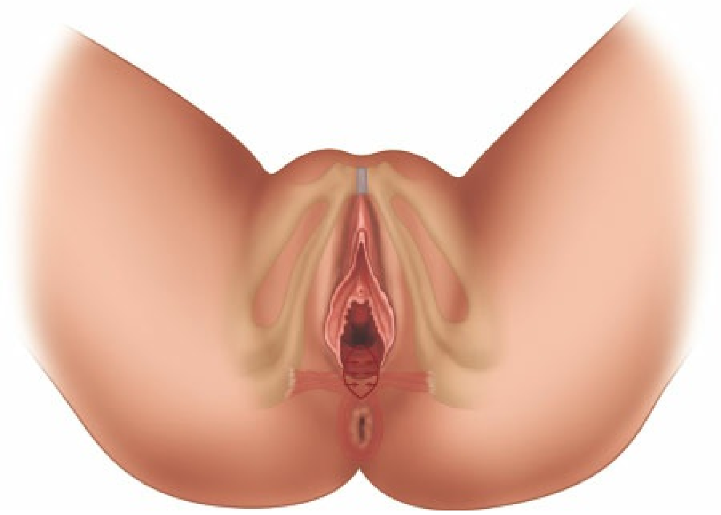

Figure 115.7 Perineoplasty. (From Goodman MP et al., *J Sex Med*, 7(4 Pt 1), 1565, April 2010; Courtesy of Miklos/Moore.)

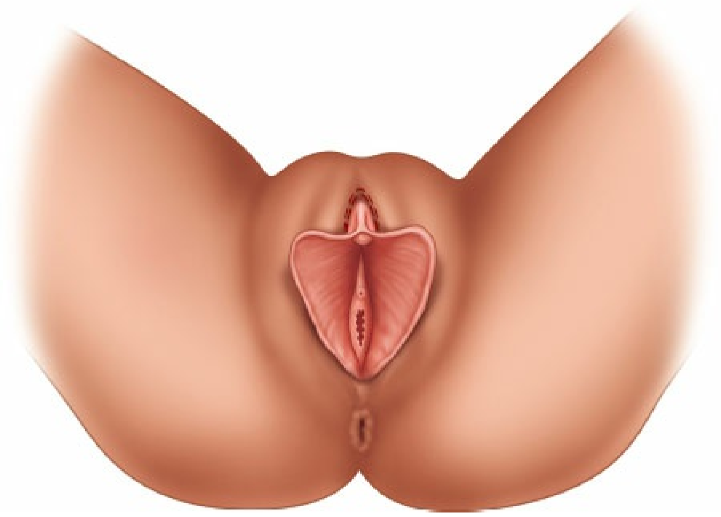

Figure 115.8 Clitoral hood reduction.

SUMMARY

Options for genital modification, be they traditional or nouveau, FGCS, vaginal rejuvenation, or FGC, are increasingly influenced by cross-cultural aspects of immigration, globalization, and the Internet, all of which has spawned a fascinating conundrum in medical ethics and public policy that has turned female genitalia into a modern neosymbol of human rights, female autonomy, and social currency.

Is a Canadian woman with a facelift and breast augmentation (both considered unacceptable and absurd in most developing nations) who requests a "Barbie labiaplasty" under any less disturbing social influences than a Masai woman undergoing ritual genital cutting? Do either one require international monitoring of their genital management issues?

Is traditional genital cutting always traumatic, mutilating, and utterly without personal reward? It appears the answer may well be no.

Is the marketing of standard colporrhaphy techniques as "vaginal rejuvenation" a semantic trick to increase financial yield, or is it a new framework within which women opt to forego the geriatric "prolapse" label for the more youthful concept of "rejuvenation" instead?

Might we successfully introduce the notion of informed consent in ritualistic FGC? Ought we support the apparent trend toward minimal cutting done with local anesthetic carried out by a certified midwife in high-prevalence FGC countries rather than continue the minimal impact zero tolerance policies set forth by international stakeholders? [15].

Why do we accept unilateral labiaplasty in a 15-year-old secondary school elite athlete who claims asymmetry is causing her to lose her races while denying FGC to her 16-year-old immigrant neighbor who needs it in order to be marriageable?

Perhaps the answer lies in labial elongation, the only do-it-yourself option with enticing alleged benefits and minimal apparent risk.

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116 Cosmetic Vaginal Surgery

Robert D. Moore and John R. Miklos

INTRODUCTION

Vaginal rejuvenation and cosmetic genital vaginal surgery have been performed and popularized increasingly in gynecology, urogynecology, and plastic surgery. However, controversy and debate over the subject remain the most discussed issue in this area, not the in-depth surgical techniques. The line between cosmetic and medically indicated surgical procedures is a gray area, and procedures are performed for both purposes. In the current chapter, we will review the background and history of these procedures, the available data to support them, and the techniques and complications of these procedures. In addition, we will discuss some of the controversies surrounding these topics. Finally, we will also attempt to shed light on what is myth and what is science in this relatively new field of elective genital vaginal surgery for sexual function and cosmesis of the female vagina and vulva.

The current chapter is divided into two sections, the first covering vaginal rejuvenation procedures and the second covering external vaginal/vulvar cosmetic surgery. Many use the term “vaginal rejuvenation” to encompass all elective vaginal/vulvar surgery; however, we feel that it should be used only to refer to functional procedures of the internal vaginal canal and introitus that are designed to enhance sexual function, which includes ensuring adequate support of the pelvic floor and then internal vaginal canal repairs and repair of the introitus. Similarly, cosmetic vaginal surgery to many just means labiaplasty or labial minora reduction; however, one will see in the second section of the chapter that it is much more comprehensive than this. Therefore, we have defined “cosmetic vaginal/vulvar surgery” as cosmetic or aesthetic procedures of the outside of the vagina and/or vulva, including labiaplasty, labia minora reduction, excess or redundant clitoral prepuce reduction, labia majora reduction or augmentation, labia majora divergence repair, perineal skin reduction, and mons pubis reduction. In most instances, to achieve the outcome desired by the woman, a combination of these external cosmetic procedures needs to be done, truly bringing in the “art” of aesthetic surgery.

VAGINAL REJUVENATION

Vaginal rejuvenation has also been defined to include perineoplasty and vaginoplasty, which are techniques to “tighten” the vaginal canal and to elevate and strengthen the perineal body [1]. The purpose of these procedures is not to correct pelvic floor defects, but they are modifications of traditional colporrhaphy designed to repair the damage from childbirth and are frequently performed concomitantly with reconstructive procedures for pelvic organ prolapse. These procedures involve vaginal reconstructive techniques to anatomically modify the vaginal caliber by decreasing the diameter of the vaginal canal while reconstructing the perineal body and the vaginal introitus in an attempt to enhance sexual gratification for the woman [2–4]. Utilizing this definition, one realizes that this is not a new field at all, i.e., gynecologists have been dealing with sexual dysfunction related to vaginal pathology, resulting mostly from vaginal childbirth for hundreds of years. However, the implication of this definition is to actually give credence to women’s complaints of altered sexual function secondary to vaginal relaxation/looseness (Figure 116.1a through c) and possibly to perform vaginal repairs prior to developing signs or symptoms of true prolapse or incontinence. Many women who are candidates for vaginal rejuvenation have symptoms and clinical findings of prolapse. Therefore, a proper repair must involve restoring the foundation of pelvic floor support and encompass some of the newer concepts of vaginal rejuvenation in the repair.

Prolapse and vaginal relaxation occurring after vaginal childbirth is not a new concept. We have clear evidence that vaginal delivery increases the risk of vaginal support problems, vaginal relaxation, prolapse, and incontinence. Various pathophysiological studies have demonstrated marked changes after vaginal delivery to levator muscles [5,6], nerves [7], and pelvic support [8]. It is obvious that parous women are more likely to have pelvic organ prolapse, fecal incontinence, and urinary incontinence than women who have not borne children [9]. There is ample epidemiological evidence that vaginal delivery appears to be the strongest risk factor for pelvic floor disorders [10]. As evident in the Women's Health Initiative [11], women who had borne at least one child were twice as likely to have uterine prolapse, rectocele, and cystocele as nulliparas, after adjusting for age, ethnicity, body mass index, and other factors. The amount of damage at the time of vaginal childbirth has also been shown to be strongly correlated with sexual function. At 6 months postpartum, women with an intact perineum or first-degree perineal tear were less likely to experience sexual dysfunction than those with higher degree of perineal tear [12,13]. Interestingly, 80.4% of urogynecologists stated that they would agree to perform elective primary cesarean section on request [14].

Prolapse and Sexual Function

Female sexual dysfunction is defined as a disorder of sexual desire, arousal, orgasm, and/or sexual pain contributing to personal distress [15]. Sexual dysfunction is a multifactorial disorder; biological, psychosocial, and relational factors can contribute to female sexual dysfunction. Among these factors, the pelvic floor appears to have an important influence. Dysfunction of vaginal support leading to incontinence, prolapse, and sexual dysfunction is highly prevalent [16].

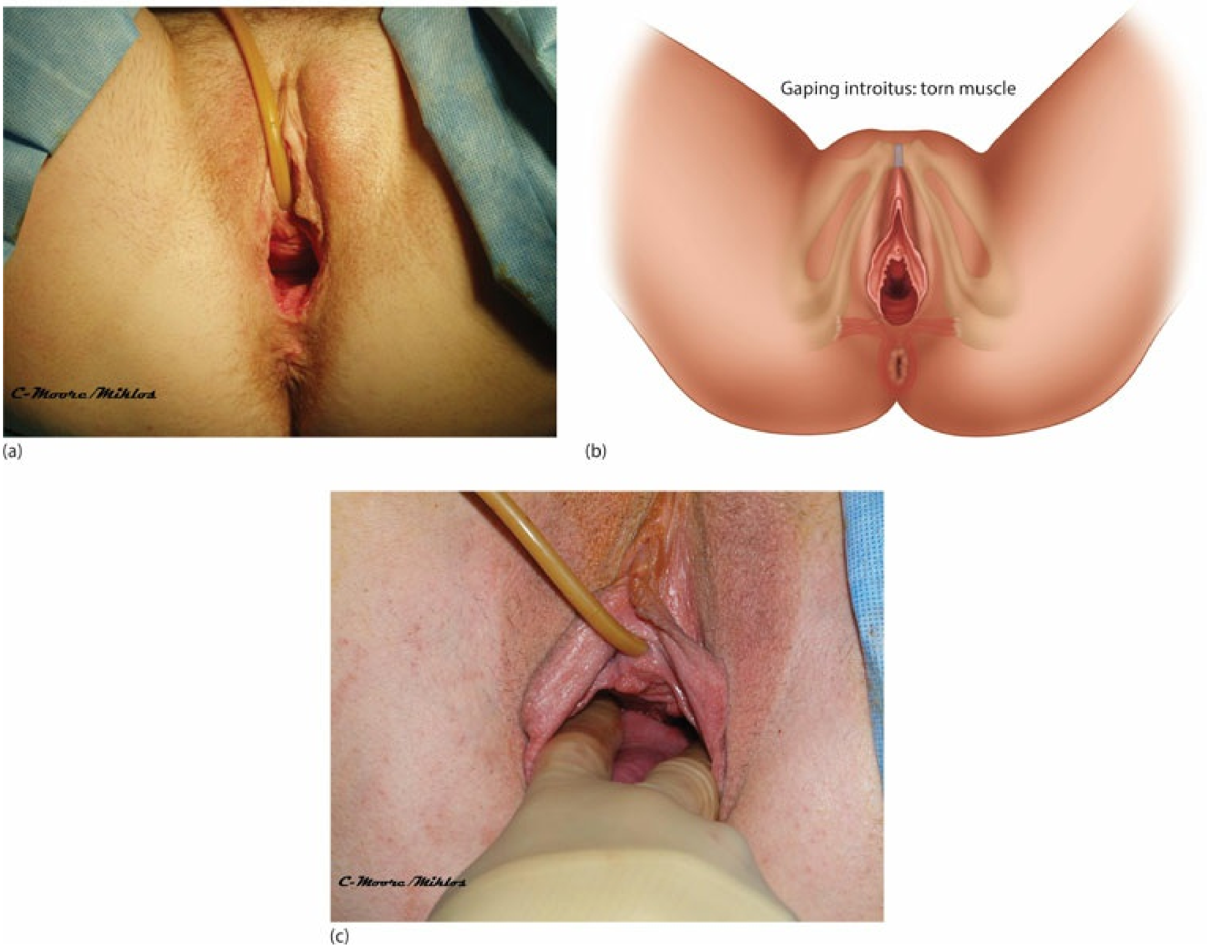


Figure 116.1 (a–c) Vaginal laxity and damaged perineum. (Courtesy of Robert D. Moore and John R. Miklos.

It is beyond the scope of this chapter to review all of the anatomy, neuroanatomy of pelvic floor support, and its relation to sexual function, however, suffice it to say that we do have good evidence that vaginal childbirth, as well as some other environmental and genetic factors, can lead to issues with pelvic floor support, which in turn can affect sexual function. Again, repairs of pelvic floor and vaginal support have been completed for many, many years, and one would not argue that one of the goals of any of these repairs is to "restore sexual function"; therefore, we must make the assumption that vaginal relaxation and prolapse affects sexual function in a negative way.

The literature also supports this theory. There have been many studies published in the literature that confirm, with validated sexual function questionnaires, that prolapse affects sexual function and, when repaired, function improves (Tables 116.1 and 116.2). These studies have confirmed that prolapse, albeit a more severe form of vaginal relaxation, but certainly relaxation, does adversely impact sexual function.

We feel that the posterior vaginal wall anatomically controls most of the vaginal caliber secondary to its relationship to the levator ani and genital hiatus and repair of this wall is a major portion of most rejuvenation-type procedures. Therefore, studies evaluating rectocele repairs may have more of a direct correlation to vaginal caliber and sexual function. Bradner et al. reported that posterior repair had a positive impact on sexual function. They examined the FSFI score before and after surgical rectocele repair in sexually active patients who had symptomatic rectoceles. There were significant improvements of FSFI score in domains of sexual desire, satisfaction, and pain [30]. Tunuguntla and Gousse found that while posterior repair with levatorplasty leads to sexual dysfunction and pain in many women, that actually posterior colporrhaphy completed alone, with the avoidance of levator ani plication, improves sexual function [34]. Komesu et al. investigated the effect of posterior repair on sexual function by using PISQ score. They included a cohort of patients who underwent pelvic floor reconstructive surgery with and without posterior repair and found that both groups significantly improved in sexual function [27]. Paraiso et al. compared three different methods of posterior rectocele repair, including one that utilized a graft and reported that all three approaches resulted in statistically significant improvements in the PISQ score [25].

Table 116.1 Pelvic Organ Prolapse Effects on Sexual Function

Author, year	Study design	*n*	Objective	Population	Sexual function measurement	Results
Ellerkmann et al. [17]	Prospective observational study	237	To compare the symptoms that are related to pelvic floor dysfunction with the location and severity of the coexisting prolapse	Patients with symptomatic pelvic organ prolapse came to Johns Hopkins Medicine.	The Pelvic Floor Dysfunction Questionnaire	Increasing severity of POP is associated with sexual dysfunction.
Barber and Maher [18]	Multiarmed clinical trial	343	To compare sexual function in women with urinary incontinence and pelvic organ prolapse	343 community-dwelling women older than 45 years with urinary incontinence or advanced prolapse.	The condition-specific sexual function questionnaire	33.3% POP group felt that prolapsed or urine leakage affected their ability to have sexual relations compared with 10% of urinary incontinence group ($p = 0.02$).
Novi et al. [19]	Unmatched case control	60	To compare sexual function in women with vs. without POP	30 women with pelvic organ prolapse and it was compared with 30 unmatched controls without evidence of prolapse.	PISQ	Pelvic organ prolapse appears to have a significant negative impact on sexual function compared with control (81.4 ± 7.3 vs. 106.4 ± 15.5, $p < 0.001$).
Botros et al. [20]	Identical twin study	542	To assess the impact of childbirth on sexual function	276 identical, sexually active twins.	PISQ-12	Nulliparous women reported superior sexual satisfaction scores compared with parous women, regardless of age and mode of delivery (102.5 vs. 93.5, $p < 0.001$).
Srikrishna et al. [21]	Prospective observational study	43	To evaluate the expectations and goals of women undergoing surgery for POP	Women with symptomatic POP were recruited from the waiting list for pelvic floor reconstructive surgery.	The prolapse quality-of-life (pQoL) questionnaire	20% women were dissatisfied with their sex lives as a result of their prolapse.

Table 116.2 POP Repair Improved Sexual Function Studies

Author, year	Study design	*n*	Objective	Population	Sexual function measurement	Results
Barber et al. [22]	Multiarmed clinical trial	343	To compare sexual function in women with urinary incontinence and pelvic organ prolapse	343 community-dwelling women older than 45 years with urinary incontinence or advanced prolapse	The condition-specific sexual function questionnaire	Fewer patients with POP reported that their prolapsed affected their ability to have sexual relations 6 months after vaginal reconstructive surgery than at baseline (0% vs. 33%, $p < 0.01$).
Rogers et al. [23]	Prospective observational	269	To assess sexual function in women after surgery for stress urinary incontinence and/or pelvic organ prolapse at 3 and 6 months	Women underwent a variety of anti-incontinence and reconstructive surgeries	PISQ	Sexual function scores improved after surgery (89 vs. 95, $p < 0.001$).
Stoutjesdijk et al. [24]	Prospective observational	67	To compare sexual function in women with POP before and after vaginal reconstructive surgery	Women who underwent vaginal reconstructive surgery	The urogenital distress inventory and incontinence impact questionnaire revisited	There was a significant improvement of dyspareunia after surgery. The ability to have intercourse, the satisfaction, and the frequency of intercourse improved although not significantly.
Paraiso et al. [25]	Randomized controlled trial	106	To compare outcomes of three different rectocele repair techniques (posterior colporrhaphy, site-specific rectocele repair, or site-specific rectocele repair augmented with a porcine small intestinal submucosa graft)	Patients undergoing surgery for stage II or greater posterior vaginal wall prolapse	PISQ-12	PISQ-12 improved significantly in all groups postoperatively ($p < 0.001$), with no differences between groups.
Handa et al. [26]	The CARE trial	224	To describe sexual function before and after sacrocolpopexy	Stress-continent women planning abdominal sacrocolpopexy for stage II–IV prolapse	PISQ-12	Among women who were sexually active before and after surgery, the mean PISQ-12 score improved significantly (34.1 ± 5.2, $p < 0.001$).
Komesu et al. [27]	Multicenter prospective cohort	73	To determine the effect of posterior repair (PR) on sexual function in patients who have undergone incontinence and/or pelvic reconstructive surgery	Sexually active patients who had undergone pelvic reconstructive and/or incontinence procedures	PISQ	Significantly improved their PISQ scores in both PR and non-PR groups, without a difference between groups.

Azar et al. [28]	Prospective observational	60	To evaluate the effect of surgical repair of POP on female sexual function	Women with POP	FSFI	Sexual function was improved 12–16 weeks postoperatively (15.9 ± 10.7 vs. 21.9 ± 11.1, $p < 0.05$).
Kuhn et al. [29]	Prospective observational	70 female, 64 male	To determine the male and female sexual function before and 4 months after surgery for POP	Sexually active heterosexual couples with symptomatic cystocele, rectocele, or vault descent	FSFI	In women, FSFI scores improved significantly in the domains desire, arousal, lubrication, overall satisfaction, and pain. In men, sexual drive, and overall satisfaction improved significantly.
Bradner et al. [30]	Prospective observational	68	To evaluate sexual function before and after surgical rectocele fascial repair in sexually active patients who suffer from symptomatic rectoceles	Sexually active female patients who were to undergo rectocele fascial repair for symptomatic rectoceles	FSFI	Significant improvement for desire ($p < 0.001$), satisfaction ($p < 0.0001$), and pain ($p < 0.0001$).
Lakeman et al. [31]	Prospective observational	29	To evaluate the effects of vaginal prolapse surgery on vaginal vasocongestion, vaginal wall sensibility, and sexual function	Patients scheduled for vaginal prolapse surgery	FSFI	Improvement of sexual function after prolapse surgery (20.5 vs. 23.3, $p = 0.30$).
Thibault et al. [32]	Multicenter prospective	148	To evaluate the impact of laparoscopic sacrocolpopexy on symptoms, health-related quality of life (HRQL), and sexuality among women with symptomatic urogenital prolapse (UGP)	Patients with symptomatic POP who undergo laparoscopic sacrocolpopexy	PISQ-12	Postoperative sexual function had improved significantly (35.42 vs. 32.07, $p < 0.05$).
Kim et al. [33]	Prospective observational	143	To evaluate the effect of surgical repair of POP on female sexual function	Patients scheduled to undergo surgery for POP stages II–IV	FSFI, PISQ-12	Improvement of PISQ score from 25.0 ± 4.95 to 28.33 ± 5.1 postoperatively ($p < 0.001$). No differences of pre- and post-op FSFI ($p = 0.08$); however, only the satisfaction domain score significantly increased ($p = 0.029$).

Vaginal Relaxation and Effect on Sexual Function and Sensation

It is clear from the aforementioned data that prolapse has a role with causing sexual dysfunction. The difficulty with this is that sexual function is multifactorial and can, because of this, be a very difficult area to study. It is also clear from these studies that vaginal repair improves sexual function and sexual quality of life, but is it because of the prolapse creating discomfort causing the woman to avoid intercourse or because of self-image issues regarding the prolapse? Or is it because vaginal relaxation and prolapse may cause decreased sensation leading to sexual dysfunction, i.e., feeling less, having a harder time achieving orgasm, or feeling self-conscious about the fact that she feels her vagina is loose, stretched, or relaxed?

Ozel and White recently published one of the first reports evaluating libido, sexual excitement, vaginal sensation, and ability to orgasm in a group of women with prolapse compared to women without prolapse. They found that women with prolapse and vaginal relaxation were significantly more likely to report an absence of libido, lack of sexual excitement during intercourse, and a much lower frequency of achieving orgasm during intercourse (all statistically significant) compared to women with the same demographics without prolapse (i.e., multiparous, similar age, marital status, etc.) [35]. This is a landmark study as it is one of the first studies evaluating the sensation of the vagina and the changes it may undergo following relaxation of the tissues that causes prolapse.

We have shown that vaginal prolapse can affect sexual function and its repair can improve sexual function and ability to orgasm. It therefore seems to make sense that if women present with an enlarged genital hiatus, or widened vaginal canal without symptomatic prolapse, this may also affect sensation and sexual function. Many women do present with these symptoms and until recently were told that there was nothing wrong and there were no options to improve her sexual sensation or function (Figure 116.2a through d).

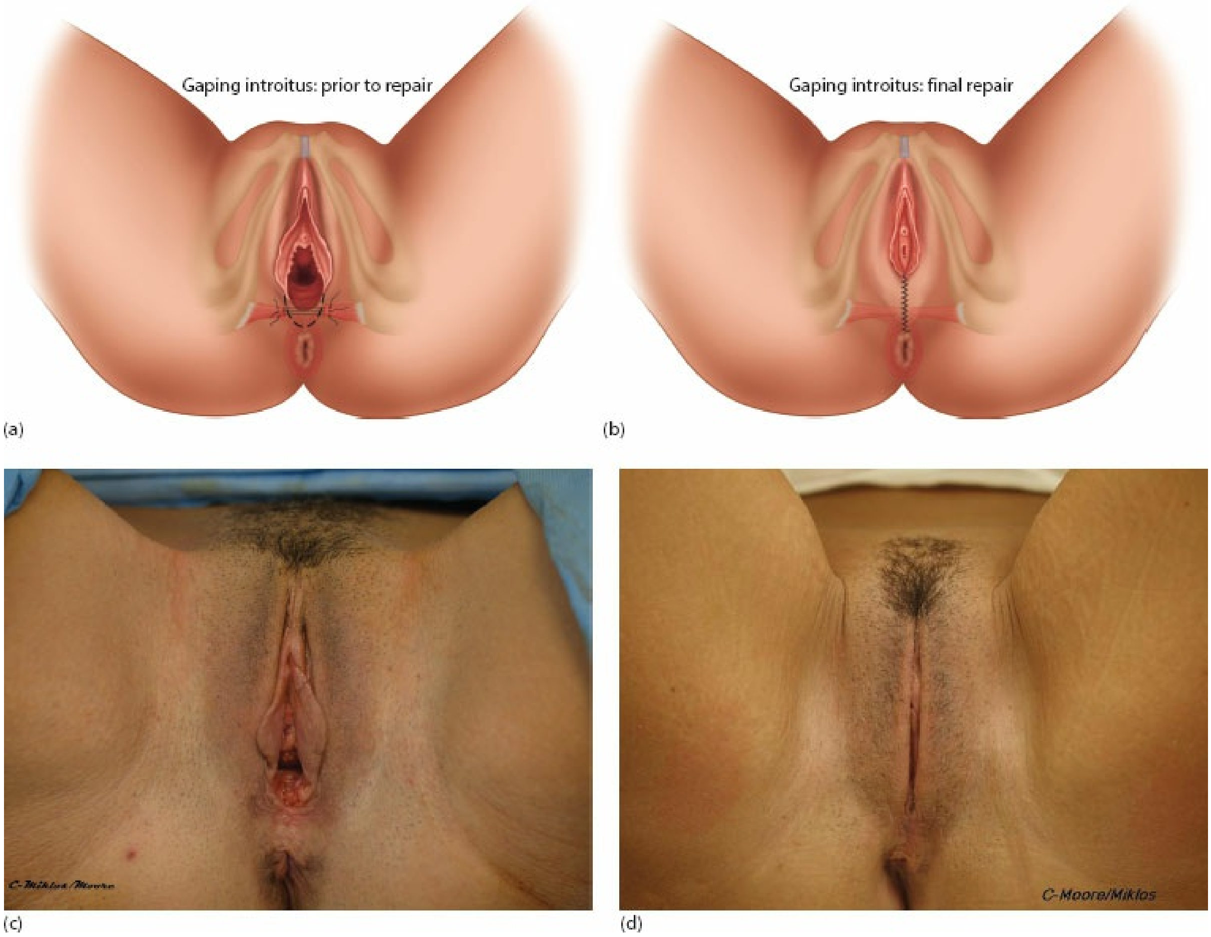

Gaping introitus: prior to repair
Gaping introitus: final repair
(a)
(b)
C-Miklos/Moore
(c)
C-Moore/Miklos
(d)

Figure 116.2 (a) Prerepair; (b) postrepair; (c) prerepair; (d) postvaginoplasty rejuvenation. (Courtesy of

Robert D. Moore and John R. Miklos.)

The theory that vaginal size is related to sexual sensation was first confirmed by Pardo et al. [2] in a study of a group of women who presented with symptoms of a wide or relaxed vagina and were interested in vaginal repair for sexual function alone. The women had no symptoms of prolapse or incontinence. Inclusion criteria included a sensation of a wide or loose vagina alone in combination with a decrease or lack of ability to reach orgasm. Exclusion criteria included symptomatic prolapse (cystocele, rectocele, or vault/uterine prolapse), dyspareunia, primary anorgasmia, or psychological impairment (all patients had psychological evaluation). Fifty-three patients were included in the study, and 96% of the patients experienced decreased vaginal sensation, 73% described difficulty achieving orgasm, and 27% could not reach orgasm. All but two patients had previous vaginal deliveries. Following surgical repair of the vaginal caliber and tightening of the vagina itself, 90% of women reported their sexual satisfaction was much or sufficiently improved and 94% of women were able to reach orgasm. This confirmed that vaginal size has a direct impact on sensation and ability to orgasm and when repaired sexual function improves.

Data Supporting Vaginal Rejuvenation and Improved Sexual Function (Table 116.3)

Pardo et al. published an additional follow-up study in a second group of women confirming their initial findings that vaginal size has a direct impact on sensation and ability to orgasm and when repaired sexual function improves [36].

Matlock and Simopoulos also conducted a study to evaluate sexual function in women presenting with subjective symptoms of vaginal relaxation with or without stress urinary incontinence following laser vaginal rejuvenation using PISQ score. Ninety-six patients who underwent the procedure completed PISQ before and 6 months after surgery. All patients presented with chief complaint of relaxed vagina and decreased sensation during intercourse. Of those, 65% had stage II POP-Q. This finding suggests that early pelvic organ prolapse may manifest as vaginal relaxation. The overall sexual function improved after surgery. There were only 13% of women with decreased PISQ score postoperatively. In addition, 53% reported increased intensity of orgasm during sexual intercourse [38].

Goodman et al. led a recent multicenter U.S. study on women undergoing female genital plastic surgery including vaginoplasty/perineoplasty for vaginal relaxation affecting sexual function. This study gathered data from diverse practices and surgical specialties with surgeons who utilize more than a single technique to achieve their desired outcome [39]. Preoperatively, 70% of women reported their sexual function was fair/poor. Postoperatively, it was found that 86% of 81 women following vaginoplasty/perineoplasty for sexual function reported enhanced sexual function following repair with only 1% reporting a negative effect on sexual function, confirming that repair of the vaginal caliber may lead to improved sexual function in women presenting with relaxation. Eighty-three percent of women reported “satisfied” with the outcome of vaginal rejuvenation. The predominate reasons for surgery from the physicians’ and patients’ perspective were feeling of looseness and lack of coital friction and sexual pleasure. A literature review by Goodman indicated that female genital plastic surgery procedures including vaginal rejuvenation appear to fulfill the majority of patient’s desires for cosmetic and functional improvement as well as enhancement of the sexual experience. The majority of patients reported improvement of overall satisfaction and subjective enhancement of sexual function and body image [39].

Most recently, we evaluated sexual function outcomes in a group of women ($n = 78$) presenting for vaginal rejuvenation/vaginoplasty procedure for a chief complaint of vaginal laxity and decreased sensation with intercourse. Outcomes were analyzed utilizing the validated Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire-12 (PISQ-12) before and at least 6 months after repair with vaginal rejuvenation/vaginoplasty procedure (VR). Compared preoperatively and postoperatively, the overall sexual function (total PISQ-12) statistically improved (30.3 ± 6.6 vs. 38.2 ± 5.2, $p < 0.001$). All individual scores statistically improved except in three categories in which there was no change (Q1-desire, Q5-pain, and Q11-partner premature ejaculation). Overall sexual satisfaction improved as well as subcategories of increased sexual excitement during intercourse and overall increase in intensity of orgasms. Pain with intercourse subscores was found to be no different from preoperatively to postoperatively [40].

VAGINAL REJUVENATION: SURGICAL TECHNIQUES

Importance of Proper Evaluation and Diagnosis

Proper preoperative evaluation is a vital process for a patient who presents with an interest in surgery to repair what she conceives is a loose or relaxed vagina and would like it tightened for sexual enhancement or to correct the feeling of having a “wide-open” vagina, i.e., vaginal rejuvenation surgery. This includes proper medical history, psychosocial evaluation for sexual dysfunction, and/or sexual satisfaction prior to any of the anatomical changes she may have noted since childbirth. Marital or relationship issues or concerns and an evaluation of her expectations of surgery and the reasoning why she is interested in the procedure should be discussed as well. Sexual dysfunction is very complex and multifactorial, and of course, a surgical procedure to repair vaginal support and reduce the vaginal caliber will not reverse or change psychological or psychosocial sexual dysfunction arising from previous abuse, primary anorgasmia, relationship issues, depression, or other more complex psychological dysfunctions.

In addition to a medical and psychosocial history, an adequate urogynecology history and physical exam must be completed. Sexual dysfunction related to a sense of a relaxed or loose vagina may be the first sign of the beginning stages of pelvic floor dysfunction and prolapse; therefore, an adequate history must be taken. We have actually found that as many as 50%–75% of patients who present for vaginal rejuvenation, when asked, have symptoms including urinary incontinence, voiding dysfunction such as overactive bladder or difficulty emptying, feelings of pressure or the sense that their organs are falling, defecatory dysfunction, or dyspareunia related to the uterus being hit during intercourse because of prolapse. It is vitally important to have an adequate understanding of the symptoms that prolapse can cause, and we use validated questionnaires such as the UDI-6, IIQ-7, and the PISQ-IR [41] to evaluate patients for these symptoms as well as a general urogynecological history form. If significant symptoms of urogynecological pathology are present, this must be evaluated preoperatively so that it can be addressed properly during surgery. Any prolapse that is present *must* be repaired properly at the time of surgery including uterine/vault prolapse, enterocele, cystocele, or rectocele as vaginal rejuvenation procedures do *not* adequately treat these defects. The foundation of the pelvic floor support must be intact prior to any technique that will tighten the caliber of the vagina or introitus.

Table 116.3 Vaginal Rejuvenation Studies on Female Sexual Function

Author, year	Study design	*n*	Population	Intervention	Outcomes	Results	Follow-up (month)	Complications
Pardo et al. [2]	Prospective observational	53	Women with wide vagina and decrease or lack of ability to reach orgasm	Colpoperineoplasty (dissected with a YAG laser)	Patients' sexual activity, fulfillment of expectations, and vaginal width using a site questionnaire	90% much or sufficiently improved of sexual satisfaction. 4% tighter vagina, able to achieve orgasm. 74% expectation fulfilled completely.	15	4% regretted having procedures.
Pardo et al. [36]	Prospective observational	100	Women with wide vagina and decrease or lack of ability to reach orgasm	Colpoperineoplasty	Patients' sexual activity, fulfillment of expectations, and vaginal width using a site questionnaire	95% tighter vagina during the intercourse. 85% achieve vaginal orgasm. 79% expectation fulfilled completely.	4	4% regretted having the procedures. 2 (0.02%) minor surgical complications
Adamo and Corvi [37]	Prospective observational	40	Women with wide vagina	Lateral colporrhaphy	Sexual sensitivity	95% improvement of vaginal sensation and wide vagina after 6 months. 80% partners noticed improvement.	1.5	5% local infection 2.5% postoperative vaginal bleeding
Matlock and Simopolous [38]	Retrospective	96	Women undergoing laser vaginal rejuvenation	Laser-assisted anterior and posterior repair w/perineorrhaphy	Comparing pre- and postoperative sexual function with PISQ-12 score	53% reported increased intensity orgasm with intercourse. Only 13% had decreased PISQ-12 scores.	6	
Goodman et al. [39]	Multicenter cross-sectional	258	Women undergoing female genital plastic surgery	Vaginoplasty/perineoplasty procedures ($n = 81$)	Preoperative sexual functioning per procedure, overall patient satisfaction per procedure, patient's perception of effect on her partner's sexual enjoyment, per procedure, complications	85% mild/significant enhanced sexual function. 86% satisfaction. Subjective improvement in sexual functioning for both women and their sexual partners ($p = 0.008$).	6–42	4% temporary stricture of vaginal apex 2% wound dehiscence 2% excessive postoperative pain 2% inadequate tightening 2% microtear at 1-year follow-up 2% introital tightening 2% bleeding after first sexual intercourse 2% felt sutures inside vagina 2% introital narrowing
Moore et al. [40]	Prospective observational	78	Women presenting for vaginal rejuvenation/vaginoplasty procedure for a chief complaint of vaginal laxity and decreased vaginal sensation with intercourse	Vaginal rejuvenation	Comparing pre- and postoperative sexual function using PISQ-12 score	Mean PISQ-12 improvement from 30.3 ± 6.6 to 38.2 ± 5.2 ($p < 0.001$).	>6	

Surgical Procedures

The surgical procedure required is determined by the patient's physical exam. Again, many women who present to be interested in vaginal rejuvenation-type surgery, or surgery to correct a feeling of a loose or wide vagina, are found to have prolapse in the form of cystocele, rectocele, or uterine/vault prolapse. In most instances, it is POP-Q stage II or less; however, it is present and should be repaired. This is what determines what surgery will need to be done as *the prolapse must be corrected first*, prior to any rejuvenation procedures being completed, and is really the first step in an overall repair or "rejuvenation" of the vagina and pelvic floor. If significant uterine/vault prolapse and/or anterior compartment (cystocele) defects are encountered, these typically should be repaired abdominally/laparoscopically/robotically prior to addressing the posterior compartment and the caliber of the vagina.

Rejuvenation of the Vaginal Canal and Introitus

Repair of the posterior vaginal wall and the introitus are the key aspects to any vaginal rejuvenation procedure. Vaginal rejuvenation surgeries are alterations and modifications of vaginal repairs for prolapse that focus on the final diameter and caliber of the vagina and attempt to restore it back to its prechildbirth state. They do however go far beyond the simple traditional posterior repairs and perineoplasty of old. The focus of these older procedures is simply to restore and reduce the bulge, whereas the focus of vaginal rejuvenation is to restore the caliber of the vagina and genital hiatus back to prechildbirth state from the introitus all the way up to the apex. They are much more extensive and meticulous procedures. No drop-offs or dips should be felt and there should be no tension placed on the levators that causes lateral banding of the vagina. Additionally, the cosmetic appearance of the introitus and perineal body is also taken into account and requires intricate dissection and repair to not only restore function of the introitus but also obtain an appearance that the woman desires. That look typically is one of the vaginal opening being closed, not gaping or wide open with a normal length perineal body that does not bulge out following the repair. This look is sometimes difficult to obtain, without making the introitus too tight, which will cause pain with intercourse.

Posterior Wall, Introitus, and Rejuvenation

The posterior vaginal wall is the focus of any vaginal rejuvenation procedure. In a woman with a mild cystocele or mild relaxation of the anterior vaginal wall, a small anterior colporrhaphy can be completed to take care of this prior to repair of the posterior wall. However, one needs to be very careful with this as if the repair of the anterior wall is too aggressive, it will lead to lateral banding and constriction of the vagina, before the posterior wall is even started.

An incision is made at the introitus, typically in trapezoid pattern, that will also be used in the perineoplasty portion of the procedure (Figure 116.3a and b). A small incision is then made in a vertical fashion on the posterior wall, and the vaginal epithelium is dissected off the underlying rectovaginal fascia all the way laterally out to the levators (Figure 116.3c and d). The dissection must be taken all the way up to the apex of the vagina, as the repair needs to incorporate the entire posterior wall to restore the caliber of the full length of the vagina (Figure 116.3e). The dissection of the vaginal epithelium may be completed with a laser, as championed by Dr. David Matlock, or completed utilizing more standard techniques with sharp scissors or electrocautery. Care of course needs to be taken with any electrical energy source near the rectum. If a rectocele is present, the fascia is repaired in a site-specific fashion with delayed absorbable suture for the first layer of the repair. This may be a lateral repair of the defects, a midline placation, or a combination (Figure 116.3f). The caliber of the vagina is then addressed by plication of the rectovaginal fascia in the midline with delayed absorbable sutures. Levator plication is avoided; however, the diameter of the vagina is constantly measured, and several layers of plication may be needed to reduce the genital hiatus and reduce the caliber of the vagina to an appropriate level (Figure 116.3g through j). A small amount of vaginal epithelium is then excised and the incision closed in a running fashion.

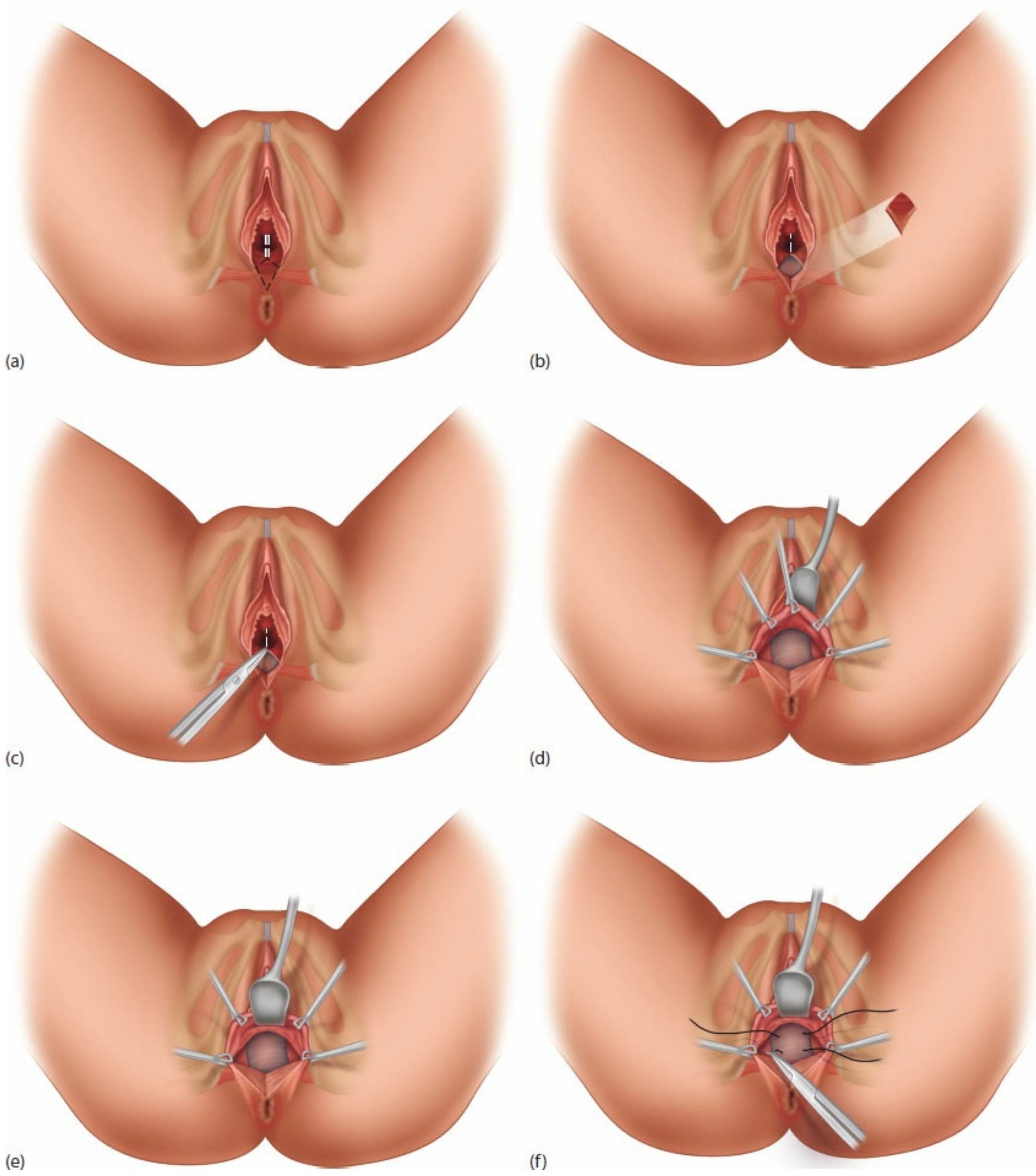
A perineoplasty is then completed, involving a very meticulous and detailed dissection out laterally to obtain the lacerated edges of the deep and superficial transverse perineal muscles and bringing them back together in the midline to achieve uniformity at the same level of the posterior wall repair. The inferior edges of the labia majora that will make up the posterior forchette of the vaginal opening must be marked at the beginning of the procedure so that these edges match up during the closure to form the vaginal opening. An appropriate amount of skin must also be excised from the perineum and introitus to result in a cosmetically pleasing appearance of the opening of the vagina for the patient. A multilayer (typically this may involve four or five layers) is completed at the perineum and introitus (Figure

116.3k through m).

When a repair is primarily for vaginal relaxation for sexual function, it becomes a much more meticulous dissection and repair as the surgeon has to constantly be judging and measuring vaginal caliber to try to restore the entire vaginal length to its prechildbirth state. If this is not done, then the results will be poor and the patients' sexual function may not change or they will be worse secondary to pain, vaginal shortening, scar tissue formation, and/or constrictions.

Postoperative Care

Routine postoperative care is given to patients undergoing vaginal surgery. Many of the procedures are undertaken on an outpatient basis, and the surgery is completed under spinal or general anesthesia. A pudendal block may also be completed prior to or during the procedure to help decrease postoperative pain. Vaginal packing is left in for a short period of time and removed prior to the patient being discharged. Routine instructions for vaginal surgery are given to the patient and she is seen in follow-up at 4 weeks postoperatively. The vaginal introitus and caliber are assessed, and if felt necessary, the patient will begin perineal massage in warm water bath for 1–2 weeks prior to resuming sexual relations.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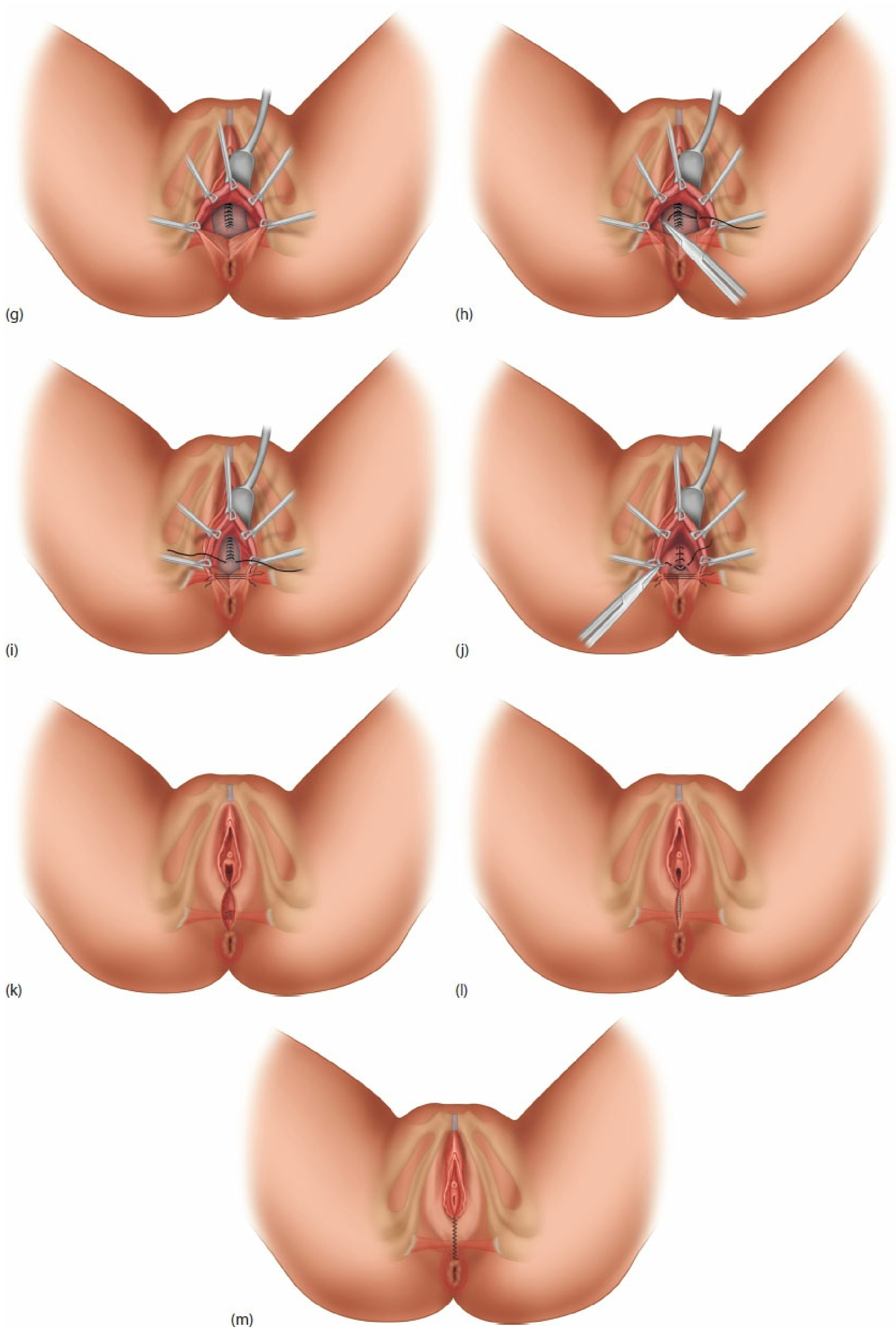

Figure 116.3 (a–f) Vaginal rejuvenation dissection and initial suture placement. (Courtesy of Robert D.

Moore and John R. Miklos.) (g–m) Vaginal rejuvenation suture placement, multilayer repair and perineal body repair. (Courtesy of Robert D. Moore and John R. Miklos.)

Risks/Complications

The potential complications of vaginal rejuvenation are infection, bleeding, wound dehiscence, dyspareunia, inadequate tightening, introital narrowing, and rectoperineal fistula. According to a study of 248 women by Goodman et al., 2% of women had temporary stricture of the vaginal apex, 1% wound dehiscence, 2% excessive postoperative pain, 2% inadequate tightening, 1% microtearing of the perineum with intercourse at 1-year follow-up, 2% introital overtightening, and 2% bleeding after first sexual intercourse [42].

Conclusion

Vaginal rejuvenation surgery is one of the latest trends in elective vaginal surgery for women. It is a repair of the vaginal caliber in women who suffer from decreased vaginal sensation or of feelings of a loose or wide vagina that affects their sexual life. In many instances, women who present with these symptoms are found to have other pelvic pathologies such as prolapse that must also be addressed during any repair contemplated. Sexual dysfunction or decreased sexual sensation may be the first symptoms that women suffer from in the progression of prolapse, and therefore, a proper exam is vital prior to any repair. We have ample evidence that prolapse and vaginal relaxation can create sexual dysfunction and that repair may reverse these changes in many women. It is important to note that when dealing with sexual dysfunction due to vaginal laxity alone, the surgical repair must be very meticulous and exact in order to enhance sensation and function and not impair it. This sums up the statement "The Art of Surgery"!

COSMETIC VAGINAL SURGERY

Aesthetic Surgery of the External Vagina and Vulva

Introduction

There have been many studies and research on the relationship between a woman's body image and her sexual function. However, little research exists on the relationship between a woman's genital image and her sexual function. Realizing one's genital image is part of one's body image; it is easy to understand how many women might feel sexually inhibited if they are not comfortable with the appearance of their vagina, vulva, or external genitalia. A survey of 3627 women found that women with positive body images reported more sexual activity, initiation of sexual activity, orgasm, sex with lights on, and greater comfort undressing in front of their partners, trying new sexual behaviors, and pleasing their partner [43].

Cosmetic vaginal surgery is currently steamrolling its way into mainstream culture. However as with every new trend, there are always those who oppose change. There have been many negative comments and editorials written suggesting that both the doctors and the patients should not be pursuing cosmetic vaginal surgery [44–46]. Many of those who imposingly opine are often ignorant of the patient and their disposition as well as their medical conditions and their associated symptoms [47]. Patients can suffer from a variety of physical and emotional symptoms. Physical symptoms are usually associated with wearing certain types of clothing; engaging in activities such as walking, jogging, exercise, and bicycling; and finally intercourse. Yet, other patients are afflicted with emotional problems such as embarrassment, anxiety, and a loss of self-esteem.

Cosmetic vaginal surgery does not always begin and end with labia minora reduction surgery, i.e., labiaplasty. There are many different techniques that can be applied to enhance a woman's genital cosmetic image. To understand the techniques, a basic understanding of the external genitalia is essential before undertaking surgical procedures.

Anatomy

The vulva is made up of the external genitalia including the mons pubis, clitoris, prepuce or clitoral hood, labia minora, labia majora, urethral meatus, hymen, and vestibule (Figure 116.4). The mons pubis is the adipose-laden area that lies superior to the pubic symphysis. This area is naturally covered with pubic hair and is a natural cushion during the impact of intercourse. The adipose area of the mons is contiguous with that of the hair-bearing labia majora. The labia majora are found bilaterally and converge both anteriorly above the clitoral prepuce and posteriorly at the perineum. The prepuce is actually the clitoral hood and acts like a protective covering over the clitoral gland. Usually, the very distal tip of the clitoris remains uncovered and exposed. The labia minora are bilateral mucosal–cutaneous refolds located between the labia majora and vulvar vestibule. While there is a wide range of normal anatomic variants, in general, the labia minora are semicircular with a 3 cm long base and a free edge extending from the clitoris to the posterior commissure. The medial mucosal surface is derived from the primitive urogenital sinus and is shiny and pink. The free edge and the lateral cutaneous surface that are derived from the urethral folds are more deeply pigmented [48]. However, the deeper pigment tends to be a darker pink initially and then begins to darken with hormonal changes often but not always associated with pregnancy. Obviously, just like any other part of the human body, there are multiple normal variants of this anatomy. Just like a nose, all the structures can be anatomically similar but cosmetically dissimilar. The most common of all described cosmetic vaginal surgery is labia minora reduction or labiaplasty [48–51].

Labia Minora Reduction (Labiaplasty)

Labia minora protruding past the distal edge of the labia majora can be of concern to women. As mentioned earlier, this condition can constitute a functional or cosmetic problem. Such an enlargement can be bilateral or unilateral in nature (Figures 116.5 and 116.6). Labial enlargement can be congenital as described by Caparo [52] and Radman [53] or can also be the result of androgenic hormones, manual stretching, and chronic irritation [52–55].

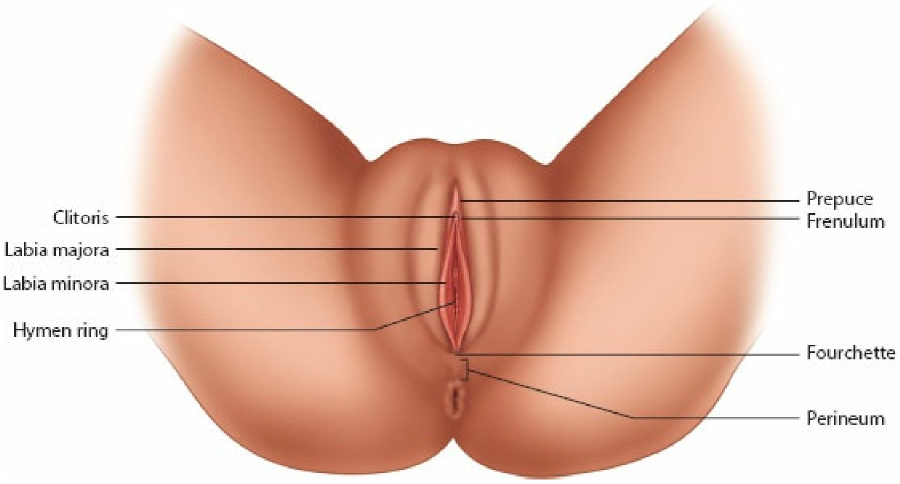

Figure 116.4 Normal external anatomy. (Courtesy of Robert D. Moore and John R. Miklos.)

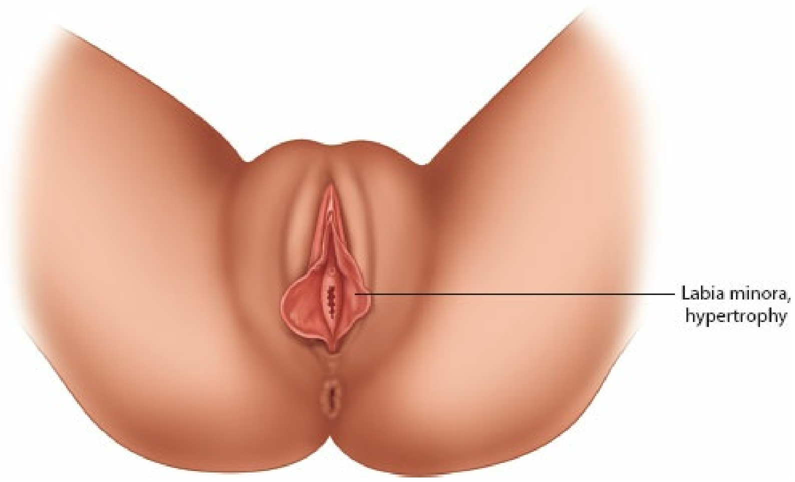

Figure 116.5 Labia minora hypertrophy. (Courtesy of Robert D. Moore and John R. Miklos.)

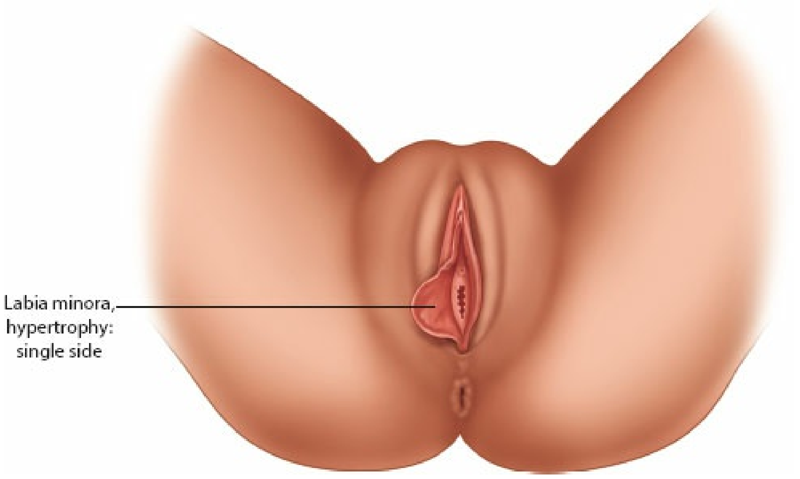

Figure 116.6 Unilateral labia hypertrophy. (Courtesy of Robert D. Moore and John R. Miklos.)

Rouzier et al. reported on 163 women who received labial reduction surgery. The primary reason for patients requesting this surgery was aesthetic dissatisfaction in 87% of cases, discomfort in clothing in 64%, discomfort when taking part in sports in 26%, and entry dyspareunia by invagination of the protuberant tissue in 43% [49]. We reported on a study of 131 patients undergoing labia minora reduction surgery and revealed the patients' indications for having the surgery: 37% strictly cosmetic reasons, 32% strictly for physical symptoms, and 31% a combination of cosmetic reasons and physical symptoms [52].

Although there are still few papers on labial reduction surgery, there are a number of different techniques described in the literature. The two most commonly utilized techniques are known as excision or contouring technique and the wedge resection technique. The authors employ both techniques depending upon the patients' requests and desires. If the patients prefer to keep the darkened pigmented labial border, we tend to utilize the wedge resection technique. However, it has been the authors' experience that most of their patients prefer to have a pinker or lighter look to the edges of their labia. In this situation, in an attempt to fulfill the desires of the patient, we utilize the contouring technique [51].

The contouring or excisional technique is a more time-consuming operation and directly excises the edge of the labia minora (Figure 116.7a through d). Though all surgeries are surgeon dependent, this operation is less reproducible than the wedge technique because it requires more artistic aptitude. There are multiple skin folds that need to be excised, reduced, and brought together to achieve a natural anatomic appearance of the entire external vulvar region. The edges should be contoured or removed in an artistic fashion instead of the commonly described term amputation. The term amputation seems to insinuate the protruding labia should just be "cut off" in a straight vertical fashion, which does not result in aesthetically pleasing results and can cause pain and discomfort. The procedure should not be completed with this type of "amputation" technique. Time and care should be put into the incision and the excision of the protruding aspect of the labia. It should be removed in a curvilinear fashion at the level or below the level of the labia majora. The amount of tissue removed should be in direct correlation to the patient's desire. Aggressive excision can result in complete amputation resulting in an undesirable result (Figure 116.8). The results of a contouring surgery should be aesthetically pleasing yet address any associated physical dysfunction. Most women state that they do not want their labia minora to protrude beyond the majora and are interested in a smooth, sleek appearance of the external vulva. This was confirmed in a recent study of 550 women who presented for labial reduction surgery at our specialty center in Atlanta. Of the 550 women who were presenting for labial reduction, 97.8% of them desired for their labia minora to be reduced to the level of or below the level of the labia majora [56].

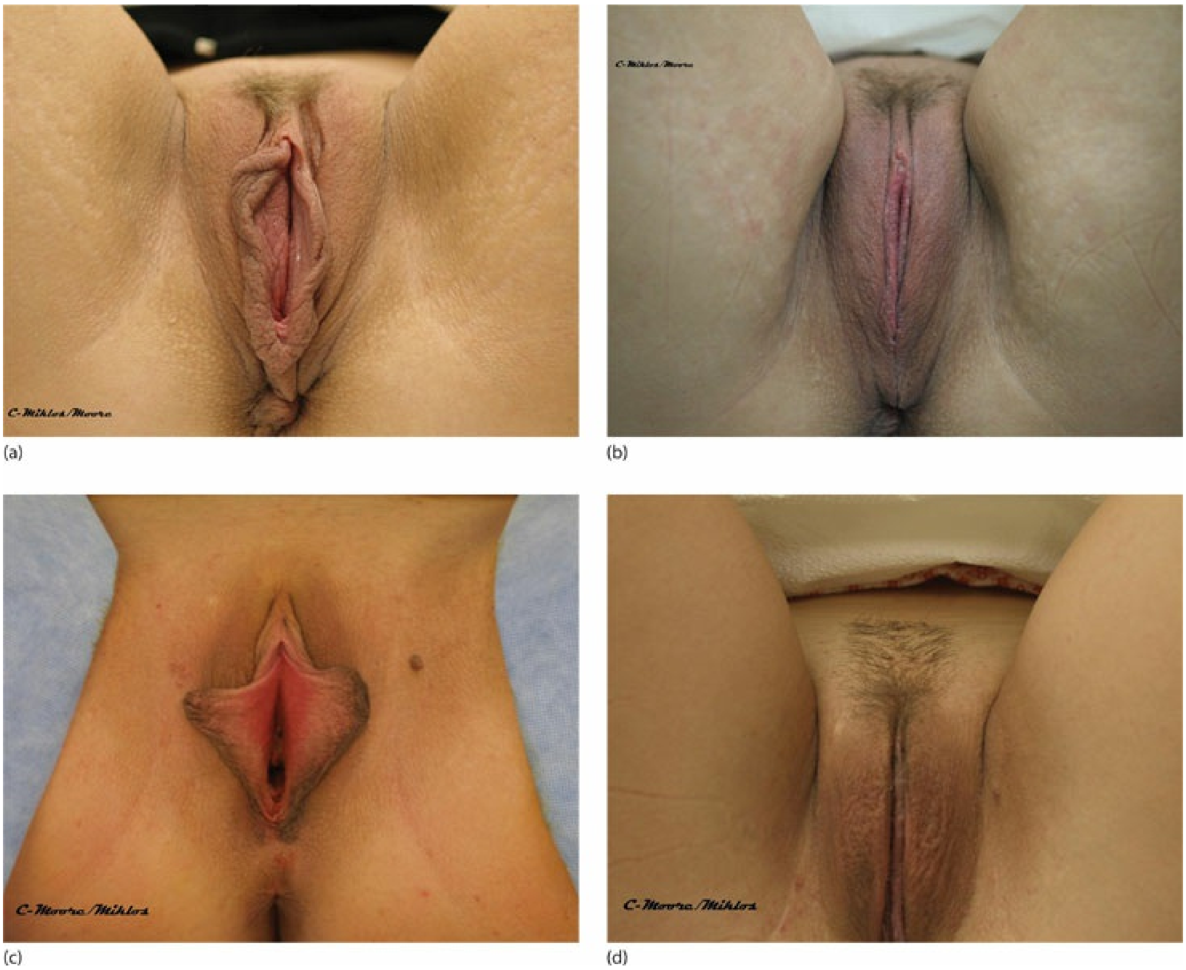

Figure 116.7 (a) Preoperative labiaplasty; (b) postlabioplasty; (c) preoperative labiaplasty; (d) postlabiaplasty. (Courtesy of Robert D. Moore and John R. Miklos.)

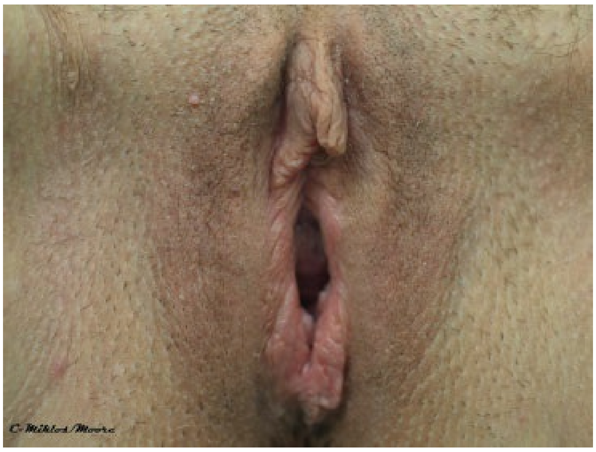

Figure 116.8 Excessive labia minora removed/amputated. (Courtesy of Robert D. Moore and John R. Miklos.)

The authors utilize the wedge resection technique in patients who wish to maintain the darkened skin edges of the labia. The technique was first described in the literature by Alters in 1998, where he utilized the technique on four patients [46]. In this case series, it is suggested that excision or contouring the protuberant edges removes the natural contour and color. Interestingly, many patients do not feel that the darkened skin edges are a normal color but instead the result of aging and hormonal changes. This is no different than the skin discoloration that happens on hands or the areola of the breast. This was also confirmed in a recent study of 550 women presenting for labiaplasty at our center in Atlanta. Of the 238 women, 72% of women felt their skin edges were dark or pigmented and 96% preferred that their skin edges be pink following the procedure [56]. The authors feel the wedge technique is less time consuming and requires less artistic impression; however, it does not address the excess prepuce that is a problem with many women presenting with labial hypertrophy (Figure 116.9).

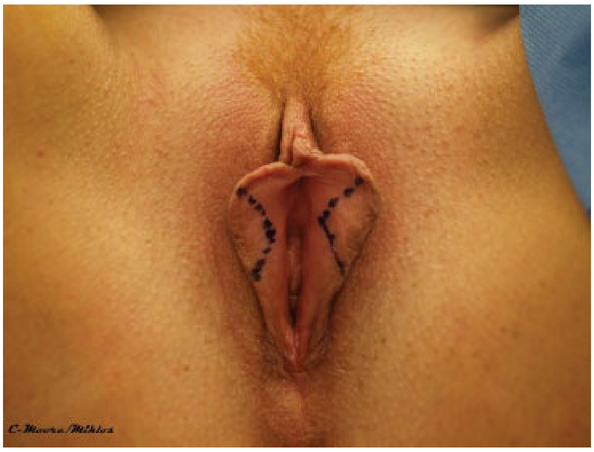

Figure 116.9 Wedge technique. (Courtesy of Robert D. Moore and John R. Miklos.)

Redundant Lateral Prepuce

In our practice, approximately 80% of patients also complain of redundant prepuce when they consult for labia minora reduction (Figure 116.10). This is strictly a cosmetic problem and not a functional problem. We have not had patients complain of symptoms from redundant lateral prepuce except occasionally feeling that it has a negative effect on clitoral sensation. On examination, patients will often point out the lateral excessive tissue, which is adjacent to the clitoral hood bilaterally, or that the clitoral hood is elongated and hangs down a great deal below the majora. If the patient wants to have her labia minora reduced via a contouring technique, often the redundant prepuce will inhibit the surgeon from getting good cosmetic results unless the prepuce redundancy is reduced or removed. The reason why the redundant prepuce becomes an issue is because of its anatomic insertion. The origin of the prepuce starts laterally to the prepuce and then inserts usually at an acute angle into the lateral aspect of the labia minora (Figure 116.10). An excision of the labia minora without addressing the redundant prepuce can result in poor cosmesis (Figure 116.11).

Excess Superior Prepuce Reduction (Clitoral Hood Lift)

As described earlier, we have coined the term “redundant prepuce” in patients who have an extra layer of prepuce *lateral or adjacent* to the clitoral hood. Patients with excess prepuce have excessive prepuce at its normal anatomic position. In other words, the prepuce is in the right spot but there is just an excessive amount of it or an elongation of the clitoral hood itself (Figure 116.12a and b). Excess superior prepuce or clitoral hood elongation may be a purely cosmetic issue, or patients may complain of difficulty accessing the clitoris, thus making clitoral orgasms difficult to achieve. Surgical resection, if done correctly, can bring favorable results for patients with excess prepuce. Performed incorrectly, it can result in hypersensitivity and chronic pain or even severe scar limiting any access to the clitoris.

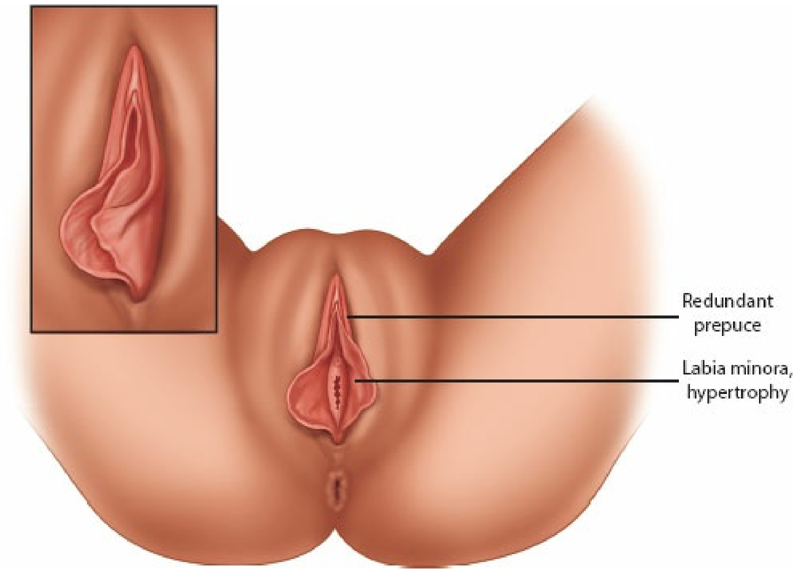

Figure 116.10 Redundant prepuce. (Courtesy of Robert D. Moore and John R. Miklos.)

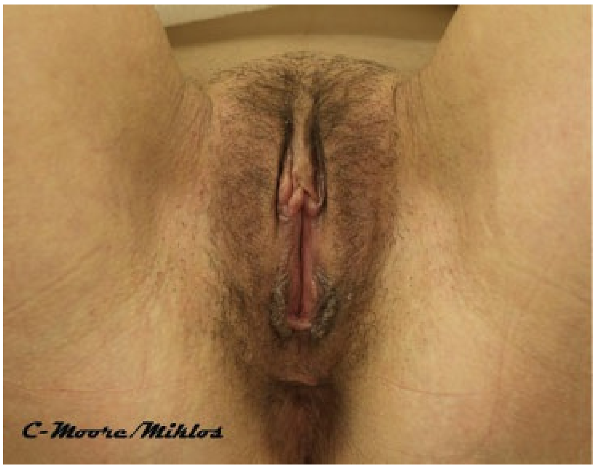

Figure 116.11 Botched labiaplasty. Excessive minora removed with no prepuce reduction. (Courtesy of Robert D. Moore and John R. Miklos.)

Labia Majora Reduction

Patients complain of "drooping," "sagging," or "hanging" majora or the majora is just too large and protruding in appearance. Many women state that this skin is very loose and makes the appearance of the external vaginal area appear "old." They are looking for a youthful "plumpness" of the labia majora, without much laxity or wrinkling. The sagging labia majora may be the result of weight gain and weight losses, which seem to be often associated with pregnancy or in patients who have had bariatric surgery. The saggy skin of the labia majora may be the result of stretching during the weight gain, and then with sudden weight loss, the skin hangs because it has lost some of its elasticity. It can also occur due to aging and/or childbearing (Figure 116.13).

Still others complain of enlarged labia majora and on examination do not have sagging skin. These patients tend to have taut skin because it is filled with excessive adipose deposits. This in essence results in lipodystrophy of the labia majora and labia majora hypertrophy. In many cases, women who have had abdominoplasties and/or liposuction of the abdominal region end up with an asymmetrically enlarged mons pubis. This area also in many cases has excess deposits of fatty tissue and, if not reduced at time of abdominoplasty, ends up protruding out or hanging down. These patients often complain they cannot wear tight clothing or they are embarrassed in a swimming garment because they feel as if their vulva and/or mons is protruding. These patients can benefit from liposuction of the mons pubis and labia majora areas (Figure 116.14a and b).

Labia Majora Convergence

Cosmetic surgical patients are very consumer savvy and often are quite specific about their cosmetic desires. Many of our patients will have pictures and/or medical illustrations, which represent their desired cosmetic results. Another common request, we have coined “labia majora convergence” surgery. Patients can have labia majora divergence both anteriorly at the mons pubis or directly anterior to the clitoral hood and posteriorly at the perineum (Figure 116.15a and b). Surgical correction of the divergence results in convergence of both or either the anterior division of posterior aspect of the labia majora.

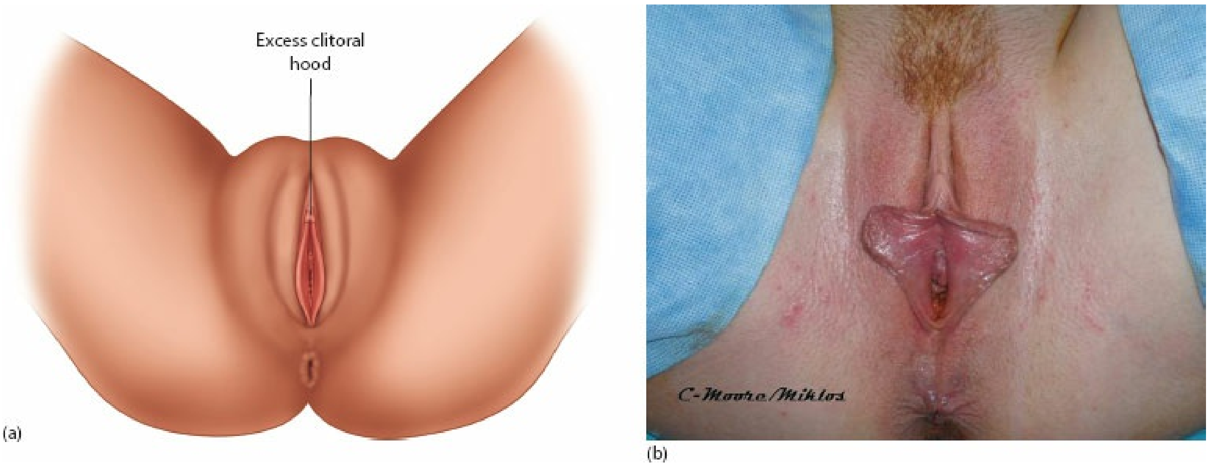

Figure 116.12 (a) Elongated clitoral hood; (b) labia hypertrophy with elongated hood. (Courtesy of Robert D. Moore and John R. Miklos.)

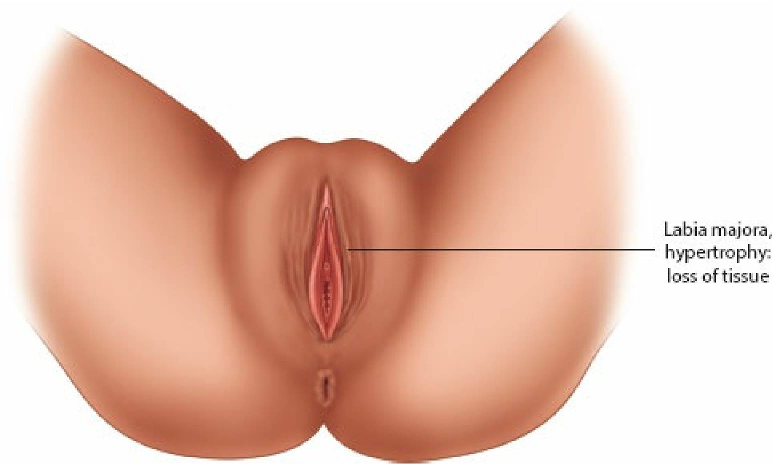

Figure 116.13 Sagging majora. (Courtesy of Robert D. Moore and John R. Miklos.)

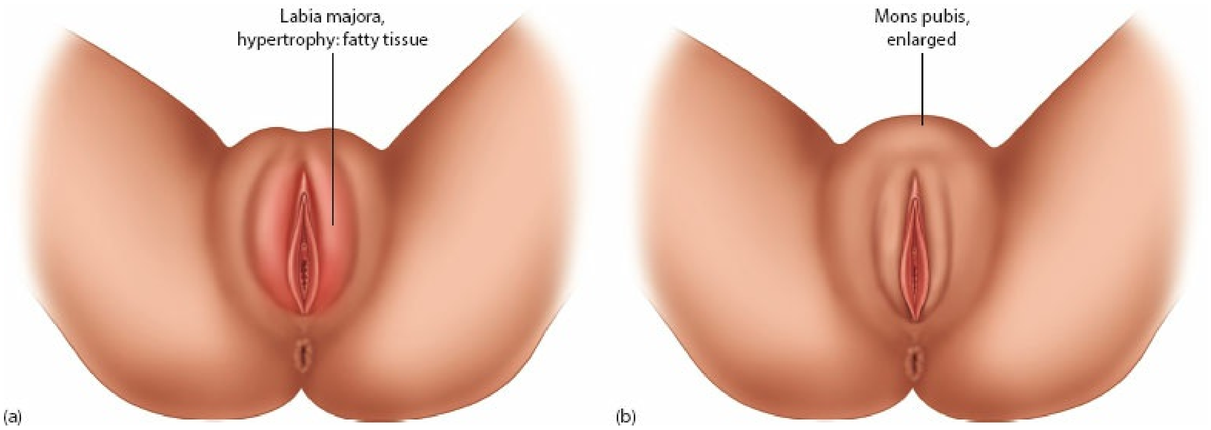

Figure 116.14 (a) Labia majora hypertrophy; (b) excess majora and mons fat. (Courtesy of Robert D. Moore and John R. Miklos.)

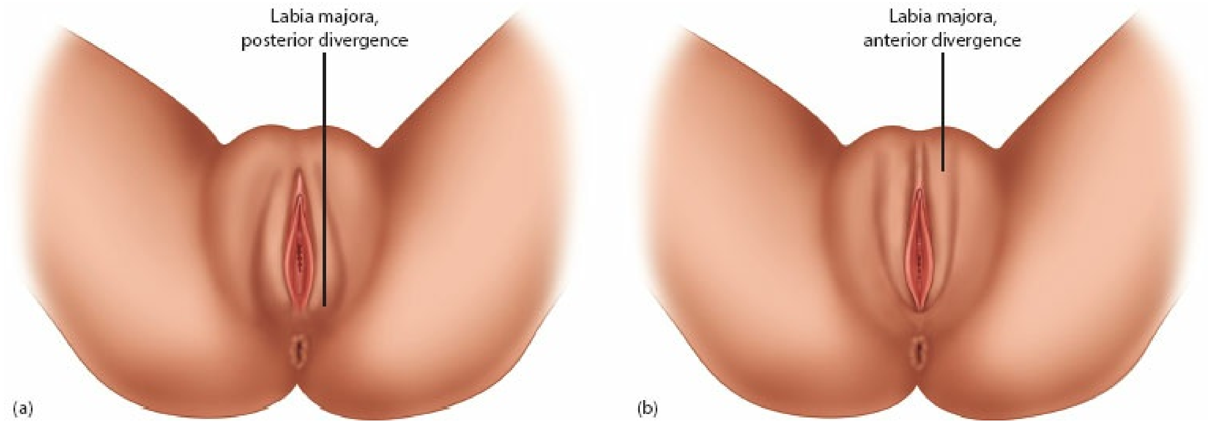

Figure 116.15 (a and b) Labia majora divergence. (Courtesy of Robert D. Moore and John R. Miklos.)

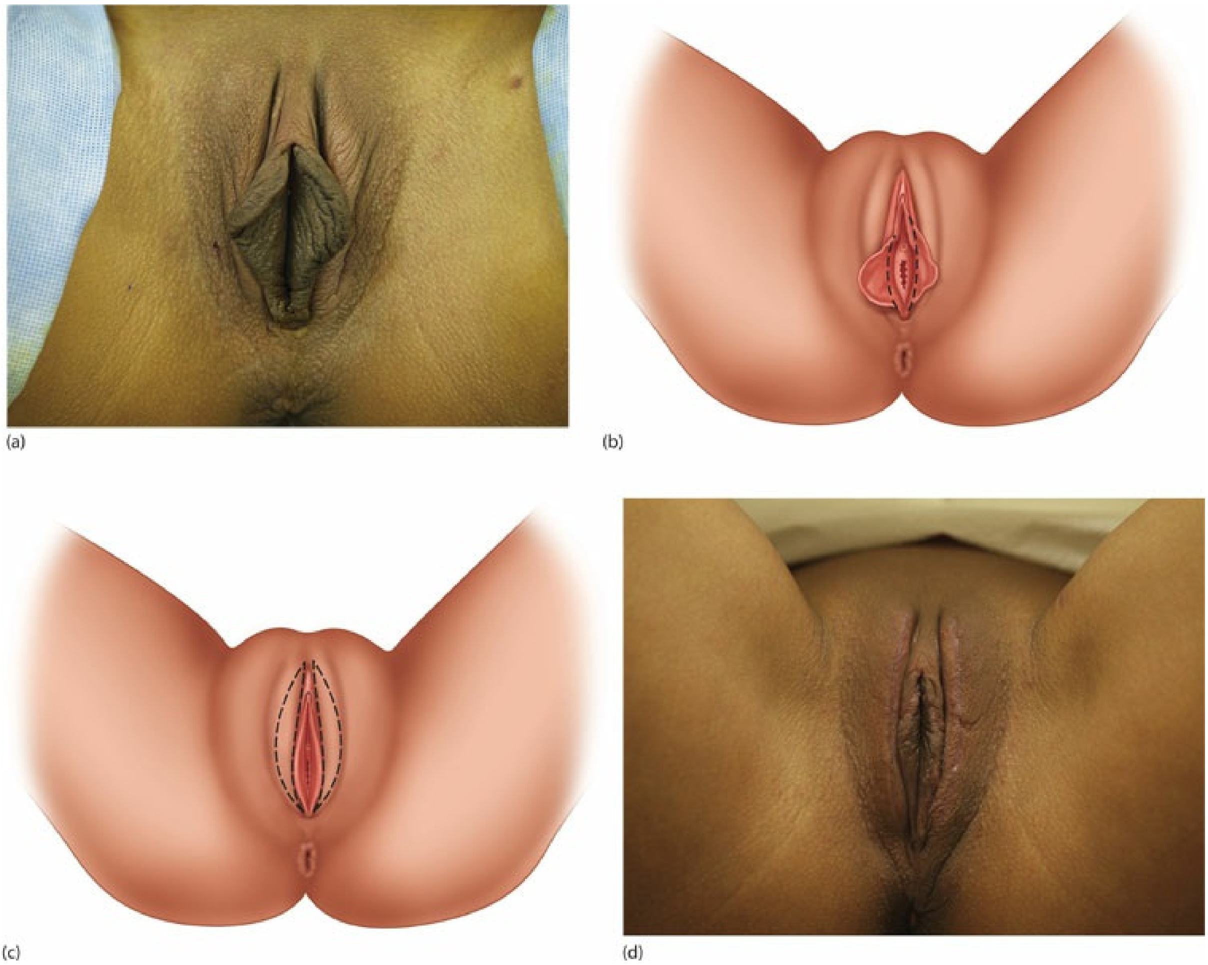

Figure 116.16 (a) Preoperative labia minora and majora; (b) labia minora incision lines; (c) labia majora reduction incision lines; (d) postoperative labia minora and majora reduction. (Courtesy of Robert D. Moore and John R. Miklos.)

Combined Vulvar Procedures

Many patients request and ultimately require combined procedures to achieve their desired results. When completing labia majora reduction concomitantly with labia minora reduction, the surgeon needs to be very careful in keeping the incisions separated to prevent the incisions from healing together. Typically, the minora are completed first and then the majora (Figure 116.16a through d).

CONCLUSION

Cosmetic vaginal surgery is a newly emerging frontier in our dynamic and body image–conscious society. Still in its infancy, this discipline will continue to mature and take on a life of its own. Partially spurred by our ever-pervasive process of globalization, the Internet, and the desire to “antiage” and remain youthful in appearance and function, cosmetic vaginal surgery is here to stay. A woman’s desire to enjoy life to its fullest does require a good body image, and *sometimes* a little surgical help might be necessary to help maintain that body image.

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117 Urological Complications of Gynecological Surgery

Monica L. Richardson and Craig V. Comiter

During gynecological surgery, the structures of the lower urinary tract are particularly at risk due to the close proximity of the pelvic organs to the ureters and bladder. Therefore, all pelvic surgeons should be familiar with ways to prevent and manage such complications. This chapter focuses on the iatrogenic causes of bladder and ureteral injury, strategies to prevent and recognize them, and management of postoperative repair.

INCIDENCE

The overall rate of urinary tract injury during benign hysterectomy can range between 1% and 4.8% [1–3]. In one large prospective study of more than 830 women, cystotomy at time of total abdominal hysterectomy found with intraoperative cystoscopy occurred in 1.7% of patients [2]. Total vaginal hysterectomy alone had an incidence of 0.4% versus 2.2% if combined with concomitant prolapse procedures [2]. In the same cohort, ureteral injury occurred in 1.7% of total abdominal hysterectomy cases and 2.6% of transvaginal hysterectomy cases [2].

Rates of bladder and ureteral injury are higher with surgery for pelvic organ prolapse and anti-incontinence procedures than benign hysterectomy alone. In patients undergoing benign hysterectomy, Vakili et al. reported a bladder injury rate of 3.6% versus 12.5% in patients undergoing concomitant anti-incontinence procedures [3]. Similarly, the rate of ureteral injury at the time of vaginal surgery for pelvic organ prolapse and anti-incontinence procedures has been reported to be 1.8%–5.1% [3–5].

PREVENTION OF INJURIES

Prior to undergoing gynecological surgery, proper patient selection and preoperative evaluation is vital to minimize the risk of unsuspected anatomic variation and to reduce the risk of surgical injury. Medical history should include obstetric history and records of prior pelvic surgery, radiation, suspected infection, or endometriosis. Any documented anatomic anomalies or urinary tract surgeries should also be reviewed. When indicated, preoperative imaging can be helpful in determining any structural changes secondary to uterine leiomyoma or other potential distorting anatomic conditions. Counseling about the risk of urinary tract injury as well as the sequela of unrecognized injuries should be undertaken prior to surgery and documented in the medical record or consent form.

Universal preplacement of ureteral catheters is not recommended for routine pelvic reconstructive or extirpative surgery. A randomized trial of more than 3000 women without prior pelvic surgery found no difference in the incidences of ureteral injury in those with preplaced ureteral catheters versus not [6]. Ureteral catheters, however, can be helpful in carefully selected women with a history of prior pelvic surgery, known retroperitoneal fibrosis, large uterine leiomyomas, or history of severe endometriosis [7]. Ureteral stents can facilitate identification of the ureters (easier to palpate) and also improve the surgeon’s ability to recognize ureteral injury or transection with obvious visualization of the brightly colored stent.

The surgeon should always identify both ureters throughout the procedure. While familiarity with normal anatomy is vital, it is those cases with abnormal anatomy that pose the highest risk. Intravenous urography or computed tomographic intravenous pyelogram may be considered if a preexisting abnormality is suspected in order to determine the ureteral course. In patients undergoing benign hysterectomy with a normal size uterus, routine utilization of an IVU is not recommended. However, patients with pelvic organ prolapse, especially those with procidentia, may have hydronephrosis prior to prolapse repair. One series of women undergoing surgery for pelvic organ prolapse who had undergone preoperative IVU reported a 7% prevalence of hydronephrosis, 14% of whom had severe dilation [8]. The incidence of hydroureteronephrosis can increase, however, with worsening pelvic prolapse. While ureteral injuries during hysterectomy occur in up to 2.5% of cases [9], routine preoperative IVU has not been shown to reduce the incidence of ureteral injury [8]. Furthermore, some patients may have a significant adverse reaction to the contrast agent, including acute renal injury and anaphylaxis.

Prompt recognition of urinary tract injury aids in the management and prevention of further complications. A properly repaired injury should prevent postoperative ureteral obstruction and ureterovaginal or vesicovaginal fistula formation. The surgeon should be meticulous regarding the inspection of the surgical field, focusing on the bladder base and distal ureters. Routine cystoscopy should always be performed following uterine, bladder, or urethral surgery to rule out associated organ injury and to observe urine efflux per ureteral orifice, thereby ruling out ureteral obstruction. Intravenous indigo carmine can be given to enhance the visualization of ureteral efflux and confirm ureteral patency.

ANATOMY

In order to prevent injury to the lower urinary tract, a surgeon must become very familiar with pelvic anatomy and proximity of the ureter to gynecological structures (Figure 117.1).

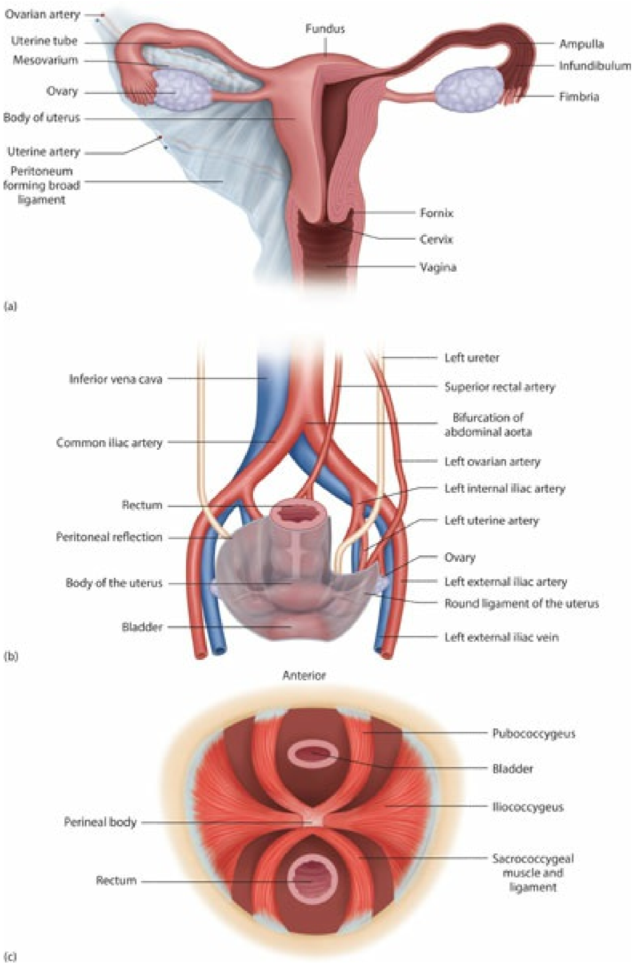

Figure 117.1 Pelvic and vreteral anatony. (a) Uterus. (b) Vaseculature. (c) Pelvic Floor.

The Ureters

Ureters are retroperitoneal tubular structures posterior to the renal artery and vein and run from the renal pelvis to the trigone of the bladder [10]. They are approximately 22–30 cm long and can be injured anywhere along this path [10–12]. The ureter courses anterior to the psoas muscle then anterior to the iliac vessels. The right ureter descends anteriorly over the duodenum and runs lateral to the inferior vena cava [10]. The left ureter travels lateral to the aorta and runs close to the descending and sigmoid colon. As the ureters approach the pelvis, they are crossed anteriorly by the ovarian vessels [10]. The right ureter enters the pelvis by crossing over the external iliac artery, while the left ureter crosses over the common iliac artery. In the middle of the pelvis, the ureter is crossed anteriorly by the uterine artery [13]. Here, it tunnels into the cardinal ligament approximately 1.5–2 cm lateral to the cervix near the internal cervical os and vaginal fornices as it enters in the trigone of the bladder [14]. It is in this area that the ureters are mostly likely to be injured during hysterectomy.

Histologically, the ureter is made of three layers that include an inner layer of transitional epithelium; a middle layer of longitudinal, circular, and smooth muscle; and an outer layer of adventitia [10]. The adventitial layer contains the blood and nerve supply as well as lymphatic drainage from the ureter [10]. The renal, ovarian, and common iliac arteries as well as the aorta all contribute to the blood supply of the ureter [12]. In the abdomen, the ureter derives its blood supply from all small arteries approaching it medially (from the aorta), where the pelvic ureter receives its blood supply from vessels approaching laterally (from the iliac arteries) [12].

The Bladder

The bladder is positioned anterior to the vagina, cervix, and lower uterine segment. The vesicouterine fold/pouch is a reflection of the anterior peritoneum that lies between the dome of the bladder and the lower uterine segment. The bladder base is opposed to the cervix and vagina with the vesicocervical and vesicovaginal fascia. The bladder is typically described as consisting of the dome superior to the trigonal ridge and the base inferiorly [12]. The base contains the trigone, including the ureters, which enter posteriorly, and the urethra, which exits at the most inferior aspect of the bladder [12].

MECHANISMS OF INJURY

The lower urinary tract can be injured in several ways. Direct trauma may include injury to the ureter by transection or clamping. It can also be devascularized or denervated by sharp or blunt dissection, typically when the dissection is carried out (unintentionally) in a subadventitial plane. Thermal injury via electrocautery or other sources of energy such as a harmonic scalpel or laser can also compromise the ureteral vascular supply. Such injuries are more likely to happen during laparoscopic surgery for hysterectomy [15–17] than with transvaginal extirpative surgery or prolapse repair. As bladder or ureteral urinary leakage secondary to thermal injury typically occurs secondary to ureteral wall necrosis, the presentation is usually delayed until several days after surgery. On the other hand, direct injury to the bladder, on the other hand, usually occurs with either laceration to the bladder wall or accidental placement of a suture or staple [18,19]. Unrecognized placement of a permanent suture or metal staple into the bladder wall may initial be asymptomatic. Over time, however, exposure of the foreign body to urine typically leads to stone formation [20]. Presentation can relate secondarily to pain, recurrent urinary tract infection, or even obstructive uropathy. Following surgery, an unrecognized lower urinary tract injury can lead to infection, abscess or hematoma formation, or edema and even frank ureteral obstruction [21]. Injury to the bladder that communicates with a vaginal incision often presents as "extraurethral" urinary leakage in the form of a genitourinary fistula [22].

SLING SURGERY

Midurethral synthetic sling surgery is currently recognized as the gold standard surgery for the treatment of female stress urinary incontinence [23]. The most common complication related to operative technique is bladder perforation during needle passage through the endopelvic fascia (from below) or through the retropubic space (from above). Reported rates of bladder perforation during midurethral sling placement range from 4% to 9% [24]. If recognized intraoperatively, bladder perforation is usually inconsequential as long as the trocar is removed and replaced outside the bladder. Urethral injury is much less common than is bladder puncture, with a recent case series documenting less than 1.0% risk [25]. Transobturator slings have been reported to have lower rates of bladder (0%–1%) and urethral injury (0.1%) [26–28] than do retropubic slings. Bladder injuries occur more often in women undergoing concomitant vaginal surgery [29].

Injury of the urethra or bladder during the vaginal dissection is best avoided by placing a urethral catheter (which drains the bladder and also allows for easy palpation of the urethra and bladder neck) by infiltrating the anterior vaginal wall with lidocaine or saline with 1:100,000 epinephrine solution (which elevated the vaginal wall from the underlying periurethral and perivesical fasciae) and by using sharp dissection rather than electrocautery or blunt dissection. The surgeon should strive to always stay superficial to the perivesical and periurethral fasciae in order to avoid injury to the urethra and bladder. Bladder perforation during needle passage is best avoided by emptying the bladder and providing finger guidance during needle passage through the retropubic space (which is not routinely done with percutaneous vaginal tape procedures for stress urinary incontinence). Following needle passage, the surgeon must always perform cystourethroscopy. If bladder perforation is appreciated, the needles should be withdrawn and then repassed more laterally. Care must be taken not to pass the needles too far laterally, which can risk injury to the external iliac vein. Following accidental bladder puncture with a small midurethral sling trocar, prolonged catheter drainage is not necessary.

If the bladder is injured during the dissection between the vaginal epithelium and pubocervical fascia, it should be immediately repaired. Transvaginal repair should be attempted if possible, closing the bladder in two layers using self-absorbing suture. If exposure is suboptimal, it may be necessary to approach the bladder transabdominally, and it may even be necessary to approach the posterior bladder wall through an intentional anterior cystotomy. Following repair of the incidental and the intentional cystotomies, catheter drainage is recommended for 1–2 weeks. Cystography is the most definitive method to determine adequate healing prior to catheter removal.

Bleeding may occur during the vaginal dissection, during perforation of the retropubic space, or during needle passage. Blood loss exceeding 500 cc or the need for blood transfusion has been reported to range from 1.4% to 2.5% [30,31]. Bleeding upon entry into the retropubic space can be difficult to manage, as it can be quite difficult to expose and ligate the perivesical venous plexus. An attempt at suture ligation is indicated, followed by packing with a laparotomy pad, or transvaginal insertion of a sponge-wrapped catheter with a 30 cc balloon into the retropubic space [32]. If bleeding is adequately controlled, then the surgery should be completed by releasing the sling from its plastic sheaths and positioned under the midurethra in a tension-free manner. The vaginal epithelium should be closed in watertight fashion and the vagina packed with gauze. Ultimately, persistent heavy bleeding may require abdominal incision and an open retropubic exploration and suture ligation. Major bleeding during needle passage may signify external iliac or femoral vessel injury, which is usually caused by exaggerated flexion of the thigh and excessively lateral passage of the needle. Symptomatic retropubic hematoma and vaginal or labial hematoma occurs with a frequency of 1%–5% [33]. Management is typically conservative, with ice packs, rest, and observation.

PROLAPSE SURGERY

During surgery for pelvic organ prolapse, the bladder can be difficult to differentiate among other prolapsed organs (such as uterine prolapse, enterocele, or even high rectocele) due to distorted anatomy. Cystotomy can be avoided by infiltrating the anterior vaginal wall with 1:100,000 epinephrine solution, using sharp dissection superficial to the pubocervical fascia, and keeping the bladder empty. Bleeding during vaginal dissection should be managed with temporary packing or with suture ligation rather than electrocautery in order to minimize the risk of vesicovaginal fistula formation. An additional way to aid in distinguishing the bladder from an enterocele or high rectocele in the setting of high-grade multicompartment pelvic organ prolapse is the “cystoscopic light test” that illuminates the urinary bladder, differentiating a large cystocele from a high rectocele or enterocele [34] (see Figure 117.2).

The bladder can be injured at the dome or above or below the trigone. If cystotomy is suspected, the bladder should be filled with blue-colored fluid to visualize any extravasation or leakage. Specific surgical management depends on the size of the injury. An injury that is less than 2 mm typically can be followed by Foley catheter drainage for 1 week and expectant management. Injuries that are greater than 2 mm but less than 1 cm either can be managed expectantly with a Foley catheter for 7 days or can be repaired. Bladder lacerations or defects greater than 1 cm should be surgically repaired in two layers—a mucosal and separate detrusor layer, performed in a watertight fashion using a self-absorbing suture. Repair should be attempted only after adequate tissue mobilization and debridement has been accomplished [35] in order to allow a watertight and tension-free repair. If more than one bladder wall injury is found, it is often easier to connect the lacerations into one large defect. It is vital to document the integrity of both ureters after cystotomy repair via direct or cystoscopic visualization of urinary efflux, as the risk of concomitant ureteral injury is as high as 10% in cases of bladder injury [36]. Extension of the cystotomy anteriorly may be necessary in order to properly visualize the bladder trigone. This allows for visualization of urinary efflux from the ureteral orifices. Intravenous indigo carmine or methylene blue should be given in order to properly visualize ureteral efflux. If efflux is not demonstrated, or if high suspicion remains, retrograde ureteral stents should be passed over a floppy-tipped wire, ideally with fluoroscopic guidance. The patient should be transferred to a fluoroscopy-ready table prior to attempting passage of a guidewire, ureteral stent, or ureteroscope, thereby minimizing the risk of additional iatrogenic ureteral injury.

A repair should only be performed after all surgery is complete, since other injuries may occur in the setting of abnormal anatomy. The cystotomy should be closed in two layers with self-absorbing suture. When the repair is completed, the closure should be tested to see if it is watertight by instilling colored fluid into the bladder catheter.

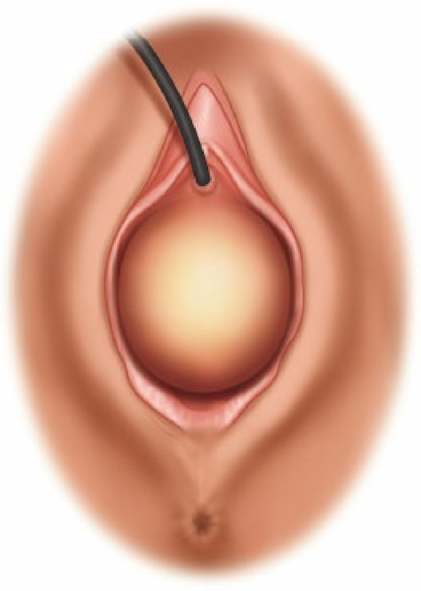

Figure 117.2 The “cystoscopic light test.”

With significant anterior wall prolapse, the trigone of the bladder can be displaced inferiorly and anteriorly, increasing the risk of ureteral occlusion during anterior wall repair. Ureteral injury can happen in prolapse repair such as cystocele repair, enterocele repair, and vaginal vault suspensions. In prolapse repairs, ureteral injury should always be recognized and remedied intraoperatively. Rates of ureteral injury have been reported to range from 1% to 11% during vaginal vault suspensions, with highest rates during uterosacral ligament suspensions [37]. Therefore, cystourethroscopy is absolutely indicated and visualization of urine efflux should be observed from both ureteral orifices. Difficulty visualizing efflux may be overcome by administration of intravenous indigo carmine and fluid challenge. If there is no efflux from the ureter, the surgeon should consider removing suspension sutures on that side as ureteral kinking is the most common cause of obstruction. Alternatively, the surgeon can attempt passage (and then removal) of a ureteral stent. Inability to pass a stent implies ureteral ligation and requires removal of the offending sutures, typically those sutures involving the cardinal ligament or posterior pubocervical fascia. Subsequent confirmation of urinary efflux should suffice, without the need for further evaluation or treatment. If a ureteral jet is not visualized, a surgeon with experience with urinary tract injury should be consulted intraoperatively. Retrograde pyelography and attempted retrograde placement of a ureteral stent are indicated. If there is doubt regarding the integrity of the ureter, an indwelling double-J ureteral stent should be left in place for 2 weeks.

If the closure is tenuous, interposition of adjacent vascularized tissue such as a labial fat pad (omental flap in abdominal surgery) between the cystotomy repair and the vagina is recommended to reduce the risk of fistulization [38]. The purpose of this flap often called a Martius flap is to introduce a new blood supply and separate the bladder and vaginal suture lines to obliterate dead space and protect from vesicovaginal fistula formation. The bladder can reepithelialize as early as 72 hours and regains its normal strength in approximately 21 days [39,40].

The bladder should be drained continuously for 2 weeks, with catheter removal following cystographic confirmation of complete healing. A proper cystogram should include retrograde filling of the bladder to at least 300 mL, as studies have shown false-negative results at lower volumes. While CT cystogram includes a multiplanar view, plain cystography must include a scout film prior to filling, an anterior/posterior film with a full bladder, and postdrainage view that can visualize any posteriorly directed extravasation that can be hidden by the full bladder.

HYSTERECTOMY

Injury to the bladder can occur at any time during vaginal or abdominal hysterectomy, but is particularly at risk while dissecting the bladder away from the lower uterus, cervix, and upper vagina during hysterectomy. This tissue plane can be straightforward to find in the absence of prior surgery, but becomes more challenging with a history of previous surgery such as cesarean section. Filling the bladder with normal saline can facilitate identification of the vesicouterine plane and help to minimize the risk of injury to the bladder wall during dissection. Sharp dissection is preferred, with avoidance of electrocautery near the bladder, thereby eliminating the risk of thermal injury.

If a bladder injury is suspected, an intraoperative test may be helpful, which includes instillation of saline or methylene blue, diluted in 200–300 cc on normal saline into the bladder. Extravasation of saline or urine into the abdomen confirms the presence of a cystotomy. Another useful sign is gas distention of the urinary drainage bag due to insufflation of CO_2 into the injured bladder during laparoscopy [21].

During benign gynecological surgery, the ureter can be injured along its path from the renal pelvis to the trigone of the bladder. A common site of ureteral injury during abdominal hysterectomy is at the pelvic brim where the ureter lies beneath the infundibulopelvic ligament [13]. Here, the surgeon should make a conscious decision to visualize the course of the ureter and ensure that it is not included in the infundibulopelvic pedicle. A second common site of injury (at risk during uterosacral ligament suspension) is the lateral pelvic side wall next to the uterosacral ligaments, often thickened in cases of endometriosis [41]. A third location (injury can occur during total hysterectomy) is at the level of the cervical internal os, where the uterine artery crosses the ureter over the iliac arteries, also known as the cardinal ligament [13,14]. Additionally, the ureter can be compromised (during excision of the cervix and vaginal cuff or even during closure of the vaginal cuff) where it passes anteriorly and lateral to the fornix of the vagina just as it enters the trigone of the bladder [13].

In order to best avoid ureteral injury during hysterectomy, the surgeon should identify the ureter at each step in the procedure. Common sites of injury that merit extra caution include ligation of ovarian vessels and uterine vessels and with closure of the vaginal cuff. Isolating the uterine vessels with meticulous dissection aids in excluding the ureter from the vascular clamp. When placing any clamp, the surgeons should only include vessels and must check that the ureter is excluded before applying the clamp. Once the uterine vessels are ligated, the ureter should then fall inferior and lateral to the pedicle. Subsequent bites should only be taken medial to this pedicle to avoid any ureteral injury. In addition, care should be taken to mobilize the bladder off the anterior cervix allowing the ureters to descend with the bladder.

If urinary tract injury is recognized intraoperatively, it should be immediately repaired in order to prevent infection, urinary leakage, or risk of fistula formation. If the surgeon is not comfortable repairing the injury, consultation with an experienced female pelvic medicine and reconstructive surgeon is recommended. All patients undergoing gynecological surgery should have sterile urine and should receive surgical site infection prophylaxis. Additional postoperative antibiotics are not indicated, even if an injury has occurred. There is a general lack of data to suggest any advantage to additional antibiotic coverage following repair of intraoperative lower urinary tract injury. During the postoperative period, fever, chemical peritonitis, abdominal or flank pain, leukocytosis, anuria, urinary leakage from wound, hydronephrosis, or hematuria may signify bladder or ureteral injury.

URETERAL REPAIR

If ureteral ligation or injury is found, and retrograde stent placement is not successful, intraoperative repair will be necessary. With injuries to the distal ureter, ureteroneocystostomy is typically favored over end-to-end ureteroureterostomy repair. Ureteroneocystostomy bypasses the site of injury and allows for straightforward proximal dissection and excision of any devascularized segment, eliminating any need for difficult dissection of the distal ureter [42]. Success rates are close to 100% with ureteral reimplantation [43–45], and the risk of ureteral obstruction is minimized by avoiding an antirefluxing anastomosis. On the other hand, ureteroureterostomy has an unacceptably high rate of stricture, due to embarrassment of the distal ureteral blood supply that typically occurs with the injury.

The location of the injury and the degree of ureteral and bladder mobility will dictate the method of implantation. While a distal ureteral injury is amenable to simple ureteral reimplantation, in the setting of a more proximal injury, a ureteroneocystostomy may be aided by a psoas bladder hitch to minimize anastomotic tension [44]. A Boari flap replacement of the distal ureter is indicated when the obstructive segment lies even more proximally [45,46]. With high or long ureteral strictures, a more complex reconstruction such as transureteroureterostomy, renal descensus, renal autotransplantation, or ileoureterocystoplasty may be necessary. Nephrectomy should be undertaken as a last resort and only in the setting of a normal contralateral renal unit [45,46]. In the rare instance of a midureteral or proximal ureteral transection, ureteroureterostomy would be preferred, but only if the anastomosis can be widely spatulated and tension-free.

Indwelling double pigtail stents are placed and usually left in place for a minimum of 6 weeks. Closed suction drains should be left in place after repairs and monitored for urine leakage. Suprapubic catheter placement is not necessary, in most cases. Foley catheter placement is indicated for 1–2 weeks if a cystotomy is necessary. Postoperative antibiotics are typically not indicated if the preoperative urinalysis was negative. Anticholinergic medication may help to reduce complaints of painful bladder spasm.

REPAIR OF URETEROVAGINAL FISTULA

The most common cause of uterovaginal fistula is total abdominal hysterectomy for either benign or malignant disease [47]. Fistulization occurs when a ureteral leak persists and the urinoma establishes a communication with the vaginal cuff. Any unexplained abdominal or flank pain or findings of costovertebral angle tenderness should alert the surgeon to the possibility of a ureteral injury. However, if there is no significant ureteral obstruction, and just extravasation, there may be no symptoms before urinary incontinence occurs. The typical presentation is one of sudden onset leakage from the vagina 1 to 4 weeks postoperatively. The patient additionally voids per urethra since there is otherwise normal filling of the bladder from the intact contralateral ureter.

In a female with vaginal leakage after pelvic surgery, a double dye test may differentiate between vesicovaginal and ureterovaginal fistulae [48]. The vagina is packed and methylene blue is given intravenously, while red carmine is instilled intravesically. The vaginal pack will stain red if a vesicovaginal fistula is present and blue if a ureterovaginal fistula is present. Alternatively, oral pyridium can be given several hours prior to bladder instillation with methylene blue, with orange staining or blue staining confirming a ureterovaginal or vesicovaginal fistula, respectively. An IVU may demonstrate varying degrees of hydronephrosis, or even a silent kidney [49]. If IVU or CT urogram is nondiagnostic, a retrograde ureterogram should demonstrate the location and magnitude of the fistula as well as any ureteral obstruction.

Management should urgently treat any ureteral obstruction with an internal ureteral stent if possible, or a percutaneous nephrostomy, with definitive repair via open or laparoscopic surgical repair, or even nephrectomy. Controversy exists regarding timing of repair, with some surgeons performing immediate, while others advocate early upper tract drainage followed be delayed ureteral repair [50–55]. While the surgery may be somewhat less cumbersome by waiting several months for inflammation to subside, the results for early versus delayed repair are comparable [56].

Retrograde ureteropyelography is recommended and may be diagnostic and therapeutic if a stent can be passed. If a ureteral catheter cannot be passed, the diagnosis of a distal obstruction remains and spontaneous healing is unlikely. Should a stent be placed to bypass the fistula, spontaneous healing is likely, but may still require further intervention [57,58].

If retrograde ureteral stenting is unsuccessful, antegrade percutaneous nephrostomy is recommended. With decompression of the kidney, the obstruction is relieved, and access for antegrade ureteral stenting is achieved. If spontaneous healing does not occur, an attempt at anterograde stenting is recommended. Once a stent is placed, there is a 50%–70% chance that the ureterovaginal fistula will heal without the need for open surgical intervention [57,58]. Because of the chance of ureteral structuring, close follow-up is needed.

If neither anterograde nor retrograde ureteral access is successful, open surgical repair is indicated.

Early surgical repair may be undertaken if there is no significant urosepsis and if renal function is relatively preserved. See Chapter 10.3 for description of ureteral reimplantation techniques.

CONCLUSIONS

Lower urinary tract injury during gynecological surgery is a well-known complication but, with careful preparation and attention to proper surgical technique, can be prevented in the vast majority of cases. Meticulous surgical technique and familiarity with pelvic anatomy are essential for every gynecological surgery. Intraoperative discovery of bladder or ureteral injury can be accomplished with careful inspection, cystoscopy, or from concern due to proximity of suture, ligation, or thermal use. Repair should always be attempted at time of recognition to decrease any future morbidity, complications, and urogenital fistula. If an injury is found, a urologist or urogynecologist with experience in FPMRS procedures should be consulted for repair. Patients who present postoperatively with fever, abdominal or flank pain, vomiting, ileus, low urine output or leakage of urine from the vagina, or incision raise concern for lower urinary tract injury. Repair of ureteral injuries should start with an attempt at retrograde or antegrade stenting, and if that fails, advanced surgical repair or reconstruction may be necessary.

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Appendix A

Standardization of Terminology

Dirk De Ridder and Marcus J. Drake

INTRODUCTION

We could not imagine a scientific world without standards and definitions. Clearly, this applies in the clinical sciences, where widely accepted definitions of signs, conditions, and diagnosis are essential. Worldwide agreement on standards is needed to allow exchange of data, ideas, and patient information. Although we might think that definitions cannot be changed anymore once they have been defined, we must realize that making or updating of definitions and standards at regular intervals is necessary to refine our understanding of the underlying concepts. With scientific progress, our understanding improves steadily and our definitions can be refined. Even seemingly "unvariable" standard units are subject to change, as is illustrated by this story by J.R. Chong on the definition of the kilogram [1]:

> 40 feet underground, in a secured and temperature and humidity controlled vault lies kilogram number 20. It consists of a platinum and iridium cylinder that is the perfect embodiment of the kilogram. The enlightenment and French revolution in the late 18th century spurred to the idea of standardization. People could only be free if they could calculate for themselves the weight and cost of things they bought. The French government created the kilogram in 1795 defining it as the mass of a liter of distilled water at a temperature of melting ice. A century later the treaty of the meter established the kilogram as an international standard. The foundation of the standard was a cylinder of 90% platinum and 10% iridium created in 1878 that became known as Le Grand K. Forty copies are made and distributed to governments around the world. Another 50 were made later. About every 50 years, the national prototypes are returned to the headquarters of the international bureau of weights and measures in France to be compared with the international prototype. During the first major comparison about 1950, scientists noticed discrepancies between the average mass of Le Grand K and its copies. At the last major kilogram comparison about 1990, some of the copies had gained as much as 132 mcg. A few had lost up to 665 mcg. There was no way to tell what was changing Le Grand K or its copies. This variability has impact on the world of precision physics which uses the kilogram as the basis for their standard measurements, from the force of gravity to the Ampere or Planck's constant, the omnipresent figure of quantum mechanics.
>
> In essence no one really knows today what the kilogram is. The kilogram has kicked off an international race to redefine the measure. Instead of using an object, scientists are searching for some property of nature or scientific constant, such as the vibrations of the cesium atom to define the second. The kilogram is the last of seven base units in international system of units that are still based on a physical object; a remnant of the era before relativity and quantum mechanics transformed the understanding of the universe. In fact at least 6 kg copies have been lost or damaged over the years. Two ideas have emerged as the leading contenders to redefine the kilogram. One involves counting the trillion trillion atoms in the most perfect silicon sphere ever made. The other idea was to measure the electrical current necessary to balance a 1 kg weight against earth's gravity. But serious complications have occurred in both approaches.

This story illustrates the relativity of so-called fixed standards and definitions. They should rather be seen as concepts under continuous evaluation and refinement.

Applying this to the terminology of the lower urinary tract, it becomes obvious that clinical definitions will potentially require modification as well. When the International Continence Society (ICS) produced the 2002 report on definitions of lower urinary tract function, some criticisms were expressed, despite the fact that these definitions were a product of an intensive consensus process [2]. Over subsequent years, it was increasingly clear that the 2002 definition of overactive bladder (OAB) has advanced our understanding and clinical effectiveness considerably. Nonetheless, a point will come where this terminology will benefit from review on the basis of increasing evidence from the literature

[3–5].

The selection of a good standard to compare new standards or definitions against is of utmost importance. While in the past, urodynamic findings were seen as the gold standard, recently, patient-centered or clinical observations have become the more evident yardstick [6]. This is illustrated by a study by Irwin et al., where the current ICS definitions of the lower urinary tract symptoms (LUTS) and currently used alternative definitions of these LUTS were compared [7]. This study noted that the ICS definitions for increased daytime frequency (the subject's perception of urinating too often by day) and for nocturia adequately described bladder symptoms within the OAB population when assessed by the level of symptom bother. In this population, the predominant manifestation of OAB was a combination of urgency with one or more other OAB symptoms. The nocturia definition adequately described the bladder symptoms in the OAB population. However, bother increased dramatically when nocturia was defined as two or more episodes per night. Also, voiding and postmicturition LUTS are common in those with the OAB, which contrasts with the prevailing perception that individuals with OAB symptoms predominantly experience storage LUTS. This study suggests that conclusions drawn from the ICS definitions from 2002 and assumptions based on these definitions might not be entirely true in a real-life world. Care must be taken with the interpretation of definitions.

In addition, the evidence base can provide important developments that can affect the appropriateness of established definitions. For example, the definition of nocturnal polyuria may better be based on nocturnal urine production or nocturnal voided volumes rather than on a diurnal urine production pattern [8].

In a study by Brubaker et al. including 655 participants, the proportion of women with mixed urinary incontinence (MUI) varied from 8.3% to 93.3%, depending on the MUI definition [9].

The current definitions may not adequately categorize clinically relevant urinary incontinence subgroups. For research reporting, MUI subcomponents of stress and urge urinary incontinence should be described separately rather than as a single dimension.

Another example is the ICS definition on painful bladder. Depending on the comparator standard, the outcome may vary considerably. Warren et al. showed that the ICS definition categorized 66% of 138 patients whom study investigators and caregivers had diagnosed as having interstitial cystitis/painful bladder syndrome (IC/PBS) [10]. Furthermore, those who met the ICS definition did not differ in important ways from those who did not. These findings were taken to suggest that the ICS definition may not be sufficiently sensitive. The definition of PBS/IC or bladder pain syndrome (PBS) is now subject to vigorous debate [11]. The ICS will issue a new standardization on terminology for chronic pelvic pain in 2015.

Thus, defining and standardizing are very important to allow exchange of clinical and scientific data. Given their central importance, the development of such standards needs to follow rigorous standards of evidence-based medicine and governance.

THE MAKING OF DEFINITIONS AND STANDARDS

Several processes exist to create standards or definitions, ranging from a simple expert consensus meeting to a structured Delphi process. When an international standard is produced, the process by which this was done should be transparent and explicitly mentioned in the publication.

The international standardization office is a well-known international organization that creates standards for many industrial applications. Recently, their methodology has also been implemented in hospital logistic processes and even in clinical settings. Their guidelines for creating a new standard include some key steps:

1. *Proposal stage*: The first step in the development of a new standard is to confirm the clinical need. This could be done by a working or interest group that submits a proposal to a relevant committee. If the committee accepts this proposal and if a sufficient number of people declare their commitment to participate, the next steps can follow.
2. *Preparatory stage*: A working group of experts is set up under the leadership of a chairperson. This group will prepare a working draft. Successive iterations of the draft may be considered until the working group is satisfied that it has developed the best technical solution for the problem being addressed.
3. *Committee stage*: As soon as a first draft is available, it will be registered by the central office. It

is then forwarded to independent external and internal experts. Successive working drafts may be considered until consensus is reached on the technical content. Once consensus has been attained, the text is presented as a draft standard.

4. *Enquiry stage*: The draft standard document is circulated to all members for commenting within a defined time period. Criteria for acceptation can be set, e.g., a proportion of votes needed. If the approval criteria are not met, the text is returned to the committee for further study and revision. The revised version can then again be circulated until consensus is reached.
5. *Approval stage*: The final draft is circulated to all members for a final yes or no vote. Criteria for acceptance or rejection can be defined. If technical comments are received during this period, they are no longer considered at this stage, but registered for consideration during a future revision of the standard text.
6. *Publication stage*: Once the final draft has been approved, only minor editorial changes, if and where necessary, are introduced into the final text. The final text is sent to the international peer-reviewed journal of choice and can then be referred to as the new standard.
7. *Review of international standards*: Standardization documents need to be reviewed over time to ensure they remain contemporaneous and consistent with the evidence base.

This cycle of standardization is widely accepted within industry and quality control organizations, but has only recently been adopted into clinical medicine. It has now been adapted for use as the basis of ICS standardizations [12].

WHAT IS CONSENSUS?

Currently, most clinical standards are based on consensus processes, usually governed by experts in the field of interest. The selection of the experts is not always transparent, and the way meetings are held is likewise usually not transparent and not really described in resulting publications. Several types of bias might affect the outcome of this type of approach.

There are several types of consensus methods that can be used to explicate the judgmental approach that is often needed in clinical and diagnostic situations where no definitive standard exists [13]:

1. *Interactive or consensus groups*: These techniques are the most informal. They are unstructured, with little direction coming from a group leader. As such, this technique is highly dependent on the motivation and personalities of the involved participants. Participants generate their own discussions around the issues of interest and proceed as they see fit. This process is particularly at risk of being dominated or steered by one or two opinion leaders or strong personalities within the group. Group dynamics are sometimes difficult to control and they may influence the outcome of the discussion.
2. *Nominal group techniques*: Participants in the group privately generate a list of their own ideas about the topic or questions of interest. In the next phase, participants share their ideas with the rest of the group, with ideas being recorded for the whole group to refer back to at a later point. After everyone's ideas are presented, a focused discussion is led by the facilitator to clarify issues and ideas. The final phase is for participants to rank or rate each item that was generated. This step is again done individually, without further group discussion. This method allows for each individual to have the same degree of input into the outcome, while still allowing for a face-to-face discussion.
3. *Delphi technique*: The Delphi technique was originally developed in the 1950s by the RAND Corporation as a research technique to gather expert opinion in a systematic way. This process has the following four attributes: (i) anonymity, (ii) iteration with control feedback, (iii) statistical group response, and (iv) expert input. Using this process, experts are polled individually and anonymously by a self-administered questionnaire completed by mail or e-mail. The Delphi technique progresses iteratively, with repeated questionnaire administration after feedback from the preceding round. After each round, information and responses from the questionnaire are tabulated at the coordinating center and anonymously provided as feedback to the entire group as part of the subsequent round's questionnaire. The Delphi is complete after there has been a convergence of opinion to a predefined level of agreement or after a certain number of iterations have been completed (usually 3 or 4). Cronbach's α can be used to assess

the variability among the responders.
4. *NIH process*: In this method, the members of the consensus panel act as a jury and debate on facts presented to them by a group of content experts.

After the formal presentation phase is over, members of the jury meet to discuss a topic of interest and draft a consensus document, often addressing a number of predefined questions put to them by the scientific organizing committee of the conference.

After this document is drafted, the findings of the jury are presented, and often further discussion with experts occurs, either in person or by e-mail after the symposium. The final phase of this process is a publication of the final consensus statement.

This process attempts to avoid the biases inherent to experts in the many fields where controversies exist. The disadvantage of this process, however, also lies in the lack of content expertise among the panel. Because of this, the validity of the recommendations may suffer and the acceptance by opinion leaders in the scientific committee community may be diminished.

There have been no studies comparing the results of using different consensus methods to address a particular question. In fact, it is probably not the choice of an individual technique but the way in which any of these techniques is applied that matters most. Key principles are as follows:

1. An explicit and transparent method for recruiting expert participants with disclosure of conflicts of interest
2. A comprehensive data-driven approach to inform item generation and production
3. Limiting the opportunity for strong personalities with firmly held convictions to have undue influence
4. The use of thresholds for the agreement or consensus
5. A process for facilitating ongoing iterative improvements in the consensus results

CONFOUNDING FACTORS

Many collective decision-making processes must balance individual preferences and incentives with the need for collective unity. Psychological research has established certain patterns of behavior in this context [14]. Behavior such as stubbornness, the presence of outlying individuals, or the awareness of opposing incentives apparently improved the collective performance of the entire group. The preferences of minorities seemed to win consistently in these experiments. The results of this kind of experiment may help us to avoid or control biases induced by group dynamics. Approaches to managing group dynamics derived from these experiments are potentially very beneficial.

UPDATING STANDARDS

Progressive advances in knowledge and clinical practice and the necessary adaptations of health economies to cope with new developments mean that standards have to respond to remain relevant. In the field of gynecology, the revision of the standardization of terminology of lower urinary tract function [15] is just such a development.

A modular approach is a realistic way forward, where the “core terminology” is the backbone for several related modules (Figure A.1). This core terminology should define the key concepts, while the modules should define or standardize specific applications of the core terminology. Applied to the lower urinary tract, the core terminology could exist of definitions of incontinence and symptoms, pelvic organ anatomy, etc., while modules could apply this to patient groups (neurological disease, children, the elderly) or could apply this to technical examinations (e.g., urodynamics, imaging techniques) and the relevant basic science models. This approach allows for a dynamic set of standards and is central to the ICS approach (http://www.ics.org/Documents/Documents.aspx?FolderID=189).

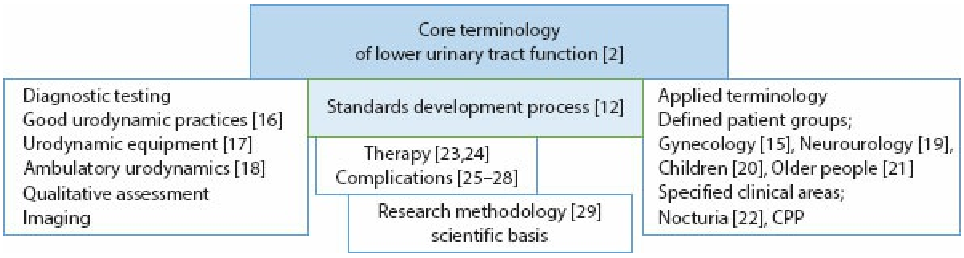
Core terminology
of lower urinary tract function [2]
Diagnostic testing
Good urodynamic practices [16]
Urodynamic equipment [17]
Ambulatory urodynamics [18]
Qualitative assessment
Imaging
Standards development process [12]
Therapy [23,24]
Complications [25–28]
Research methodology [29]
scientific basis
Applied terminology
Defined patient groups;
Gynecology [15], Neurourology [19],
Children [20], Older people [21]
Specified clinical areas;
Nocturia [22], CPP

Figure A.1 A modular approach to terminology in the clinical and scientific field of urinary tract function and dysfunction espoused by the International Continence Society. CPP, chronic pelvic pain.

CONCLUSION

At this point in time, standardization and terminology definitions in clinical medicine are often designed by some form of consensus process. Scientific societies should invest in further professionalization of these processes within their society. In other words, “standardization should be standardized.”

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Appendix B

The Standardization of Terminology of Lower Urinary Tract Function: Report from the Standardization Subcommittee of the International Continence Society*

Paul Abrams, Linda Cardozo, Magnus Fall, Derek Griffiths, Peter F.W.M. Rosier, Ulf Ulmsten, Philip van Kerrebroeck, Arne Victor, and Alan J. Wein

INTRODUCTION

This report presents definitions of the symptoms, signs, urodynamic observations, and conditions associated with lower urinary tract dysfunction (LUTD) and urodynamic studies (UDS) for use in all patient groups from children to the elderly.

The definitions restate or update those presented in previous International Continence Society (ICS) Standardisation of Terminology reports [1–18] and those recently published on urethral function [10] and nocturia [16]. The published ICS report on the technical aspects of urodynamic equipment [13] is complemented by the new ICS report on urodynamic practice [15]. In addition, there are four published ICS outcome reports [5,9,11,12].

New or changed definitions are all indicated; however, recommendations concerning technique are not included in the main text of this report.

The definitions have been written to be compatible with the WHO publication International Classification of Functioning, Disability and Health-2 (ICIDH-2) published in 2001, and the International Classification of Diseases-10 (ICD-10). As far as possible, the definitions are descriptive of observations, without implying underlying assumptions that may later prove to be incorrect or incomplete. By following this principle, the ICS aims to facilitate comparison of results and enable effective communication by investigators who use urodynamic methods. This report restates the ICS principle that symptoms, signs, and conditions are separate categories and adds a category of urodynamic observations. In addition, terminology related to therapies is included [3].

When a reference is made to the whole anatomic organ the vesica urinaria, the correct term is the bladder. When the smooth muscle structure known as the m. detrusor urinae is being discussed, then the correct term is detrusor.

It is suggested that acknowledgment of these standards in written publications be indicated by a footnote to the section “Methods and Materials” or its equivalent, to read as follows:

> Methods, definitions, and units conform to the standards recommended by the ICS, except where specifically noted.

The report covers the following areas.

LOWER URINARY TRACT SYMPTOMS

Symptoms are the subjective indicator of a disease or change in condition as perceived by the patient, carrier, or partner and may lead him or her to seek help from health-care professionals. (NEW)

Symptoms may either be volunteered or described during the patient interview. They are usually qualitative. In general, LUTS cannot be used to make a definitive diagnosis. LUTS can also indicate pathologies other than LUTD, such as urinary infection.

SIGNS SUGGESTIVE OF LUTD

Signs are observed by the physician, including simple means to verify symptoms and quantify them.

(NEW)

For example, a classic sign is the observation of leakage on coughing. Observations from frequency volume charts, pad tests, and validated symptom and quality of life questionnaires are examples of other instruments that can be used to verify and quantify symptoms.

URODYNAMIC OBSERVATIONS

Urodynamic observations are observations made during UDS. (NEW)

For example, an involuntary detrusor contraction (detrusor overactivity) is a urodynamic observation. In general, a urodynamic observation may have a number of possible underlying causes and does not represent a definitive diagnosis of a disease or condition and may occur with a variety of symptoms and signs or in the absence of any symptoms or signs.

CONDITIONS

Conditions are defined by the presence of urodynamic observations associated with characteristic symptoms or signs and/or nonurodynamic evidence of relevant pathological processes. (NEW)

TREATMENT

Treatment for LUTD: These definitions are from the 7th ICS report on lower urinary tract rehabilitation techniques [3].

LOWER URINARY TRACT SYMPTOMS

LUTSs are defined from the individual's perspective, who is usually, but not necessarily, a patient within the healthcare system. Symptoms are either volunteered by, or elicited from, the individual or may be described by the individual's caregiver.

LUTSs are divided into three groups: storage, voiding, and postmicturition symptoms.

Storage Symptoms

Storage symptoms are experienced during the storage phase of the bladder and include daytime frequency and nocturia: (NEW)

- *Increased daytime frequency* is the complaint by the patient who considers that he or she voids too often by day. (NEW) This term is equivalent to pollakisuria used in many countries.
- *Nocturia* is the complaint that the individual has to wake at night one or more times to void. (NEW)[*]
- *Urgency* is the complaint of a sudden compelling desire to pass urine, which is difficult to defer. (CHANGED)
- *Urinary incontinence* is the complaint of any involuntary leakage of urine. (NEW)[†]

In each specific circumstance, urinary incontinence should be further described by specifying relevant factors such as type, frequency, severity, precipitating factors, social impact, effect on hygiene and quality of life, the measures used to contain the leakage, and whether or not the individual seeks or desires help because of urinary incontinence.[‡]

Urinary leakage may need to be distinguished from sweating or vaginal discharge:

- *Stress urinary incontinence* is the complaint of involuntary leakage on effort or exertion or on sneezing or coughing. (CHANGED)[§]
- *Urge urinary incontinence* is the complaint of involuntary leakage accompanied by or immediately preceded by urgency. (CHANGED)[¶]
- *Mixed urinary incontinence* is the complaint of involuntary leakage associated with urgency and also with exertion, effort, sneezing, or coughing. (NEW)
- *Enuresis* means any involuntary loss of urine. (ORIGINAL) If it is used to denote incontinence during sleep, it should always be qualified with the adjective "nocturnal."
- *Nocturnal enuresis* is the complaint of loss of urine occurring during sleep. (NEW)

- *Continuous urinary incontinence* is the complaint of continuous leakage. (NEW)
- *Other types of urinary incontinence* may be situational, for example, the report of incontinence during sexual intercourse, or giggle incontinence.
- *Bladder sensation* can be defined, during history taking, by five categories:
  - *Normal*: The individual is aware of bladder filling and increasing sensation up to a strong desire to void. (NEW)
  - *Increased*: The individual feels an early and persistent desire to void. (NEW) *Reduced: The individual is aware of bladder filling but does not feel a definite desire to void. (NEW)*
  - *Absent*: The individual reports no sensation of bladder filling or desire to void. (NEW)
  - *Nonspecific*: The individual reports no specific bladder sensation, but may perceive bladder filling as abdominal fullness, vegetative symptoms, or spasticity. (NEW)[**]

Voiding Symptoms

Voiding symptoms are experienced during the voiding phase: (NEW)

- *Slow stream* is reported by the individual as his or her perception of reduced urine flow, usually compared to previous performance or in comparison to others. (NEW)
- *Splitting or spraying* of the urine stream may be reported. (NEW)
- *Intermittent stream (intermittency)* is the term used when the individual describes urine flow that stops and starts, on one or more occasions, during micturition. (NEW)
- *Hesitancy* is the term used when an individual describes difficulty in initiating micturition resulting in a delay in the onset of voiding after the individual is ready to pass urine. (NEW)
- *Straining* to void describes the muscular effort used to initiate, maintain, or improve the urinary stream. (NEW)[*]
- *Terminal dribble* is the term used when an individual describes a prolonged final part of micturition, when the flow has slowed to a trickle/dribble. (NEW)

Postmicturition Symptoms

Postmicturition symptoms are experienced immediately after micturition: (NEW)

- *Feeling of incomplete emptying* is a self-explanatory term for a feeling experienced by the individual after passing urine. (NEW)
- *Postmicturition dribble* is the term used when an individual describes the involuntary loss of urine immediately after he or she has finished passing urine, usually after leaving the toilet in men or after rising from the toilet in women. (NEW)

Symptoms associated with Sexual Intercourse

Dyspareunia, vaginal dryness, and incontinence are among the symptoms women may describe during or after intercourse. These symptoms should be described as fully as possible. It is helpful to define urine leakage as during penetration, during intercourse, or at orgasm.

Symptoms Associated with Pelvic Organ Prolapse

The feeling of a lump (“something coming down”), low backache, heaviness, dragging sensation, and the need to digitally replace the prolapse in order to defecate or micturate are among the symptoms that women with a prolapse may describe.

Genital and Lower Urinary Tract Pain[†]

Pain, discomfort, and pressure are part of a spectrum of abnormal sensations felt by the individual. Pain produces the greatest impact on the patient and may be related to bladder filling or voiding, may be felt after micturition, or may be continuous. Pain should also be characterized by type, frequency, duration, precipitating and relieving factors, and location as defined in the following:

- *Bladder pain* is felt suprapubically or retropubically, usually increases with bladder filling, and

may persist after voiding. (NEW)
- *Urethral pain* is felt in the urethra and the individual indicates the urethra as the site. (NEW)
- *Vulval pain* is felt in and around the external genitalia. (NEW)
- *Vaginal pain* is felt internally above the introitus. (NEW)
- *Scrotal pain* may or may not be localized, for example, to the testis, epididymis, cord structures, or scrotal skin. (NEW)
- *Perineal pain* is felt, in the female, between the posterior fourchette (posterior lip of the introitus) and the anus and, in the male, between the scrotum and the anus. (NEW)
- *Pelvic pain* is less well defined than, for example, bladder, urethral, or perineal pain, is less clearly related to the micturition cycle or to bowel function, and is not localized to any single pelvic organ. (NEW)

Genitourinary Pain Syndromes and Symptom Syndromes Suggestive of LUTD

Syndromes describe constellations, or varying combinations of symptoms, but cannot be used for precise diagnosis. The use of the word syndrome can only be justified if there is at least one other symptom in addition to the symptom used to describe the syndrome. In scientific communications, the incidence of individual symptoms within the syndrome should be stated, in addition to the number or individuals with the syndrome.

The syndromes described are functional abnormalities for which a precise cause has not been defined. It is presumed that routine assessment (history taking, physical examination, and other appropriate investigations) has excluded obvious local pathologies, such as those that are infective, neoplastic, metabolic, or hormonal in nature.

Genitourinary Pain Syndromes

These syndromes are all chronic in their nature. Pain is the major complaint but concomitant complaints are of lower urinary tract, bowel, sexual, or gynecologic nature:

- *Painful bladder syndrome* is the complaint of suprapubic pain related to bladder filling, accompanied by other symptoms such as increased daytime and nighttime frequency, in the absence of proven urinary infection or other obvious pathologies. (NEW)[‡]
- *Urethral pain syndrome* is the occurrence of recurrent episodic urethral pain, usually on voiding, with daytime frequency and nocturia, in the absence of proven infection or other obvious pathologies. (NEW)
- *Vulval pain syndrome* is the occurrence of persistent or recurrent episodic vaginal pain, which is either related to the micturition cycle or associated with symptoms suggestive of urinary tract or sexual dysfunction. There is no proven infection or other obvious pathologies. (NEW)[*]
- *Vaginal pain syndrome* is the occurrence of persistent or recurrent episodic vaginal pain that is associated with symptoms suggestive of urinary tract or sexual dysfunction. There is no proven vaginal infection or other obvious pathologies.
- *Scrotal pain syndrome* is the occurrence of persistent or recurrent episodic scrotal pain that is associated with symptoms suggestive of urinary tract or sexual dysfunction. There is no proven epididymo-orchitis or other obvious pathologies.
- *Perineal pain syndrome* is the occurrence of persistent or recurrent episodic perineal pain, which is either related to the micturition cycle or associated with symptoms suggestive of urinary tract or sexual dysfunction. There is no proven infection or other obvious pathologies. (NEW)[†]
- *Pelvic pain syndrome* is the occurrence of persistent or recurrent episodic pelvic pain associated with symptoms suggestive of lower urinary tract, sexual, bowel, or gynecological dysfunction. There is no proven infection or other obvious pathologies. (NEW)

Symptom Syndromes Suggestive of LUTD

In clinical practice, empirical diagnoses are often used as the basis for initial management after assessing the individual’s lower urinary tract symptoms, physical findings, and the results of urinalysis and other indicated investigations.

- *Urgency*, with or without urge incontinence, usually with frequency and nocturia, can be described as the *overactive bladder syndrome*, *urge syndrome*, or *urgency–frequency syndrome*. (NEW)

These symptom combinations are suggestive of urodynamically demonstrable detrusor overactivity, but can be due to other forms of urethrovesical dysfunction. These terms can be used if there is no proven infection or other obvious pathologies.

- *Lower urinary symptom suggestive of bladder outlet obstruction* is a term used when a man complains predominantly of voiding symptoms in the absence of infection or obvious pathology other than possible causes of outlet obstruction. (NEW)[‡]

SIGNS SUGGESTIVE OF LUTD

Measuring the Frequency, Severity, and Impact of LUTS

Asking the patient to record micturitions and symptoms[§] for a period of days provides invaluable information. The recording of micturition events can be in three main forms:

- *Micturition time chart*: This records only the times of micturitions, day and night, for at least 24 hours. (NEW)
- *Frequency volume chart*: This records the volumes voided as well as the time of each micturition, day and night, for at least 24 hours. (CHANGED)
- *Bladder diary*: This records the times of micturitions and voided volumes, incontinence episodes, pad usage, and other information such as fluid intake, the degree of urgency, and the degree of incontinence. (NEW)[¶]

The following measurements can be abstracted from frequency volume charts and bladder diaries:

- *Daytime frequency* is the number of voids recorded during waking hours and includes the last void before sleep and the first void after waking and rising in the morning. (NEW)
- *Nocturia* is the number of voids recorded during a night's sleep: Each void is preceded and followed by sleep. (NEW)
- *24-hour frequency* is the total number of daytime voids and episodes of nocturia during a specified 24-hour period. (NEW)
- *24-hour production* is measured by collecting all urine for 24 hours. (NEW)

This is usually commenced *after* the first void produced after rising in the morning and is completed by including the first void on rising the following morning.

- *Polyuria* is defined as the measured production of more than 2.8 L of urine in 24 hours in adults. It may be useful to look at output over shorter time frames [16]. (NEW) [**]
- *Nocturnal urine volume* is defined as the total volume of urine passed between the times the individual goes to bed with the intention of sleeping and the time of waking with the intention of rising. (NEW) Therefore, it excludes the last void before going to bed but includes the first void after rising in the morning.
- *Nocturnal polyuria* is present when an increased proportion of the 24-hour output occurs at night (normally during the 8 hours while the patient is in bed). (NEW) The nighttime urine output excludes the last void before sleep but includes the first void in the morning.[*]
- *Maximum voided volume* is the largest volume of urine voided during a single micturition and is determined either from the frequency/volume chart or bladder diary. (NEW)

The maximum, mean, and minimum voided volumes over the period of recording may be stated.[†]

Physical Examination

Physical examination is essential in the assessment of all patients with LUTD. It should include abdominal, pelvic, perineal, and a focused neurological examination. For patients with possible neurogenic LUTD, a more extensive neurologic examination is needed.

Abdominal

The bladder may be felt by abdominal palpation or by suprapubic percussion. Pressure suprapubically or during bimanual vaginal examination may induce a desire to pass urine.

Perineal/Genital Inspection

This allows the description of the skin (e.g., the presence of atrophy or excoriation), any abnormal anatomic features, and the observation of incontinence.

- *Urinary incontinence (the sign)* is defined as urine leakage seen during examination; this may be urethral or extraurethral.
- *Stress urinary incontinence* is the observation of involuntary leakage from the urethra, synchronous with exertion/effort, or sneezing or coughing. (CHANGED)‡

Stress leakage is presumed to be due to raised abdominal pressure.

- *Extraurethral incontinence* is defined as the observation of urine leakage through channels other than the urethra. (ORIGINAL)
- *Uncategorized incontinence* is the observation of involuntary leakage that cannot be classified into one of the above categories on the basis of signs and symptoms. (NEW)

Vaginal Examination

Vaginal examination allows the description of observed and palpable anatomic abnormalities and the assessment of pelvic floor muscle function, as described in the ICS report on pelvic organ prolapse. The definitions given are simplified versions of the definitions in that report [4]:

- *Pelvic organ prolapse* is defined as the descent of one or more of the anterior vaginal wall, the posterior vaginal wall, and the apex of the vagina (cervix/uterus) or vault (cuff) after hysterectomy. Absence of prolapse is defined as stage 0 support; prolapse can be staged from stage I to stage IV. (NEW)

Pelvic organ prolapse can occur in association with urinary incontinence and other LUTD and may on occasion mask incontinence.

- *Anterior vaginal wall prolapse* is defined as descent of the anterior vagina so that the urethrovesical junction (a point 3 cm proximal to the external urinary meatus) or any anterior point proximal to this is <3 cm above the plane of the hymen. (CHANGED)
- *Prolapse of the apical segment of the vagina* is defined as any descent of the vaginal cuff scar (after hysterectomy) or cervix below a point that is 2 cm less than the total vaginal length above the plane of the hymen. (CHANGED)
- *Posterior vaginal wall prolapse* is defined as any descent of the posterior vaginal wall so that a midline point on the posterior vaginal wall 3 cm above the level of the hymen, or any posterior point proximal to this, is <3 cm above the plane of the hymen. (CHANGED)

Pelvic Floor Muscle Function

This can be qualitatively defined by the tone at rest and the strength of a voluntary or reflex contraction as strong, weak, or absent or by a validated grading system (e.g., Oxford 1–5). A pelvic muscle contraction may be assessed by visual inspection, palpation, electromyography, or perineometry. Factors to be assessed include strength, duration, displacement, and repeatability.

Rectal Examination

Rectal examination allows the description of observed and palpable anatomic abnormalities and is the easiest method of assessing pelvic floor muscle function in children and men. In addition, rectal examination is essential in children with urinary incontinence to rule out fecal impaction.

- *Pelvic floor muscle function* can be qualitatively defined, during rectal examination, by the tone at rest and the strength of a voluntary contraction, as strong, weak, or absent. (NEW)

Pad Testing

Pad testing may be used to quantify the amount of urine lost during incontinence episodes, and methods range from a short provocative test to a 24-hour pad test.

URODYNAMIC OBSERVATIONS AND CONDITIONS

Urodynamic Techniques

There are two principal methods of urodynamic investigation:

1. *Conventional UDS* normally take place in the urodynamic laboratory and usually involve artificial bladder filling. (NEW)
   a. *Artificial bladder filling* is defined as filling the bladder, via a catheter, with a specified liquid at a specified rate. (NEW)
2. *Ambulatory UDS* are defined as a functional test of the lower urinary tract, utilizing natural filling and reproducing the subject's everyday activities.*
   a. *Natural filling* means that the bladder is filled by the production of urine rather than by an artificial medium.

Both filling cystometry and pressure flow studies (PFS) of voiding require the following measurements:

- *Intravesical pressure* is the pressure within the bladder. (ORIGINAL)
- *Abdominal pressure* is taken to be the pressure surrounding the bladder. In current practice, it is estimated from rectal, vaginal, or, less commonly, extraperitoneal pressure or a bowel stoma. The simultaneous measurement of abdominal pressure is essential for the interpretation of the intravesical pressure trace. (ORIGINAL)
- *Detrusor pressure* is that component of intravesical pressure that is created by forces in the bladder wall (passive and active). It is estimated by subtracting abdominal pressure from intravesical pressure. (ORIGINAL)

Filling Cystometry

The word "cystometry" is commonly used to describe the urodynamic investigation of the filling phase of the micturition cycle. To eliminate confusion, the following definitions are proposed:

- *Filling cystometry* is the method by which the pressure/volume relationship of the bladder is measured during bladder filling. (ORIGINAL)

The filling phase starts when filling commences and ends when the patient and urodynamicist decide that "permission to void" has been given.†

Bladder and urethral function, during filling, need to be defined separately.

The rate at which the bladder is filled is divided into the following:

- *Physiological filling rate* is defined as a filling rate less than the predicted maximum—predicted maximum body weight in kilogram divided by four, expressed as milliliter per minutes [17]. (CHANGED)
- *Nonphysiological filling rate* is defined as a filling rate greater than the predicted maximum—predicted maximum body weight in kilogram divided by four expressed as milliliter per minutes [8]. (CHANGED)

Bladder storage function should be described according to bladder sensation, detrusor activity, bladder compliance, and bladder capacity.[‡]

Bladder Sensation during Filling Cystometry

- *Normal bladder sensation* can be judged by three defined points noted during filling cystometry and evaluated in relation to the bladder volume at that moment and in relation to the patient's symptomatic complaints.
- *First sensation of bladder filling* is the feeling the patient has, during filling cystometry, when he or she first becomes aware of the bladder filling. (NEW)
- *First desire to void* is defined as the feeling, during filling cystometry, that would lead the patient to pass urine at the next convenient moment, but voiding can be delayed if necessary. (CHANGED)
- *Strong desire to void* is defined, during filling cystometry, as a persistent desire to void without the fear of leakage. (ORIGINAL)
- *Increased bladder sensation* is defined, during filling cystometry, as an early first sensation of bladder filling (or an early desire to void) and/or an early strong desire to void, which occurs at low bladder volume and which persists. (NEW)[*]
- *Reduced bladder sensation* is defined, during filling cystometry, as diminished sensation throughout bladder filling. (NEW)
- *Absent bladder sensation* means that, during filling cystometry, the individual has no bladder sensation. (NEW)
- *Nonspecific bladder sensations*, during filling cystometry, may make the individual aware of bladder filling, for example, abdominal fullness or vegetative symptoms. (NEW)
- *Bladder pain*, during filling cystometry, is a self-explanatory term and is an abnormal finding. (NEW)
- *Urgency*, during filling cystometry, is a sudden compelling desire to void. (NEW)[†]
- *The vesical/urethral sensory threshold* is defined as the least current that consistently produces a sensation, perceived by the subject during stimulation at the site under investigation [3]. (ORIGINAL)

Detrusor Function during Filling Cystometry

In everyday life, the individual attempts to inhibit detrusor activity until he or she is in a position to void. Therefore, when the aims of the filling study have been achieved, and when the patient has a desire to void, normally the "permission to void" is given (see "filling cystometry" earlier). That by the change in detrusor moment is indicated on the urodynamic trace and all detrusor activity before this "permission" is defined as "involuntary detrusor activity."

- *Normal detrusor function* allows bladder filling with little or no change in pressure. No involuntary phasic contractions occur despite provocation. (ORIGINAL)
- *Detrusor overactivity* is a urodynamic observation characterized by involuntary detrusor contractions during the filling phase, which may be spontaneous or provoked. (CHANGED)[‡]

There are certain patterns of detrusor overactivity:

- *Phasic detrusor overactivity* is defined by a characteristic waveform and may or may not lead to urinary incontinence. (NEW)[§]
- *Terminal detrusor overactivity* is defined as a single involuntary detrusor contraction occurring at cystometric capacity, which cannot be suppressed, and results in incontinence, usually resulting in bladder emptying (voiding). (NEW)[¶]
- *Detrusor overactivity incontinence* is incontinence due to an involuntary detrusor contraction. (NEW)

In a patient with normal sensation, urgency is likely to be experienced just before the leakage episode.[**]

Detrusor overactivity may also be qualified, when possible, according to cause, for example,

- *Neurogenic detrusor overactivity* when there is a relevant neurologic condition.

This term replaces the term “detrusor hyperreflexia.” (NEW)

- *Idiopathic detrusor overactivity* when there is no defined cause. (NEW)

This term replaces “detrusor instability.”[††]

In clinical and research practice, the extent of neurologic examination/investigation varies. It is likely that the proportion of neurogenic to idiopathic detrusor overactivity will increase if a more complete neurologic assessment is carried out.

Other patterns of detrusor overactivity are seen; for example, the combination of phasic and terminal detrusor overactivity and the sustained high-pressure detrusor contractions seen in spinal cord injury patients when attempted voiding occurs against a dyssynergic sphincter.

- *Provocative maneuvers* are defined as techniques used during urodynamics in an effort to provoke detrusor overactivity, for example, rapid filling, use of cooled or acid medium, postural changes, and hand washing. (NEW)

Bladder Compliance during Filling Cystometry

- *Bladder compliance* describes the relationship between change in bladder volume and change in detrusor pressure. (CHANGED)[*]

Compliance is calculated by dividing the volume change (DV) by the change in detrusor pressure (Dp_{det}) during that change in bladder volume ($C = V.Dp_{det}$). It is expressed in mL/cmH_2O.

A variety of means of calculating bladder compliance has been described. The ICS recommends that two standard points should be used for compliance calculations: the investigator may wish to define additional points. The standards points are as follows:

1. The detrusor pressure at the start of bladder filling and the corresponding bladder volume (usually zero).
2. The detrusor pressure (and corresponding bladder volume) at cystometric capacity or immediately before the start of any detrusor contraction that causes significant leakage (and therefore causes the bladder volume to decrease, affecting compliance calculation). Both points are measured excluding any detrusor contraction.

Bladder Capacity during Filling Cystometry

- *Cystometric capacity* is the bladder volume at the end of the filling cystometrogram, when “permission to void” is usually given. The end point should be specified, for example, if filling is stopped when the patient has a normal desire to void. The cystometric capacity is the volume voided together with any residual urine. (CHANGED)[†]
- *Maximum cystometric capacity*, in patients with normal sensation, is the volume at which the patient feels he or she can no longer delay micturition (has a strong desire to void). (ORIGINAL)
- *Maximum anesthetic bladder capacity* is the volume to which the bladder can be filled under deep general or spinal anesthetic and should be qualified according to the type of anesthesia used, the speed of filling, the length of time of filling, and the pressure at which the bladder is filled. (CHANGED)

Urethral Function during Filling Cystometry

The urethral closure mechanism during storage may be competent or incompetent:

- *Normal urethral closure mechanism* maintains a positive urethral closure pressure during

bladder filling even in the presence of increased abdominal pressure, although it may be overcome by detrusor overactivity. (CHANGED)
- *Incompetent urethral closure mechanism* is defined as one that allows **leakage of urine in the absence of a detrusor contraction**. (ORIGINAL)
- *Urethral relaxation incontinence* is defined as leakage due to urethral relaxation in the absence of raised abdominal pressure or detrusor overactivity. (NEW)[‡]
- *Urodynamic stress incontinence* is noted during filling cystometry and is defined as the involuntary leakage of urine during increased abdominal pressure, in the absence of a detrusor contraction. (CHANGED)

Urodynamic stress incontinence is now the preferred term to "genuine stress incontinence."[¶]

Assessment of Urethral Function during Filling Cystometry

- *Urethral pressure measurement*
    - *Urethral pressure* is defined as the fluid pressure needed to just open a closed urethra. (ORIGINAL) *The urethral pressure profile* is a graph indicating the intraluminal pressure along the length of the urethra. (ORIGINAL)
    - *The urethral closure pressure profile* is given by the subtraction of intravesical pressure from urethral pressure. (ORIGINAL)
    - *Maximum urethral pressure* is the maximum pressure of the measured profile. (ORIGINAL)
    - *Maximum urethral closure pressure* is the maximum difference between the urethral pressure and the intravesical pressure. (ORIGINAL)
    - *Functional profile length* is the length of the urethra along which the urethral pressure exceeds intravesical pressure in women.
    - *Pressure "transmission" ratio* is the increment in urethral pressure on stress as a percentage of the simultaneously recorded increment in intravesical pressure.

- *Abdominal leak point pressure* is the intravesical pressure at which urine leakage occurs due to increased abdominal pressure in the absence of a detrusor contraction. (NEW)[*]
- *Detrusor leak point pressure* is defined as the lowest detrusor pressure at which urine leakage occurs in the absence of either a detrusor contraction or increased abdominal pressure. (NEW)[†]

Pressure Flow Studies

Voiding is described in terms of detrusor and urethral function and assessed by measuring urine flow rate and voiding pressures.

- *PFS* of voiding are the methods by which the relationship between pressure in the bladder and urine flow rate is measured during bladder emptying. (ORIGINAL)

The voiding phase starts when "permission to void" is given or when uncontrollable voiding begins and ends when the patient considers voiding has finished.

Measurement of Urine Flow

Urine flow is defined either as *continuous*, that is, without interruption, or as *intermittent*, when an individual states that the flow stops and starts during a single visit to the bathroom in order to void. The continuous flow curve is defined as a *smooth*, arc-shaped curve, or *fluctuating* when there are multiple peaks during a period of continuous urine flow:[‡]

- *Flow rate* is defined as the volume of fluid expelled via the urethra per unit time. It is expressed in milliliter per second. (ORIGINAL)
- *Voided volume* is the total volume expelled via the urethra. (ORIGINAL)
- *Maximum flow rate* is the maximum measured value of the flow rate after correction for artifacts. (CHANGED)

- *Voiding time* is total duration of micturition, i.e., includes interruptions. When voiding is completed without interruption, voiding time is equal to flow time. (ORIGINAL)
- *Flow time* is the time over which measurable flow actually occurs. (ORIGINAL)
- *Average flow rate* is voided volume divided by flow time. The average flow should be interpreted with caution if flow is interrupted or there is a terminal dribble. (CHANGED)
- *Time to maximum flow* is the elapsed time from onset of flow to maximum flow. (ORIGINAL)

Pressure Measurements during PFS

The following measurements are applicable to each of the pressure curves: intravesical, abdominal, and detrusor pressure.

- *Premicturition pressure* is the pressure recorded immediately before the initial isovolumetric contraction. (ORIGINAL)
- *Opening pressure* is the pressure recorded at the onset of urine flow (consider time delay). (ORIGINAL)
- *Opening time* is the elapsed time from initial rise in detrusor pressure to onset of flow. (ORIGINAL)

This is the initial isovolumetric contraction period of micturition. Flow measurement delay should be taken into account when measuring opening time.

- *Maximum pressure* is the maximum value of the measured pressure. (ORIGINAL)
- *Pressure at maximum flow rate* is the lowest pressure recorded at maximum measured flow rate. (ORIGINAL)
- *Closing pressure* is the pressure measured at the end of measured flow. (ORIGINAL)
- *Minimum voiding pressure* is the minimum pressure during measurable flow. This is not necessarily equal to either the opening or closing pressures.
- *Flow delay* is the time delay between a change in bladder pressure and the corresponding change in measured flow rate.

Detrusor Function during Voiding

- *Normal detrusor function*

Normal voiding is achieved by a voluntarily initiated continuous detrusor contraction that leads to complete bladder emptying within a normal time span and in the absence of obstruction. For a given detrusor contraction, the magnitude of the recorded pressure rise will depend on the degree of outlet resistance. (ORIGINAL)

- *Abnormal detrusor activity* can be subdivided:
    - *Detrusor underactivity* is defined as a contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or a failure to achieve complete bladder emptying within a normal time span. (ORIGINAL)
    - *Acontractile detrusor* is one that cannot be demonstrated to contract during UDS. (ORIGINAL)[*]
    - *Postvoid residual* is defined as the volume of urine left in the bladder at the end of micturition. (ORIGINAL)[†]

Urethral Function during Voiding

Normal urethral function during voiding is defined as a urethra that opens and is continuously relaxed to allow the bladder to be emptied at a normal pressure. (CHANGED)

Abnormal urethral function may be due to either obstruction to urethral overactivity or a urethra that cannot open due to anatomic abnormality, such as an enlarged prostate or a urethral stricture.

- *Bladder outlet obstruction* is the generic term for obstruction during voiding and is characterized by increased detrusor pressure and reduced urine flow rate. It is usually diagnosed by studying the synchronous values of flow rate and detrusor pressure. (CHANGED)[‡]

- *Dysfunctional voiding* is defined as an intermittent and/or fluctuating flow rate due to involuntary intermittent contractions of the periurethral striated muscle during voiding, in neurologically normal individuals. (CHANGED)[§]
- *Detrusor sphincter dyssynergia* is defined as a detrusor contraction concurrent with an involuntary contraction of the urethral and/or periurethral striated muscle. Occasionally, flow may be prevented altogether. (ORIGINAL)[¶]
- *Nonrelaxing urethral sphincter obstruction* usually occurs in individuals with a neurological lesion and is characterized by a nonrelaxing, obstructing urethra, resulting in reduced urine flow. (NEW)[**]

CONDITIONS

- *Acute retention of urine* is defined as a painful, palpable, or percussable bladder, when the patient is unable to pass any urine. (NEW)[††]
- *Chronic retention of urine* is defined as a nonpainful bladder, which remains palpable or percussable after the patient has passed urine. such patients may be incontinent. (NEW)[‡‡]
- *Benign prostatic obstruction* is a form of bladder outlet obstruction; it may be diagnosed when the cause of outlet obstruction is known to be benign prostatic enlargement, due to histological benign prostatic hyperplasia. (NEW)
- *Benign prostatic hyperplasia* is a term used (and reserved) for the typical histological pattern, which defines the disease. (NEW)
- *Benign prostatic enlargement* is defined as prostatic enlargement due to histological benign prostatic hyperplasia. The term “prostatic enlargement” should be used in the absence of prostatic histology. (NEW)

TREATMENT

The following definitions were published in the 7th ICS report on lower urinary tract rehabilitation techniques [3] and remain in their original form.

Lower Urinary Tract Rehabilitation

This is defined as a nonsurgical, nonpharmacological treatment for lower urinary tract function and includes the following:

- *Pelvic floor training* is defined as repetitive selective voluntary contraction and relaxation of specific pelvic floor muscles.
- *Biofeedback* is the technique by which information about a normally unconscious physiological process is presented to the patient and/or the therapist as a visual, auditory, or tactile signal.
- *Behavioral modification* is defined as the analysis and alteration of the relationship between the patient’s symptoms and his or her environment for the treatment of maladaptive voiding patterns.

This may be achieved by modification of the behavior and/or environment of the patient.

Electrical Stimulation

This is the application of electrical current to stimulate the pelvic viscera or their nerve supply.

The aim of electrical stimulation may be to directly induce a therapeutic response or to modulate lower urinary tract, bowel, or sexual dysfunction.

Catheterization

Catheterization is a technique for bladder emptying employing a catheter to drain the bladder or a urinary reservoir.

Intermittent (In/Out) Catheterization

This is defined as drainage or aspiration of the bladder or a urinary reservoir with subsequent removal of the catheter.

The following types of intermittent catheterization are defined:

- *Intermittent self-catheterization* is performed by the patient himself or herself.
- *Intermittent catheterization* is performed by an attendant (e.g., doctor, nurse, or relative).
- *Clean intermittent catheterization*: Use of a clean technique. This implies ordinary washing techniques and use of disposable or cleansed reusable catheters.
- *Aseptic intermittent catheterization*: Use of a sterile technique. This implies genital disinfection and the use of sterile catheters and instruments/gloves.

Indwelling Catheterization

This describes an indwelling catheter that remains in the bladder, urinary reservoir, or urinary conduit for a period of time longer than one emptying.

Bladder Reflex Triggering

This comprises various maneuvers performed by the patient or the therapist in order to elicit reflex detrusor contraction by exteroceptive stimuli.

The most commonly used maneuvers are suprapubic tapping, thigh scratching, and anal/rectal manipulation.

Bladder Expression

This comprises various maneuvers aimed at increasing intravesical pressure in order to facilitate bladder emptying.

The most commonly used maneuvers are abdominal straining, Valsalva maneuver, and Credé maneuver.

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ADDENDUM

Formation of the ICS Terminology Committee

The Terminology Committee was announced at the ICS meeting in Denver in 1999 and expressions of interest were invited from those who wished to be active members of the committee, and they were asked to comment in detail on the preliminary draft (the discussion paper published in *Neurourology and Urodynamics*). These are the nine authors who replied with a detailed critique by April 1, 2000, and constitute the committee: Paul Abrams, Linda Cardozo, Magnus Fall, Derek Griffiths, Peter Rosier, Ulf Ulmsten, Philip van Kerrebroeck, Arne Victor, and Alan Wein.

We thank other individuals who later offered their written comments: Jens Thorup Andersen, Walter Artibani, Jerry Blaivas, Linda Brubaker, Rick Bump, Emmanuel Chartier-Kastler, Grace Dorey, Clare Fowler, Kelm Hjalmas, Gordon Hosker, Vik Khullar, Guus Kramer, Gunnar Lose, Joseph Macaluso, Anders Mattiasson, Richard Millard, Rien Nijman, Arwin Ridder, Werner Schäfer, David Vodusek, and Jean Jacques Wyndaele.

A half-day workshop was held at the ICS Annual Meeting in Tampere (August 2000) and a 2-day meeting in London (January 2001), which produced draft 5 of the report, which was then placed on the ICS website (www.icsoffice.org). Discussions on draft 6 took place at the ICS meeting in Korea (September 2001), and draft 7 then remained on the ICS website until final submission to journals in November 2001.

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[**] These nonspecific symptoms are most frequently seen in neurologic patients, particularly those with spinal cord trauma, and in children and adults with malformations of the spinal cord.

[*] The term “nighttime frequency” differs from that for nocturia, as it includes voids that occur after the individual has gone to bed, but before he or she has gone to sleep, and voids that occur in the early morning that prevent the individual from getting back to sleep as he or she wishes. These voids before and after sleep may need to be considered in research studies, for example, in nocturnal polyuria. If this definition were used, then an adapted definition of daytime frequency would need to be used with it.

[†] In infants and small children, the definition of urinary incontinence is not applicable. In scientific communications, the definition of incontinence in children would need further explanation.

[**] The causes of polyuria are various and reviewed elsewhere but include habitual excess fluid intake. The figure of 2.8 is based on a 70 kg person voiding SPiGR40 mL/kg.

[*] The normal range of nocturnal urine production differs with age and the normal ranges remain to be defined. Therefore, nocturnal polyuria is present when sPiGR20% (young adults) to 33% (over 65 years) is produced at night. Hence, the precise definition is dependent on age.

[†] The term “functional bladder capacity” is no longer recommended as “voided volume” is a clearer and less confusing term, particularly if qualified (e.g., “maximum voided volume”). If the term bladder capacity is used, in any situation, it implies that this has been measured in some way, if only by abdominal ultrasound. In adults, voided volumes vary considerably. In children, the “expected volume” may be calculated from the formula (30 + [age in years x 30] in mL). Assuming no residual urine, this will be equal to the “expected bladder capacity.”

[‡] The original ICS definition of incontinence, “Urinary incontinence is the involuntary loss of urine that is a social or hygienic problem,” relates the complaint to quality of life (QoL) issues. Some QoL instruments have been, and are being, developed in order to assess the impact of both incontinence and other LUTS on QoL.

[§] The committee considers the term “stress incontinence” to be unsatisfactory in the English language because of its mental connotations. The Swedish, French, and Italian expression “effort incontinence” is preferable; however, words such as “effort” or “exertion” still do not capture some of the common precipitating factors for stress incontinence such as coughing or sneezing. For this reason, the term is left unchanged.

¶ Urge incontinence can present in different symptomatic forms, for example, as frequent small losses between micturitions, or as a catastrophic leak with complete bladder emptying.

* Suprapubic pressure may be used to initiate or maintain urine flow. The Credé maneuver is used by some spinal cord injury patients, and girls with detrusor underactivity sometimes press suprapubically to help empty the bladder.

† The terms “strangury,” “bladder spasm,” and “dysuria” are difficult to define and of uncertain meaning and should not be used in relation to lower urinary tract dysfunction, unless a precise meaning is stated. Dysuria literally means “abnormal urination” and is used correctly in some European countries. However, it is often used to describe the stinging/burning sensation characteristic of urinary infection. It is suggested that these descriptive words should not be used in the future.

† The ICS believes this to be a preferable term to “interstitial cystitis.” Interstitial cystitis is a specific diagnosis and requires confirmation by typical cystoscopic and histological features. In the investigation of bladder pain, it may be necessary to exclude conditions such as carcinoma in situ and endometriosis.

* The ICS suggests that the term vulvodynia (vulva pain) should not be used, as it leads to confusion between single symptom and a syndrome.

† The ICS suggests that, in men, the term prostatodynia (prostate pain) should not be used as it leads to confusion between a single symptom and a syndrome.

‡ In women, voiding symptoms are usually thought to suggest detrusor underactivity rather than bladder outlet obstruction.

§ Validated questionnaires are useful for recording symptoms, their frequency, severity, and both and the impact of LUTS on QoL. The instrument used should be specified.

¶ It is useful to ask the individual to make an estimate of liquid intake. This may be done precisely by measuring the volume of each drink or crudely by asking how many drinks are taken in a 24-hour period. If the individual eats significant quantities of water-containing foods (vegetables, fruit, salads), then an appreciable effect on urine production will result. The time that diuretic therapy is taken should be marked on a chart or diary.

‡ Coughing may induce a detrusor contraction; hence, the sign of stress incontinence is only a reliable indication of urodynamic stress incontinence when leakage occurs synchronously with the first proper cough and stops at the end of that cough.

* The term ambulatory urodynamics is used to indicate that monitoring usually takes place outside the urodynamic laboratory rather than the subject’s mobility using natural filling.

† The ICS no longer wishes to divide filling rates into slow, medium, and fast. In practice, almost all investigations are performed using medium filling rates, which have a wide range. It may be more important during investigations to consider whether or not the filling rate used during conventional urodynamic studies (UDS) can be considered physiologic.

‡ While bladder sensation is assessed during filling cystometry, the assumption that it is sensation from the bladder alone, without urethral or pelvic components, may be false.

* The assessment of the subject’s bladder sensation is subjective, and it is not, for example, possible to quantify “low bladder volume” in the definition of “increased bladder sensation.”

† The ICS no longer recommends the terms “motor urgency” and “sensory urgency.” These terms are often misused and have little intuitive meaning. Furthermore, it may be simplistic to relate urgency just to the presence or absence of detrusor overactivity when there is usually a concomitant fall in urethral pressure.

‡ There is no lower limit for the amplitude of an involuntary detrusor contraction, but confident interpretation of low-pressure waves (amplitude smaller than 5 cm H2O) depends on “high-quality” urodynamic technique. The phrase “which the patient cannot completely suppress” has been deleted from the old definition.

§ Phasic detrusor contractions are not always accompanied by any sensation, or may be interpreted as a first sensation of bladder filling, or as a normal desire to void.

¶ “Terminal detrusor overactivity” is a new ICS term: It is typically associated with reduced bladder sensation, for example, in the elderly stroke patient when urgency may be felt as the voiding contraction occurs. However, in complete spinal cord injury patients, there may be no sensation whatsoever.

** ICS recommends that the terms “motor urge incontinence” and “reflex incontinence” should no longer be used as they have no intuitive meaning and are often misused.

†† The terms “detrusor instability” and “detrusor hyperreflexia” were both used as generic terms, in the English-speaking world and in Scandinavia, prior to the first ICS report in 1976. As a compromise, they were allocated to idiopathic and neurogenic overactivity, respectively. As there is no real logic or intuitive meaning to the terms, the ICS believes they should be abandoned.

* The observation of reduced bladder compliance during conventional filling cystometry is often related to relatively fast bladder filling: the incidence of reduced compliance is markedly lower if the bladder is filled at physiologic rates, as in ambulatory urodynamics.

† In certain types of dysfunction, the cystometric capacity cannot be defined in the same terms. In the absence of sensation, the cystometric capacity is the volume at which the clinician decides to terminate filling. The reason(s) for terminating filling should be defined, for example, high detrusor filling pressure, large infused volume, or pain. If there is uncontrollable voiding, it is the volume at which this begins. In the presence of sphincter incompetence, the cystometric capacity may be significantly increased by occlusion of the urethra, for example, by Foley catheter.

‡ Fluctuations in urethral pressure have been defined as the “unstable ure-thra.” However, the significance of the fluctuations and the term itself lack clarity, and the term is not recommended by the ICS. If symptoms are seen in association with a decrease in urethral pressure, a full description should be given.

§ In patients with stress incontinence, there is a spectrum of urethral characteristics ranging from a highly mobile urethra with good intrinsic function to an immobile urethra with poor intrinsic function. Any delineation into categories such as “urethral hypermobility” and “intrinsic sphincter deficiency” may be simplistic and arbitrary and requires further research.

* The leak pressure point should be qualified according to the site of pressure measurement (rectal, vaginal, or intravesical) and the method by which pressure is generated (cough or Valsalva). Leak point pressures may be calculated in three ways from the three different baseline values that are in common use: zero (the true zero of intravesical pressure), the value of pves measured at zero bladder volume, or the value of pves immediately before the cough or Valsalva (usually at 200 or 300 mL bladder capacity). The baseline used and the baseline pressure should be specified.

† Detrusor leak point pressure has been used most frequently to predict upper tract problems in neurologic patients with reduced bladder compliance. ICS has defined it “in the absence of a detrusor contraction” although others will measure DLPP during involuntary detrusor contractions.

‡ The precise shape of the flow curve is decided by detrusor contractility, by the presence of any abdominal straining, and by the bladder outlet [11].

* A normal detrusor contraction will be recorded as a high pressure if there is high outlet resistance, normal pressure if there is normal outlet resistance, or low pressure if urethral resistance is low.

† If after repeated free flowmetry no residual urine is demonstrated, then the finding of residual urine during UDS should be considered an artifact, due to the circumstances of the test.

‡ Bladder outlet obstruction has been defined for men but, as yet, not ade-quately in women and children.

§ Although dysfunctional voiding is not a very specific term, it is preferred to terms such as “nonneurogenic neurogenic bladder.” Other terms such as “idiopathic detrusor sphincter dyssynergia,” or “sphincter overactivity voiding dysfunction” may be preferable. However, the term “dysfunctional voiding” is very well established. The condition occurs most frequently in children. While it is felt that pelvic floor contractions are responsible, it is possible that the intraurethral striated muscle may be important.

¶ Detrusor sphincter dyssynergia typically occurs in patients with a supra-sacral lesion, for example, after high spinal cord injury, and is uncommon in lesions of the lower cord. Although the urethral and periurethral striated muscles are usually held responsible, the smooth muscle of the bladder neck or urethra may also be responsible.

** Nonrelaxing sphincter obstruction is found in sacral and infrasacral lesions such as meningomyelocele and after radical pelvic surgery. In addition, there is often urodynamic stress incontinence during bladder filling. This term replaces “isolated distal sphincter obstruction.”

†† Although acute retention is usually thought of as painful, in certain cir-cumstances, pain may not be a presenting feature, for example, when due to prolapsed intervertebral disk, postpartum, or after regional anesthesia such as an epidural anesthetic. The retention volume should be significantly greater than the expected normal bladder capacity. In patients after surgery, due to bandaging of the lower abdomen or abdominal wall pain, it may be difficult to detect a painful, palpable, or percussable bladder.

‡‡ The ICS no longer recommends the term “overflow incontinence.” This term is considered confusing and lacking a convincing definition. If used, a precise definition and any associated pathophysiology, such as reduced urethral function, or detrusor overactivity/low bladder compliance, should be stated. The term chronic retention excludes transient voiding difficulty, for example, after surgery for stress incontinence, and implies significant residual urine; a minimum figure of300 mL has been previously mentioned.

Appendix C

International Urogynecological Association/International Continence Society Joint Report on the Terminology for Female Pelvic Floor Dysfunction*

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INTRODUCTION

There is currently no single document addressing all elements required for diagnoses in the area of female pelvic floor dysfunction in a comprehensive way. Indeed, the diagnoses themselves have not been all completely defined. The term "diagnosis" is defined as "the determination of the nature of a disease: *clinical,* made from a study of the symptoms and signs of a disease; and *laboratory*," multiple options mentioned [1]. Such a specific report would require a full outline of the terminology for all symptoms, signs, urodynamic investigations for female pelvic floor dysfunction, the imaging associated with those investigations, and the most common diagnoses.

It may have been possible in the past to combine all the terminology for lower urinary tract function in men, women, and children into one report. The International Continence Society (ICS) has provided leadership in terminology for lower urinary tract dysfunction over decades employing combined or generic reports. The 1988 report by the Committee on the Standardization of Terminology [2] is one such example. With the increasing specificity and complexity of female diagnoses, a combined report may now be an anachronism. The 2002 report [3] still provided the traditional core terminology and some useful modifications, many of which are repeated in this document. However, it also revealed evidence that (1) a coherent and user-friendly combined report may be starting to become too difficult and (2) the terminology for women, due to the absence of specific diagnoses as well as other female-specific terminology, may not have been advantaged by this approach [4]. The need for standardized terminology in female pelvic floor dysfunction to enable accurate communication for clinical and research purposes has been highlighted for some time [5]. There is indeed the need for a general terminology, forming a "backbone" or "core" terminology to which more specific terminologies can be attached.

A female-specific terminology report should be as follows:

1. *As user-friendly as possible*: It should be able to be understood by all clinical and research users.
2. *Clinically based*: Symptoms, signs, and validated investigations should be presented for use in forming workable diagnoses. Sections 1 through 3 will address symptoms, signs, urodynamic investigations, and current associated pelvic imaging modalities routinely used in the office or urodynamic laboratory to make those diagnoses. A number of related radiological investigations as well as magnetic resonance imaging (MRI) have also been included. The detailed description of electromyography (EMG) and related nerve conduction, reflex latency, and other sensory studies contained in reference [2] will again [3] not be reinstated here. This report does not specifically address terminology for neurogenic pelvic floor dysfunction.

Section 4 will address the most common diagnoses of pelvic floor dysfunction. The terms [3] "urodynamic observation" and "condition" (nonmedical) have not been used in this report. The scope of the report will exclude (1) more invasive investigations requiring anesthetic and (2) evidence-based treatments for each diagnosis.

3. *Able to indicate origin and to provide explanations*: Where a term's existing definition (from one of multiple sources used) is deemed appropriate, that definition will be included and duly referenced. A large number of terms in female pelvic floor function and dysfunction, because of their longterm use, have now become generic, as apparent by their listing in medical dictionaries.

Where a specific explanation is deemed appropriate to explain a change from earlier definitions or to qualify the current definition, this will be included as a note to this appendix (superscript numbers 1, 2, 3, etc.). Wherever possible, evidence-based medical principles will be followed.

As in earlier ICS reports [2,3], when a reference is made to the whole anatomical organ, the vesica urinaria, the correct term is the bladder. When the smooth muscle structure known as the m. detrusor urinae is being discussed, then the correct term is detrusor.

It is suggested that acknowledgment of these standards in written publications related to female pelvic floor dysfunction be indicated by a footnote to the section "Methods and Materials," or its equivalent, to read as follows: "Methods, definitions, and units conform to the standards jointly recommended by the International Continence Society and the International Urogynecological Association, except where specifically noted."

SECTION 1: SYMPTOMS

Symptom: Any morbid phenomenon or departure from the normal in structure, function, or sensation experienced by the woman and indicative of disease [1] or a health problem. Symptoms are either volunteered by, or elicited from the individual, or may be described by the individual's caregiver [2,3].

1A: Urinary Incontinence Symptoms[*]

1. *Urinary incontinence (symptom)*: Complaint of involuntary loss of urine.
2. *Stress (urinary) incontinence*: Complaint of involuntary loss of urine on effort or physical exertion (e.g., sporting activities) or on sneezing or coughing. NB: "*activity-related incontinence*" might be preferred in some languages to avoid confusion with psychological stress.
3. *Urgency (urinary) incontinence*: Complaint of involuntary loss of urine associated with urgency.[†]
4. *Postural (urinary) incontinence: (NEW)* Complaint of involuntary loss of urine associated with change of body position, e.g., rising from a seated or lying position.[‡]
5. *Nocturnal enuresis*: Complaint of involuntary urinary loss of urine that occurs during sleep [3].
6. *Mixed (urinary) incontinence*: Complaint of involuntary loss of urine associated with urgency and also with effort or physical exertion or on sneezing or coughing.
7. *Continuous (urinary) incontinence*: Complaint of continuous involuntary loss of urine [3,6].
8. *Insensible (urinary) incontinence: (NEW)* Complaint of urinary incontinence where the woman has been unaware of how it occurred.
9. *Coital incontinence: (NEW)* Complaint of involuntary loss of urine with coitus. This symptom might be further divided into that occurring with penetration and that occurring at orgasm.

1B: Bladder Storage Symptoms

1. *Increased daytime urinary frequency*: Complaint that micturition occurs more frequently during waking hours than previously deemed normal by the woman [7].[§]
2. *Nocturia*: Complaint of interruption of sleep one or more times because of the need to micturate [3].[¶]
3. *Urgency*: Complaint of a sudden, compelling desire to pass urine that is difficult to defer.[**]
4. *Overactive bladder (OAB, urgency) syndrome*: Urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of urinary

tract infection (UTI) or other obvious pathologies.

1C: Sensory Symptoms

Sensory symptoms: A departure from normal sensation or function, experienced by the woman during bladder filling [1]. Normally, the individual is aware of increasing sensation with bladder filling up to a strong desire to void [3].

1. *Increased bladder sensation*: Complaint that the desire to void during bladder filling occurs earlier or is more persistent to that previous experienced. NB: This differs from urgency by the fact that micturition can be postponed despite the desire to void.
2. *Reduced bladder sensation*: Complaint that the definite desire to void occurs later to that previously experienced despite an awareness that the bladder is filling.
3. *Absent bladder sensation*: Complaint of both the absence of the sensation of bladder filling and a definite desire to void [3].

1D: Voiding and Postmicturition Symptoms

Voiding symptoms: A departure from normal sensation or function, experienced by the woman during or following the act of micturition [1].

1. *Hesitancy*: Complaint of a delay in initiating micturition.
2. *Slow stream*: Complaint of a urinary stream perceived as slower compared to previous performance or in comparison with others.
3. *Intermittency*: Complaint of urine flow that stops and starts on one or more occasions during voiding.
4. *Straining to void*: Complaint of the need to make an intensive effort (by abdominal straining, Valsalva, or suprapubic pressure) to either initiate, maintain, or improve the urinary stream.
5. *Spraying (splitting) of urinary stream*: Complaint that the urine passage is a spray or split rather than a single discrete stream.
6. *Feeling of incomplete (bladder) emptying*: Complaint that the bladder does not feel empty after micturition.
7. *Need to immediately revoid*: Complaint that further micturition is necessary soon after passing urine.
8. *Postmicturition leakage*: Complaint of a further involuntary passage of urine following the completion of micturition.
9. *Position-dependent micturition: (NEW)* Complaint of having to take specific positions to be able to micturate spontaneously or to improve bladder emptying, for example, leaning forward or backward on the toilet seat or voiding in the semistanding position.
10. *Dysuria*: Complaint of burning or other discomfort during micturition. Discomfort may be intrinsic to the lower urinary tract or external (vulvar dysuria).
11. *(Urinary) retention: (NEW)* Complaint of the inability to pass urine despite persistent effort.

1E: POP Symptoms

Prolapse symptoms: A departure from normal sensation, structure, or function, experienced by the woman in reference to the position of her pelvic organs. Symptoms are generally worse at the times when gravity might make the prolapse worse (e.g., after long periods of standing or exercise) and better when gravity is not a factor, for example, lying supine. Prolapse may be more prominent at times of abdominal straining, for example, defecation.

1. *Vaginal bulging*: Complaint of a “bulge” or “something coming down” through the vaginal introitus. The woman may state she can either feel the bulge by direct palpation or see it aided with a mirror.
2. *Pelvic pressure*: Complaint of increased heaviness or dragging in the suprapubic area and/or pelvis.
3. *Bleeding, discharge, infection*: Complaint of vaginal bleeding, discharge, or infection related to

dependent ulceration of the prolapse.

4. *Splinting/digitation*: Complaint of the need to digitally replace the prolapse or to otherwise apply manual pressure, for example, to the vagina or perineum (splinting), or rectally (digitation) to assist voiding or defecation.
5. *Low backache*: Complaint of low, sacral (or "periodlike") backache associated temporally with pelvic organ prolapse (POP).

1F: Symptoms of Sexual Dysfunction

A departure from normal sensation and/or function experienced by a woman during sexual activity.

1. *Dyspareunia*: Complaint of persistent or recurrent pain or discomfort associated with attempted or complete vaginal penetration[*]
2. *Superficial dyspareunia*: Complaint of pain or discomfort on vaginal entry or at the vaginal introitus
3. *Deep dyspareunia*: Complaint of pain or discomfort on deeper penetration (mid- or upper vagina)
4. *Obstructed intercourse*: Complaint that vaginal penetration is not possible due to obstruction
5. *Vaginal laxity*: Complaint of excessive vaginal laxity
6. *Other symptoms* [9,10][†]

1G: Symptoms of Anorectal Dysfunction[‡]

1. *Anal incontinence (symptom)*: Complaint of involuntary loss of feces or flatus
2. *Fecal incontinence*: Complaint of involuntary loss of feces [11]
   a. Solid
   b. Liquid
   c. Passive fecal incontinence (such as soiling without sensation or warning or difficulty wiping clean)
   d. Coital fecal incontinence (occurring with vaginal intercourse)
3. *Flatal incontinence*: Complaint of involuntary loss of flatus [11]
4. *Fecal (rectal) urgency*: Sudden, compelling desire to defecate that is difficult to defer
5. *Fecal (flatal) urgency incontinence*: Involuntary loss of feces (flatus) associated with urgency
6. *Straining to defecate*: Complaint of the need to make an intensive effort (by abdominal straining or Valsalva) to either initiate, maintain, or improve defecation
7. *Feeling of incomplete (bowel) evacuation*: Complaint that the rectum does not feel empty after defecation
8. *Diminished rectal sensation*: Complaint of diminished or absent sensation in the rectum [11]
9. *Constipation*: Complaint that bowel movements are infrequent and/or incomplete and/or there is a need for frequent straining or manual assistance to defecate (Rome II criteria)[*]
10. *Rectal prolapse*: Complaint of external protrusion of the rectum
11. *Rectal bleeding/mucus*: Complaint of the loss of blood or mucus per rectum

1H: Lower Urinary Tract Pain and/or Other Pelvic Pain[†]

1. *Bladder pain*: Complaint of suprapubic or retropubic pain, pressure, or discomfort, related to the bladder, and usually increasing with bladder filling. It may persist or be relieved after voiding [3].
2. *Urethral pain*: Complaint of pain felt in the urethra and the woman indicates the urethra as the site [3].
3. *Vulval pain*: Complaint of pain felt in and around the vulva [3].
4. *Vaginal pain*: Complaint of pain felt internally within the vagina, above the introitus [3].
5. *Perineal pain*: Complaint of pain felt between the posterior fourchette (posterior lip of the introitus) and the anus [3].
6. *Pelvic pain*: The complaint of pain perceived to arise in the pelvis, not associated with

symptoms suggestive of lower urinary tract, sexual, bowel, or gynecological dysfunction. It is less well defined than the aforementioned types of localized pain.
7. *Cyclical (menstrual) pelvic pain*: Cyclical pelvic pain related to menses that raises the possibility of a gynecological cause.
8. *Pudendal neuralgia*: Burning vaginal or vulval (anywhere between the anus and clitoris) pain associated with tenderness over the course of the pudendal nerves. Recently, five essential criteria (Nantes criteria) have been proposed for the diagnosis of pudendal neuropathy [13]: (1) pain in the anatomical region of pudendal innervation, (2) pain that is worse with sitting, (3) no waking at night with pain, (4) no sensory deficit on examination, and (5) relief of symptoms with a pudendal block.
9. *Chronic lower urinary tract and/or other pelvic pain syndromes*.[‡]

1I: Lower UTI

1. *UTI*: Scientific diagnosis of a UTI is the finding of microbiological evidence of significant bacteriuria and pyuria[§]
2. *Recurrent UTIs*: At least three symptomatic and medically diagnosed UTI in the previous 12 months.[¶]
3. *Other related history*: For example, hematuria and catheterization.

SECTION 2: SIGNS

Sign: Any abnormality indicative of disease or a health problem, discoverable on examination of the patient; an objective indication of disease [1] or a health problem.

2A: Urinary Incontinence Signs

All examinations for urinary incontinence are best performed with the woman's bladder comfortably full.

1. *Urinary incontinence*: Observation of involuntary loss of urine on examination; this may be urethral or extraurethral [3].
2. *Stress (urinary) incontinence (clinical stress leakage)*: Observation of involuntary leakage from the urethra synchronous with effort or physical exertion or on sneezing or coughing [3].
3. *Urgency (urinary) incontinence*: Observation of involuntary leakage from the urethra synchronous with the sensation of a sudden, compelling desire to void that is difficult to defer.
4. *Extraurethral incontinence*: Observation of urine leakage through channels other than the urethral meatus, for example, fistula.
5. *Stress incontinence on prolapse reduction (occult or latent stress incontinence)*: (*NEW*) Stress incontinence only observed after the reduction of coexistent prolapse.[**]

2B: Signs of POP

All examinations for POP should be performed with the woman's bladder empty (and if possible an empty rectum). An increasing bladder volume has been shown to restrict the degree of descent of the prolapse [14]. The choice of the woman's position during examination, for example, left lateral (Sims), supine, standing, or lithotomy, is that which can best demonstrate POP in that patient and which the woman can confirm, for example, by use of a mirror or digital palpation. The degree of prolapse may be worse later in the day (after a lengthy time in the erect position) than it is earlier in the day. The hymen remains the fixed point of reference for prolapse description [15].

1. *POP (definition)*: The descent of one or more of the anterior vaginal wall, posterior vaginal wall, the uterus (cervix), or the apex of the vagina (vaginal vault or cuff scar after hysterectomy). The presence of any such sign should be correlated with relevant POP symptoms. More commonly, this correlation would occur at the level of the hymen or beyond.
2. *POP—(POPQ)—(staging [3,15,16])*
   Stage 0: No prolapse is demonstrated.

Stage I: Most distal portion of the prolapse is more than 1 cm above the level of the hymen.
Stage II: Most distal portion of the prolapse is 1 cm or less proximal to or distal to the plane of the hymen.
Stage III: The most distal portion of the prolapse is more than 1 cm below the plane of the hymen.
Stage IV: Complete eversion of the total length of the lower genital tract is demonstrated.*

3. *Uterine/cervical prolapse*: Observation of descent of the uterus or uterine cervix.
4. *Vaginal vault (cuff scar) prolapse*: Observation of descent of the vaginal vault (cuff scar after hysterectomy) [19].†
5. *Anterior vaginal wall prolapse*: Observation of descent of the anterior vaginal wall. Most commonly this would be due to bladder prolapse (cystocele, either central, paravaginal, or a combination). Higher stage anterior vaginal wall prolapse will generally involve uterine or vaginal vault (if uterus is absent) descent. Occasionally, there might be anterior enterocele (hernia of peritoneum and possibly abdominal contents) formation after prior reconstructive surgery [19] (Figure C.1).‡
6. *Posterior vaginal wall prolapse*: Observation of descent of the posterior vaginal wall. Most commonly, this would be due to rectal protrusion into the vagina (rectocele). Higher-stage posterior vaginal wall prolapse after prior hysterectomy will generally involve some vaginal vault (cuff scar) descent and possible enterocele formation [19].§

2C: Other Pelvic Examinations/Signs [2,3,20]

The internal examinations are generally best performed with the woman's bladder empty.

1. *Vulval examination*: Abnormalities include cysts, other tumors, atrophic changes, or lichen sclerosis.
2. *Urethral inspection/palpation*
   a. *Urethral mucosal prolapse*: Prolapse, generally circumferential and larger, of the distal urethral urothelium.
   b. *Urethral caruncle*: Smaller eversion of the urethral urothelium, generally involving the posterior lip.
   c. *Urethral diverticulum*: The presence of a sac opening from the urethra. It might be suspected by a lump or tenderness along the line of the urethra or external urethral discharge on urethral massage.
3. *Vaginal examination*: Examination for vaginal length and mobility, presence of scarring and/or pain, and estrogenization. The location of any vaginal pain should be noted. Included here is any tenderness over the course of the pudendal nerve (see 1H[8] pudendal neuralgia).
4. *Bimanual pelvic examination*: Observations for any pelvic mass or unusual tenderness by vaginal examination together with suprapubic palpation.

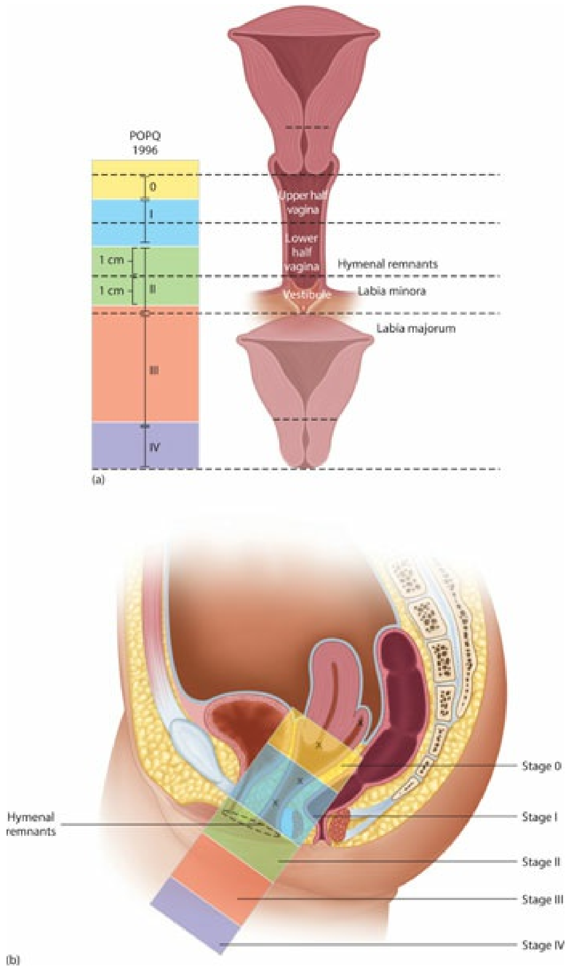


Figure C.1 (a, b) Prolapse staging—0, I, II, III, IV. (Uterine—by the position of the leading edge of the cervix.)

5. *Pelvic floor muscle function [3,20]*: Can be qualitatively defined by the tone at rest and the strength of a voluntary or reflex contraction as strong, normal, weak, or absent, or by a validated grading symptom. Voluntary pelvic floor muscle contraction and relaxation may be assessed by visual inspection, digital palpation (circumferentially), EMG dynamometry, perineometry, or ultrasound. Factors to be assessed include muscle strength (static and dynamic), voluntary muscle relaxation (absent, partial, complete), muscular endurance (ability to sustain maximal or near maximal force), repeatability (the number of times a contraction to maximal or near maximal force can be performed), duration, coordination, and displacement. It is desirable to document findings for each side of the pelvic floor separately to allow for any unilateral defects and asymmetry. The ICS Report into the standardization of terminology of pelvic floor muscle function and dysfunction [20] provides a fuller description of the assessment of pelvic floor muscle function including the following:
    a. *Normal pelvic floor muscles*: Pelvic floor muscles that can voluntarily and involuntarily contract and relax.
    b. *Overactive pelvic floor muscles*: Pelvic floor muscles that do not relax or may even contract when relaxation is functionally needed, for example, during micturition or defecation.
    c. *Underactive pelvic floor muscles*: Pelvic floor muscles that cannot voluntarily contract when this is appropriate.
    d. *Nonfunctioning pelvic floor muscles*: Pelvic floor muscles where there is no action palpable.
6. *Examination for levator (puborectalis) injury*: The puborectalis muscle may be assessed for the presence of major morphological abnormalities by palpating its insertion on the inferior aspect of the os pubis. If the muscle is absent 2–3 cm lateral to the urethra, that is, if the bony surface of the os pubis can be palpated as devoid of muscle, an “avulsion injury” of the puborectalis

muscle is likely [21].

7. *Perineal examination* [20]: When the patient is asked to cough or Valsalva, the perineum should show no downward movement; ventral movement may occur because of the guarding actions of the pelvic floor muscles.
   a. *Perineal elevation*: This is the inward (cephalad) movement of the vulva, perineum, and anus.
   b. *Perineal descent*: This is the outward (caudal) movement of the vulva, perineum, and anus.
8. *Rectal examination*: Observations can include the following:
   a. *Anal sphincter tone and strength*: Assessment on digital examination as good or poor in the absence of any quantitative assessment.
   b. *Anal sphincter tear*: May be recognized as a clear "gap" in the anal sphincter on digital examination.
   c. *Confirm presence or absence of rectocele*: And if possible, differentiate from enterocele. Diagnose perineal body deficiency.
   d. *Confirm presence or absence of fecal impaction*.
   e. *Other rectal lesions*: Intussusception, rectovaginal fistula, or tumor.
   f. *Anal lesions*: Hemorrhoids, fissure.
   g. *Other perianal lesions*: Anocutaneous fistula.

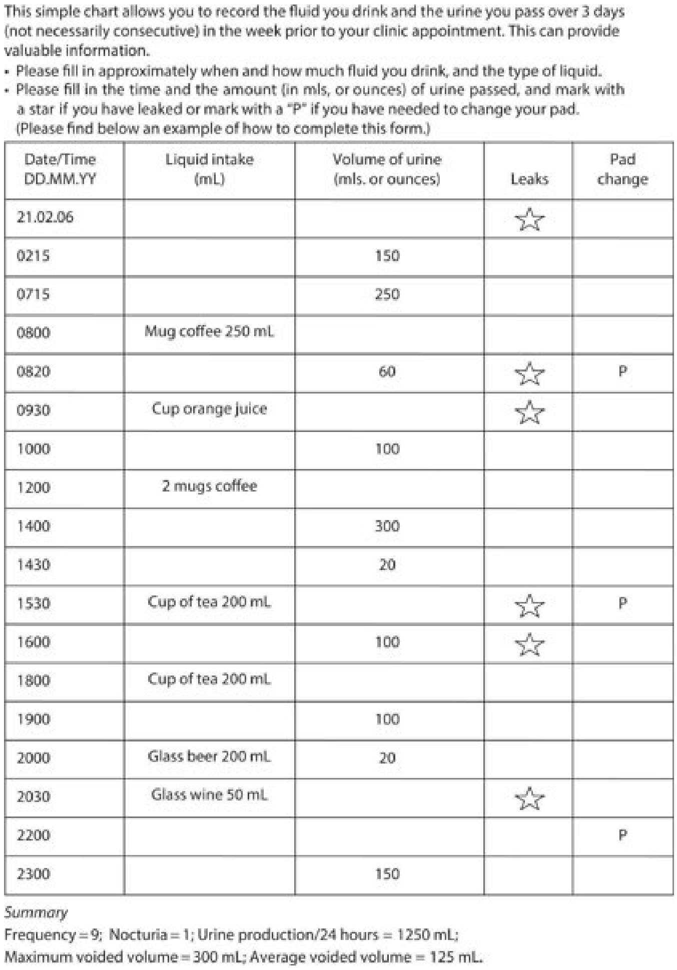
2D: Other Relevant Examinations/Signs [2]

The following general examinations and signs may be relevant:

1. *Neurological signs*: For patients with possible neurogenic lower urinary tract or pelvic floor dysfunction, there should be particular note of those neurological signs related to S2–S4, but these should be complemented by a more general neurological examination as indicated.
2. *Abdominal signs*: Among numerous possible abdominal signs are the following:
   a. *Bladder fullness/retention*: The bladder may be felt by abdominal palpation or suprapubic percussion.
   b. *Other abdominal masses*: Or distension (e.g., ascites).
   c. *Scars*: Indicating previous relevant surgery or traumas.
   d. *Renal area*: Examination for tenderness and masses.

2E: Frequency Volume Chart/Bladder Diary

1. *Frequency volume chart (FVC)*: The recording of the time of each micturition and the volume voided for at least 24 hours. Two or three days of recording (not necessarily consecutive) will generally provide more useful clinical data.
   Information obtained will confirm the following:
   a. *Daytime urinary frequency*: Number of voids by day (wakeful hours including last void before sleep and first void after waking and rising).
   b. *Nocturnal frequency/nocturia*: Number of times sleep is interrupted by the need to micturate. Each void is preceded and followed by sleep.
   c. *24-hour frequency*: Total number of daytime voids and episodes of nocturia during a specified 24-hour period.
   d. *24-hour urine production*: Summation of all urine volumes voided in 24 hours.
   e. *Maximum voided volume*: Highest voided volume recorded.
   f. *Average voided volume*: Summation of volumes voided divided by the number of voids.
   g. *Median functional bladder capacity*: Median maximum voided volume in everyday activities.



This simple chart allows you to record the fluid you drink and the urine you pass over 3 days (not necessarily consecutive) in the week prior to your clinic appointment. This can provide valuable information.

- Please fill in approximately when and how much fluid you drink, and the type of liquid.
- Please fill in the time and the amount (in mls, or ounces) of urine passed, and mark with a star if you have leaked or mark with a "P" if you have needed to change your pad. (Please find below an example of how to complete this form.)

Date/Time DD.MM.YY	Liquid intake (mL)	Volume of urine (mls. or ounces)	Leaks	Pad change
21.02.06			☆	
0215		150		
0715		250		
0800	Mug coffee 250 mL			
0820		60	☆	P
0930	Cup orange juice		☆	
1000		100		
1200	2 mugs coffee			
1400		300		
1430		20		
1530	Cup of tea 200 mL		☆	P
1600		100	☆	
1800	Cup of tea 200 mL			
1900		100		
2000	Glass beer 200 mL	20		
2030	Glass wine 50 mL		☆	
2200				P
2300		150		

Summary
Frequency = 9; Nocturia = 1; Urine production/24 hours = 1250 mL;
Maximum voided volume = 300 mL; Average voided volume = 125 mL.

Figure C.2 Example of a bladder diary.

   h. *Polyuria*: Excessive excretion of urine resulting in profuse and frequent micturition [3]. It has been defined as over 40 mL/kg body weight during 24 hours or 2.8 L urine for a woman weighing 70 kg [22].
   i. *Nocturnal urine volume*: Cumulative urine volume from voids after going to bed with the intention of sleeping to include the first void at the time of waking with the intention of rising (excludes last void before sleep).
   j. *Nocturnal polyuria*: Excess (over 20%–30%—age dependent) proportion of urine excretion (nocturnal voided volume/total 24-hour voided volume · 100%) occurs at night (or when patient is sleeping).[*]

2. *Bladder diary*: Adds to the FVC mentioned earlier, the fluid intake, pad usage, incontinence episodes, and the degree of incontinence. Episodes of urgency and sensation might also be recorded, as might be the activities performed during or immediately preceding the involuntary loss of urine. Additional information obtained from the bladder diary involves *severity of incontinence in terms of leakage episodes and pad usage* (Figure C.2).

2F: Pad Testing

Pad testing is the quantification of the amount of urine lost over the duration of testing, by measuring the increase in the weight of the perineal pads (weighed pre- and posttesting) used. This may give a guide to the severity of incontinence. Different durations from a short (1 hour) test to a 24- and 48-hour tests have been used with provocation varying from normal everyday activities to defined regimens.

SECTION 3: URODYNAMIC INVESTIGATIONS AND ASSOCIATED PELVIC IMAGING

Urodynamics: Functional study of the lower urinary tract.

Clinical sequence of testing: Urodynamic investigations generally involve a woman attending with a comfortably full bladder for free (no catheter) uroflowmetry and postvoid residual urine volume (PVR) measurement prior to filling and voiding (with catheter) cystometry.

3A: Uroflowmetry

1. *Ideal conditions for free (or spontaneous—no catheter) uroflowmetry*: Ideally, all free uroflowmetry studies should be performed in a completely private uroflowmetry room. Most modern uroflowmeters have a high degree of accuracy (±5%) though regular calibration is important [23].
2. *Urine flow*: Voluntary urethral passage of urine that may be
   a. *Continuous*: No interruption to flow.
   b. *Intermittent*: Flow is interrupted.
3. *Flow rate*: Volume of urine expelled via the urethra per unit time. It is expressed in milliliter per second [2,3].
4. *Voided volume (mL)*: Total volume of urine expelled via the urethra [2,3].
5. *Maximum (urine) flow rate (MUFR–mL/s)–*Q_{max}: Maximum measured value of the flow rate [2,3] correcting for artifacts [3].
6. *Flow time (s)*: The time over which measurable flow actually occurs [2,3].
7. *Average (urine) flow rate (AUFR–mL/s)–*Q_{ave}: Voided volume divided by the flow time [2,3] (Figure C.3).
8. *Voiding time (s)*: This is the total duration of micturition, that is, includes interruptions. When voiding is completed without interruption, voiding time is equal to flow time [2,3].
9. *Time to maximum flow (s)*: This is the elapsed time from the onset of urine flow to maximum urine flow [2,3].
10. *Interpretation of the normality of free uroflowmetry*: Because of the strong dependency of urine flow rates on voided volume [24], they are best referenced to nomograms where the cutoff for abnormally slow MUFR and AUFR has been determined and validated [23,25,26] as under the 10th centile of the respective Liverpool nomogram [26]. References to a specific urine flow rate as the lower limit of normal provided a specific volume has been voided require further validation studies [27] (Figure C.4).

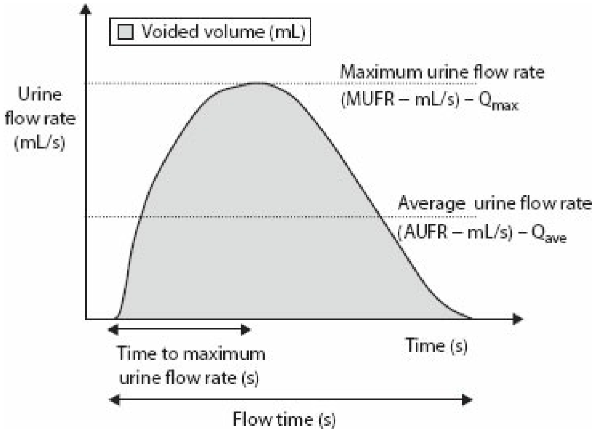


Figure C.3 A schematic representation of urine flow over time.

3B: PVR (Urine Volume)

1. *PVR*: Volume of urine left in the bladder at the completion of micturition [1,3].
2. *Conditions for PVR measurement*: PVR reading is erroneously elevated by delayed measurement due to additional renal input (1–14 mL/min) into bladder volume [28]. Ultrasonic techniques (transvaginal, abdominal, Doppler planimetry) allow immediate (within 60 seconds of micturition) measurement [28]. A short plastic female catheter provides the most effective

bladder drainage for PVR measurement [28].

3. *Assessment of normality of PVR*: Quoted upper limits of normal may reflect the accuracy of measurement. Studies using "immediate" PVR measurement (e.g., transvaginal ultrasound) suggest an upper limit of normal of 30 mL [29]. Studies using urethral catheterization (up to 10 minute delay) quote higher upper limits of normal of 50 mL [27] or 100 mL [29]. An isolated finding of a raised PVR requires confirmation before being considered significant.

3C: Cystometry: General [2,3,29]

1. *Cystometry*: Measurement of the pressure/volume relationship of the bladder during filling and/or pressure–flow study during voiding [2,30].
2. *Cystometrogram*: Graphical recording of the bladder pressure(s) and volume(s) over time [2,30].
3. *Urodynamic studies*: These usually take place in a special clinical room (urodynamic laboratory) and involve (artificial) bladder filling with a specified liquid at a specified rate [3,30].

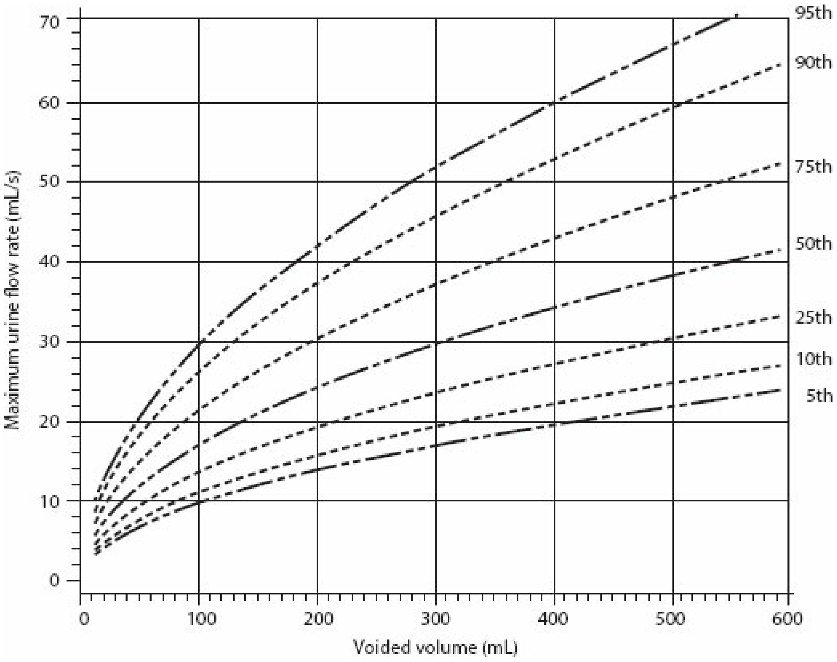


Figure C.4 Liverpool nomogram for maximum urine flow rate in women. Equation: Ln (maximum urine flow rate) = 0.511 + 0.505 · Ln (voided volume), root mean square error = 0.340. (From Van Kerrebroeck P et al., *Neurourol Urodyn*, 21, 179, 2002; Fantl JA et al., *Am J Obstet Gynecol*, 145, 1017, 1982.)

4. *Conditions for cystometry [2,3,30]*
   a. *Pressures*: All systems are zeroed at atmospheric pressure.
   b. *External pressure transducers*: Reference point is the superior edge of the pubic symphysis.
   c. *Catheter-mounted transducers*: Reference point is the transducer itself.
   d. *Initial bladder volume*: Bladder should be empty.
   e. *Fluid medium*: Usually water or saline (or contrast if radiology involved).
   f. *Temperature of fluid*: Should ideally be warmed to body temperature.
   g. *Position of patient*: Sitting position is more provocative for abnormal detrusor activity than the supine position. At some point in the test, filling might desirably take place with the patient standing.
   h. *Filling rate*: The filling rate, including any changes during testing, should be noted on the urodynamic report.
5. *Intravesical pressure (P_{ves})*: The pressure within the bladder [1–3].

6. *Abdominal pressure (P_{abd})*: The pressure surrounding the bladder. It is usually estimated from measuring the rectal pressure, though vaginal and infrequently the pressure though a bowel stoma can be measured as an alternative. The simultaneous measurement of P_{abd} is essential for the interpretation of the P_{ves} trace [2,3]. Artifacts on the detrusor pressure (P_{det}) trace may be produced by an intrinsic rectal contraction.
7. *Detrusor pressure*: The component of intravesical pressure that is created by forces in the bladder wall (passive and active). It is estimated by subtracting P_{abd} from P_{ves} [3].
8. *Ambulatory urodynamics*: These investigations are a functional test of the lower urinary tract, performed outside the clinical setting, involving natural filling and reproducing the woman’s everyday activities.

3D: Filling Cystometry [2,3,30]

1. *Filling cystometry*: This is the pressure/volume relationship of the bladder during bladder filling [1,2]. It begins with the commencement of filling and ends when a “permission to void” is given by the urodynamicist [3].
2. *Aims of filling cystometry*: These are to assess bladder sensation, bladder capacity, detrusor activity, and bladder compliance [2,3].
3. *Bladder sensation during filling cystometry*: This is usually assessed by questioning the woman in relation to the fullness of the bladder during cystometry [2].
   a. *First sensation of bladder filling*: The feeling when the woman first becomes aware of bladder filling [3].
   b. *First desire to void* [2]: The first feeling that the woman may wish to pass urine.

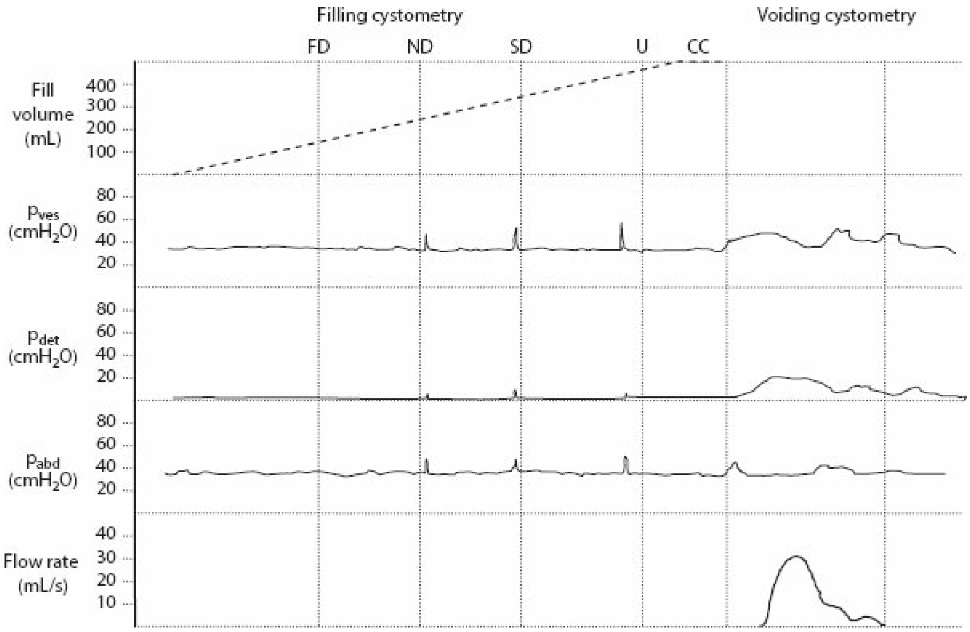


Figure C.5 Filling cystometry—normal detrusor function. Forty-eight-year-old female with urinary frequency. No phasic activity during filling. Voided with normal urine flow rate at normal detrusor voiding pressure. Normal study. *Abbreviations*: FD, first desire to void; ND, normal desire to void; SD, strong desire to void; U, urgency; CC, cystometric capacity (permission to void given).

   c. *Normal desire to void*: The feeling that leads the woman to pass urine at the next convenient moment, but voiding can be delayed if necessary.
   d. *Strong desire to void*: The persistent desire to pass urine without the fear of leakage.
   e. *Urgency*: Sudden, compelling desire to pass urine that is difficult to defer [3]*
   f. *Bladder oversensitivity—also referred to as either “increased bladder sensation” [3] or “sensory urgency” ([2] now obsolete)*: Increased perceived bladder sensation during bladder

filling with an early first desire to void; an early strong desire to void, which occurs at low bladder volume; a low maximum cystometric bladder capacity (*3D[4b]*); no abnormal increases in P_{det}.

g. *Reduced bladder sensation*: Bladder sensation is perceived to be diminished during filling cystometry.

h. *Absent bladder sensation*: The woman reports no bladder sensation during filling cystometry (Figure C.5).

i. *Pain*: The complaint of pain during filling cystometry is abnormal. Its site, character, and duration should be noted.

4. *Bladder capacity during filling cystometry*

a. *Cystometric capacity*: Bladder volume at the end of filling cystometry, when "permission to void" is usually given by the urodynamicist. This end point and the level of the woman's bladder sensation at that time, for example, "normal desire to void," should be noted.

b. *Maximum cystometric capacity*: In patients with normal sensation, this is the bladder volume when she can no longer delay micturition.

5. *Detrusor function during filling cystometry*

a. *Normal (previously "stable") detrusor function*: There is little or no change in detrusor pressure with filling. There are no involuntary phasic contractions despite provocation with activities such as postural changes, coughing, hearing the sound of running water, handwashing, etc.

b. *Detrusor overactivity*: The occurrence of involuntary detrusor contractions during filling cystometry. These contractions, which may be spontaneous or provoked, produce a wave form of variable duration and amplitude on the cystometrogram. The contractions may be phasic or terminal. Symptoms, for example, urgency and/or urgency incontinence, may or may not occur. If a relevant neurological cause is present, then *neurogenic detrusor overactivity* is noted; otherwise, *idiopathic detrusor overactivity* should be the term used (Figure C.6).

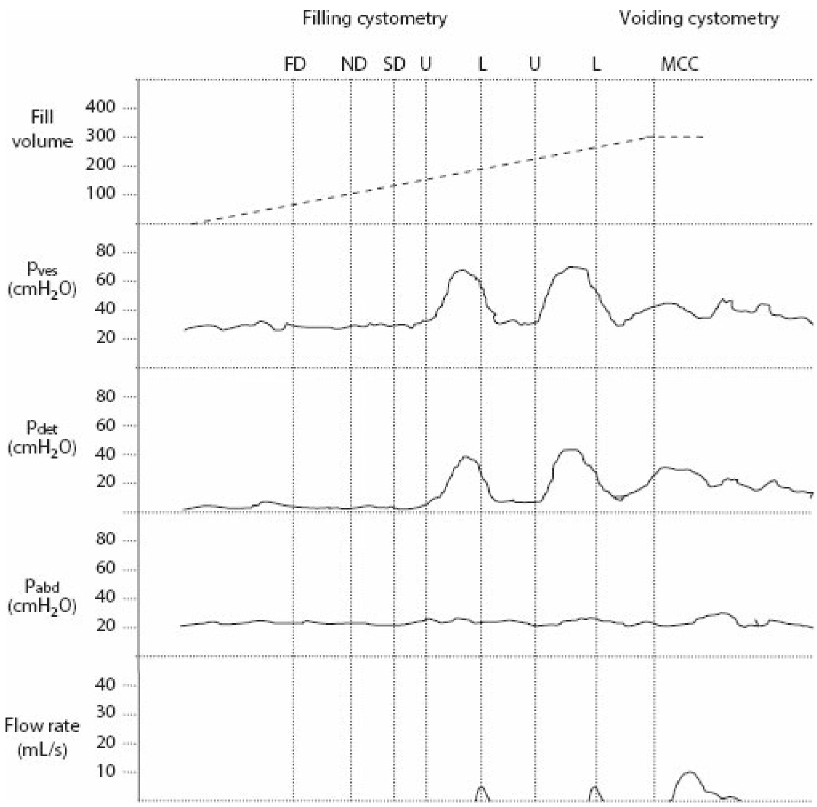


Figure C.6 Filling cystometry—detrusor overactivity. Fifty-two-year-old female with urgency and frequency. Phasic detrusor activity during filling. Leakage is associated with urgency and detrusor contractions.

Abbreviations: FD, first desire to void; ND, normal desire to void; SD, strong desire to void; U, urgency; L, leakage; MCC, maximum cystometric capacity.

   c. *Neurogenic detrusor overactivity*: This is where there is detrusor overactivity and there is evidence of a relevant neurological disorder.

6. *Bladder compliance [2,3]*: This describes the relationship between a change in bladder volume and change in P_{det} [3]. Compliance is calculated by dividing the volume change ($\otimes V$) by the change in P_{det} ($\otimes P_{det}$) during that change in bladder volume. ($C = \otimes V/\otimes P_{det}$). Compliance is expressed as mL/cmH_2O. Bladder compliance can be affected by the following:
   a. *Bladder filling*: Faster filling is more provocative. An artifact may be produced, which settles when filling is interrupted.
   b. *Contractile/relaxant properties of the detrusor*: For example, postradiation changes of the detrusor wall.
   c. *Starting point for compliance calculations [3]*: Usually, the P_{det} at the start of bladder filling and the corresponding bladder volume (usually zero).
   d. *End point for compliance calculations [3]*: The P_{det} (and corresponding bladder volume) at cystometric capacity or immediately before the start of any detrusor contraction that causes significant leakage (and therefore causes the bladder volume to decrease, affecting compliance calculations). Both points are measured excluding any detrusor contraction.

3E: Urethral Function during Filling Cystometry (Filling Urethrocystometry)

1. *Urethral pressure measurement [2,3,30]*: Urethral pressure and urethral closure pressure are idealized concepts that represent the ability of the urethra to prevent leakage. Urethral pressure is currently measured by a number of different techniques that don't tend to have consistent results, either between methods or for a single method [31]. For example, the effect of catheter rotation will be relevant when urethral pressure is measured by a catheter-mounted transducer. Urethral pressure might, nonetheless, be measured as follows:
   - At rest, with the bladder at a given volume
   - During coughing or straining
   - During the process of voiding

   a. *Urethral pressure (intraluminal)*: This is the fluid pressure needed to just open a closed urethra.
   b. *Urethral pressure profile (UPP)*: This is a graph indicating the intraluminal pressure along the length of the urethra.
      - Resting UPP: The bladder and subject are at rest.
      - Stress UPP: Defined applied stress (e.g., cough, strain, Valsalva).

      All systems are zeroed at atmospheric pressure. For external transducers, the reference point is the superior edge of the symphysis pubis. For catheter-mounted transducers, the reference point is the transducer itself. P_{ves} should be measured to exclude a simultaneous detrusor contraction. Methodology should be noted [2] including patient position, catheter type, transducer orientation, fluid and rate of infusion (if fluid-filling system), bladder volume, and rate of catheter withdrawal.
   c. *Maximum urethral pressure*: Maximum pressure in the UPP
   d. *Urethral closure pressure profile (UCPP)*: The relevant pressure is the urethral closure pressure (urethral pressure minus the P_{ves}).
   e *Maximum urethral closure pressure (MUCP)*: Maximum pressure in the UCPP, that is, the maximum difference between the urethral pressure and the P_{ves}.
   f. *Functional profile length*: The length of the urethra along which the urethral pressure exceeds P_{ves} in a woman.
   g. *Functional profile length (on stress)*: The length over which the urethral pressure exceeds the P_{ves} on stress.
   h. *Pressure "transmission" ratio*: This is the increment in urethral pressure on stress as a percentage of the simultaneously recorded increment in P_{ves}. For stress profiles obtained

during coughing, pressure transmission ratios can be obtained at any point along the urethra. If single values are given, the position in the urethra should be stated. If several transmission ratios are defined at different points along the urethra, a pressure transmission "profile" is obtained. During "cough profiles," the amplitude of the cough should be stated if possible.

2. *Urethral closure mechanism [3]*
    a. *Normal urethral closure mechanism*: A positive urethral closure pressure is maintained during bladder filling even in the presence of increased P_{abd}, although it may be overcome by detrusor overactivity.
    b. *Incompetent urethral closure mechanism*: Leakage of urine occurs during activities that might raise intra-abdominal pressure in the absence of a detrusor contraction.
    c. *Urethral relaxation incompetence ("urethral instability")*: Leakage due to urethral relaxation in the absence of raised P_{abd} or a detrusor contraction.
    d. *Urodynamic stress incontinence*: This is the involuntary leakage of urine during filling cystometry, associated with increased intraabdominal pressure, in the absence of a detrusor contraction.
3. *Leak point pressures [2,32,33]*: There are two types of leak point pressure measurement. The pressure values at leakage should be measured at the moment of leakage.
    a. *Detrusor leak point pressure (DLPP)*: This a static test. The pressure is the lowest value of the P_{det} at which leakage is observed in the absence of increased P_{abd} or a detrusor contraction. High DLPP (e.g., over 40 cmH_2O [32]) may put patients at risk for upper urinary tract deterioration or secondary damage to the bladder in the cases of known underlying neurological disorders such as paraplegia or multiple sclerosis. There are no data on any correlation between DLPP and upper tract damage in nonneurogenic patients.
    b. *Abdominal leak point pressure (ALPP)*: This is a dynamic test. It is the lowest value of the intentionally increased P_{ves} that provokes urinary leakage in the absence of a detrusor contraction [33]. The increase in pressure can be induced by a cough (CLPP) or Valsalva (VLPP). Multiple estimates at a fixed bladder volume (200–300 mL) are desirable. Catheter size will influence LPP values and should be standardized. LPP values might also be affected by many other factors such as the technique to confirm urine loss, location of catheter, type of pressure sensor, bladder volume, rate of bladder filling, and patient position. A low ALPP is suggestive of poor urethral function.[*]

3F: Voiding Cystometry (Pressure–Flow Studies)

1. *Voiding cystometry*: This is the pressure/volume relationship of the bladder during micturition [1]. It begins when the "permission to void" is given by the urodynamicist and ends when the woman considers her voiding has finished [3]. Measurements to be recorded should be the intravesical, intraabdominal, and detrusor pressures and the urine flow rate.
2. *Measurements during voiding cystometry [2,3,30]*
    a. *Premicturition pressure*: The pressure recorded immediately before the initial isovolumetric contraction.
    b. *Opening time*: The time elapsed from initial rise in pressure to the onset of flow. This is the initial isovolumetric contraction period of micturition. It reflects the time taken for the fluid to pass from the point of pressure measurement to the uroflow transducer. Flow measurement delay should be taken into account when measuring the opening time.
    c. *Opening pressure*: The pressure recorded at the onset of measured flow (consider time delay).
    d. *Maximum pressure*: Maximum value of the measured pressure.
    e. *Pressure at maximum flow*: Pressure recorded at maximum measured flow rate.
    f. *Closing pressure*: Pressure recorded at the end of measured flow.
    g. *Contraction pressure at maximum flow*: This is the difference between pressure at maximum flow and the premicturition pressure.
    h. *Flow delay*: This is the delay in time between a change in pressure and the corresponding change in measured flow rate.

Figure C.7 shows a schematic diagram of voiding cystometry.

3. *Detrusor function during voiding [2,3]*
   a. *Normal detrusor function*: Normal voiding in women is achieved by an initial (voluntary) reduction in intraurethral pressure (urethral relaxation) [34]. This is generally followed by a continuous detrusor contraction that leads to complete bladder emptying within a normal time span. Many women will void successfully (normal flow rate and no PVR) by urethral relaxation alone, without much of a rise in P_{det} [35]. The amplitude of the detrusor contraction will tend to increase to cope with any degree of bladder outflow obstruction [36].

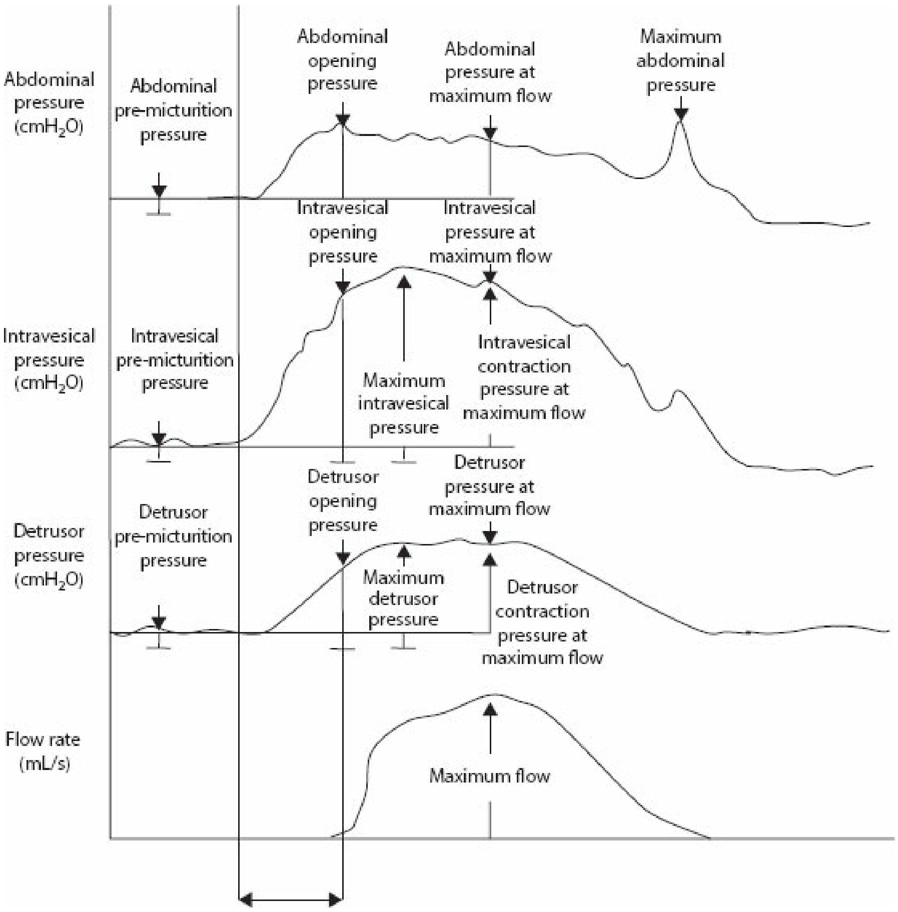

Abdominal pressure (cmH$_2$O)
Abdominal pre-micturition pressure
Abdominal opening pressure
Abdominal pressure at maximum flow
Maximum abdominal pressure
Intravesical opening pressure
Intravesical pressure at maximum flow
Intravesical pressure (cmH$_2$O)
Intravesical pre-micturition pressure
Maximum intravesical pressure
Intravesical contraction pressure at maximum flow
Detrusor opening pressure
Detrusor pressure at maximum flow
Detrusor pressure (cmH$_2$O)
Detrusor pre-micturition pressure
Maximum detrusor pressure
Detrusor contraction pressure at maximum flow
Flow rate (mL/s)
Maximum flow

Figure C.7 A schematic diagram of voiding cystometry.

   b. *Detrusor underactivity*: Detrusor contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or a failure to achieve complete bladder emptying within a normal time span.
   c. *Acontractile detrusor*: The detrusor cannot be observed to contract during urodynamic studies, resulting in prolonged bladder emptying and/or a failure to achieve complete bladder emptying within a normal time span. The term "areflexia" has been used where there is a neurological cause but should be replaced by *neurogenic acontractile detrusor*.

3G: Urethral Function during Voiding Cystometry (Voiding Urethrocystometry) [2,3,30]

This technique may assist in determining the nature of urethral obstruction to voiding. Pressure is recorded in the urethra during voiding. This may be at one specific point, for example, high-pressure zone, or it may be measured as a profile. A voiding urethral pressure profile (VUPP) uses a similar technique to that described earlier for the UPP measured during bladder filling. Simultaneous P_{ves} measurement is required. Localization of the site of the intraurethral pressure measurement is desirable.

1. *Normal urethral function*: The urethra opens and is continuously relaxed to allow micturition at a normal pressure, urine flow, and PVR.*
2. *Bladder outflow obstruction*: This is the generic term for obstruction during voiding. It is a reduced urine flow rate and/or presence of a raised PVR and an increased P_{det}.† It is usually diagnosed by studying the synchronous values of urine flow rate and P_{det} and any PVR measurements. A urethral stricture or obstruction due to higher degrees of uterovaginal prolapse or obstructed voiding after stress incontinence procedures is among the possible causes.
3. *Dysfunctional voiding*: This is characterized by an intermittent and/or fluctuating flow rate due to involuntary intermittent contractions of the periurethral striated or levator muscles during voiding in neurologically normal women. This type of voiding may also be the result of an acontractile detrusor (abdominal voiding) with EMG or videourodynamics required to distinguish between the two entities.
4. *Detrusor sphincter dyssynergia*: This is incoordination between detrusor and sphincter during voiding due to a neurological abnormality (i.e., detrusor contraction synchronous with contraction of the urethral and/or periurethral striated muscles). This is a feature of neurological voiding disorders. Neurological features should be sought. Videocystourethrography (VCU)–(radiological imaging [VCU]) is generally valuable to conclude this diagnosis.

3H: Ultrasound Imaging [38]

1. *Ultrasound in urogynecology*: Ultrasound has become an increasingly frequent adjunct investigation in urogynecology and female urology both in the office and in the urodynamic laboratory.
2. *Modalities in current routine clinical use*
   a. *Perineal*: Curved array probe applied to the perineum. This term incorporates transperineal and translabial ultrasound.
   b. *Introital*: Sector probe applied to the vaginal introitus.
   c. *Transvaginal (TV)*: Intravaginal curvilinear, linear array, or sector scanning.
   d. *Transabdominal (TA)*: Curvilinear scanning applied to the abdomen.
3. *Current routine possible uses of ultrasound in urogynecology and female urology*
   a. *Bladder neck descent/mobility/opening*
      - Position of bladder neck at rest and on Valsalva.‡

NB: Ideally, the Valsalva should be standardized, but it is appreciated that at present, a reliable noninvasive method is lacking. Consensus has not been reached on criteria for excessive bladder neck mobility nor the relationship of this finding to a diagnosis of urodynamic stress incontinence [37].

- Position of bladder neck during pelvic floor contraction.
- Retrovesical angle: That is, angle between proximal urethra and trigonal surface of the bladder. o Urethral rotation: That is, rotation of the proximal urethra on Valsalva.§
- Angle gamma: That is, angle defined by lines from the inferoposterior symphyseal margin to the bladder neck at rest and on Valsalva.¶

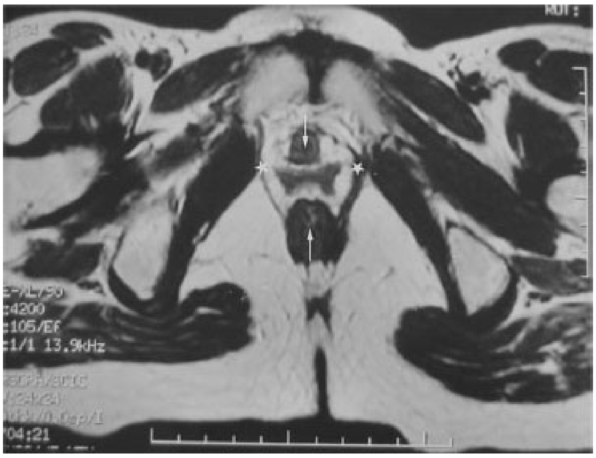


Figure C.8 Axial T2-weighted image of the pelvic floor of a healthy nulliparous Caucasian woman showing measurement of the anteroposterior diameter of the genital hiatus between the arrows from midurethra to midanus at the level of the lower border of the pubic symphysis. Transverse diameter (width) of the levator hiatus was measured between the stars at the point of maximum extension of the levator muscles at the level of the urinary bladder and proximal urethra. (From Rizk DE et al., *Am J Obstet Gynecol*, 191, 83, 2004.)

- Urethral funneling: That is, opening of the proximal third of the urethra during coughing or on Valsalva.[*]
- Urine loss: Full urethral opening during coughing, Valsalva,[†]

Figure C.8 shows a number of possible measurements using MRI.

a. *PVRs*: See Section *3B*.
b. *Intercurrent pelvic pathology*: For example, uterine and adnexal pathology.
c. *Uterine version*: Anteverted or retroverted; flexion at the level of the isthmus [39].[‡]
d. *Bladder abnormalities*: For example, tumor and foreign body.
e. *Urethral abnormality*: For example, diverticulum.
f. *Postoperative findings*: For example, bladder neck position and mobility, position of meshes, tapes, or implants.
g. *Pelvic floor/levator defects*: Bladder neck elevation during pelvic floor contraction.
h. *Descent of pelvic organs*: Visualization of descent of the bladder, uterine cervix, and rectum during Valsalva and coughing.

4. *3D and 4D ultrasound*: The potential of 3D ultrasound in urogynecology and female urology is currently being researched with validated applications likely to be included in future updates of this report and/or separate ultrasound reports. Applications with the most current research include (1) major morphological abnormalities such as levator defects [40] and (2) excessive distensibility of the puborectalis muscle and levator hiatus ("ballooning"—[41]). The additional diagnostic potential of 4D (i.e., the addition of movement) ultrasound awaits clarification by further research.
5. *Other assessments*: Synchronous ultrasound screening of the bladder and/or urethra and measurement of the bladder and P_{abd} during filling and voiding cystometry.
6. *Anal ultrasound (endosonography) [42]*: This is the gold standard investigation in the assessment of anal sphincter integrity. There is a high incidence of defecatory symptoms in women with anal sphincter defects.

3I: Radiological Imaging

1. *Modalities in current routine clinical use*
   a. *VCU [43]*: Synchronous radiological screening of the bladder and measurement of the bladder and P_{abd} during filling and voiding cystometry. When indicated for complex cases, VCU allows direct observation of the effects of bladder events, the position and conformation

of the bladder neck in relation to the pubic symphysis, bladder neck closure during rest and stress, diverticula of the bladder and urethra, vesicovaginal and urethrovaginal fistulae, vesicoureteric reflux, and voiding events.

2. *Other modalities*: None of these are office or urodynamic laboratory based.
   a. *Intravenous urography [43]*: This provides an anatomical outline of the urinary tract including a nephrogram prior to passage of the contrast to the calyces, renal pelvis, ureter, and bladder.
   b. *Micturating cystogram [44]*: The principal use is the detection of vesicoureteric reflux, some fistulae, and diverticula.
   c. *Defecography [42]*: This demonstrates normal anatomy of the anorectum as well as disorders of rectal evacuation. Barium paste is inserted rectally prior to defecation over a translucent commode. Measurement of the anorectal angle is allowed with evidence of the presence, size, or emptying of any rectocele. Enteroceles, rectal intussusception, and mucosal prolapse might be diagnosed as well as a spastic pelvic floor (anismus).
   d. *Colporectocystourethrography (colpocystodefecography) [43]*: This involves the instillation of radiopaque media into the bladder, vagina, and rectum simultaneously for pelvic floor evaluation with images obtained during rest and straining.

3J: Magnetic Resonance Imaging [45,46]

1. *MRI in urogynecology and female urology*
   MRI *provides* the opportunity to examine the soft tissue structures of the pelvic support apparatus in toto. It is noninvasive, has excellent soft tissue contrast resolution without exposure to ionizing radiation, and allows the study of function of pelvic floor structures under different dynamic conditions such as increased P_{abd} during Valsalva [45,46]. Several anatomical landmarks used for pelvic measurements are also easily identified in MRI and most measurements are thus highly reproducible. Currently, the clinical value of these examinations is still under investigation with its impact on therapeutic decisions not yet fully evaluated.
2. *Current possible measurements using MRI in urogynecology and female urology [45,46]*
   a. *Bladder neck and cervical descent/mobility*
      – Position of bladder neck and cervix at rest and on Valsalva.
      – Pubococcygeal line: A line extending from the inferior border of the pubic symphysis to the last joint of the coccyx. Bladder neck or cervical descent >2 cm below this line with straining indicates weakness of the pelvic floor. If alternative landmarks are used in scientific papers, they should be clearly described.
   b. *Intercurrent pelvic pathology*: For example, fibroids and ovarian pathology.
   c. *Uterine version*: Anteverted or retroverted and flexion at the isthmus [47].
   d. *Bladder abnormalities*: For example, tumor and foreign body.
   e. *Urethral abnormality*: For example, diverticulum.
   f. *Postoperative findings*: For example, bladder neck mobility.
   g. *Pelvic floor measurements/levator defects*: Assessment of the configuration of pelvic floor muscles, in particular, the levator ani.
   h. *Descent of pelvic organs*.

NB: Diagnostic ability may be enhanced by the use of 3D MRI. New techniques with high-speed sequence of pictures allow a functional MRI.

DIAGNOSES (MOST COMMON)*

This report again [2,3] highlights the need to base diagnoses for female pelvic floor dysfunction on the correlation between a woman’s symptoms, signs, and any relevant diagnostic investigations.

A: Urodynamic Stress Incontinence

Definition: As noted in Section *3E(2d)*, this diagnosis by *symptom, sign, and urodynamic investigations* involves the finding of involuntary leakage during filling cystometry, associated with increased intra-abdominal pressure, in the absence of a detrusor contraction.[†]

B: Detrusor Overactivity

1. *Definition*: As noted in Section *3D(5b)*, this diagnosis by *symptoms and urodynamic investigations* is made in women with lower urinary tract symptoms (more commonly OAB—type symptoms—section 1B[4]) when involuntary detrusor muscle contractions occur during filling cystometry.[‡]

C. Bladder Oversensitivity

Definition: Bladder oversensitivity, a diagnosis made by *symptoms and urodynamic investigations*, is more likely to occur in women with symptoms of frequency and nocturia and a voiding diary showing a clearly reduced average voided volume. Also referred to as "increased bladder sensation" [3], bladder oversensitivity replaces the now obsolete term of "sensory urgency" [50,51]. As noted in Section *3D(3f)*, it can be defined as an increased perceived bladder sensation during bladder filling *1C(1)* with specific cystometric findings of (1) an early first desire to void *3D(3b)*; (2) an early strong desire to void, which occurs at low bladder volume *3D(3d)*; (3) a low maximum cystometric bladder capacity *3D(4b)*; and (4) no abnormal increases in P_{det} [50,51]. Specific bladder volumes at which these findings occur will vary in different populations. There should be no known or suspected UTI.[§]

D: Voiding Dysfunction

1. *Definition*: Voiding dysfunction, a diagnosis by *symptoms and urodynamic investigations*, is defined as abnormally slow and/or incomplete micturition [53]. Abnormal slow urine flow rates and abnormally high postvoid residuals, the basis of this diagnosis, are outlined in Sections *3A(10)* and *3B(3)*. This diagnosis should be based on a repeated measurement to confirm abnormality.[*]
2. *Further evaluation—pressure–flow studies (voiding cystometry)*: Pressure–flow studies are indicated to evaluate the cause of any voiding dysfunction. Some possible causes have been already defined: *3F(3b) detrusor underactivity*, *3F(3c) acontractile detrusor*, and *3G(2) bladder outflow obstruction*.
3. *Alternative presentations*
   a. *Acute retention of urine [3]*: This is defined as a generally (but not always) painful, palpable, or percussible bladder, when the patient is unable to pass any urine when the bladder is full.
   b. *Chronic retention of urine*: This is defined as a nonpainful bladder, where there is a chronic high PVR.[†]

E: POP

Definition: This diagnosis *2B(1)* by *symptoms and clinical examination, assisted by any relevant imaging*, involves the identification of descent of one or more of the anterior vaginal wall (central, paravaginal, or combination cystocele), posterior vaginal wall (rectocele), the uterus (cervix), or the apex of the vagina (vaginal vault or cuff scar) after hysterectomy.[‡]

F: Recurrent UTIs

Definition: This diagnosis by *clinical history* assisted by *the results of diagnostic tests* involves the determination of the occurrence of at least three symptomatic and medically diagnosed UTIs over the previous 12 months[§]

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[*] “Continence” is defined as voluntary control of bladder and bowel function.

[†] “Urgency” replaces “urge” as the “accepted” terminology for the abnormal rather than the normal phenomenon.

[‡] This is a common symptom, the mechanism of which has not been adequately researched. It is uncertain whether it should be linked to 1A(2) (stress urinary incontinence) or 1A(3) (urgency urinary incontinence).

[§] Traditionally, seven episodes of micturition during waking hours have been deemed as the upper limit of normal, though it may be higher in some populations [7].

[¶] It is common to void during the night when sleep is disturbed for other reasons—for example, insomnia and lactation—this does not constitute nocturia [8]. Each void is preceded and followed by sleep.

[**] The use of the word “sudden,” defined as “without warning or abrupt,” used in earlier definitions [2,8] has been subject to much debate. Its inclusion has been continued. Grading of “urgency” is being developed.

[*] Dyspareunia, the symptom most applicable to female pelvic floor dysfunction, will depend on many factors including a woman’s introital relaxation and/or pain tolerance and her partner’s hesitancy or insistence.

[†] Other symptoms of female sexual dysfunction including (1) decreased sexual desire, (2) decreased sexual arousal, (3) decreased orgasm, and (4) abstention are less specific for female pelvic floor dysfunction and will not be defined here. The Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ) is a measure of sexual function in women with urinary incontinence or POP [9].

[‡] Symptoms of defecatory dysfunction are commonly associated with POP, particularly posterior vaginal prolapse.

[*] Rome II criteria for 1G(9) constipation: Complaint that bowel movements are infrequent (Using this definition, two or

more and three or more UTIs can occur with a prevalence of 19% and 11% respectively in women presenting with symptoms of pelvic floor dysfunction [57]. This then becomes a significant, generally intercurrent, diagnosis likely to require treatment additional to that planned for the other diagnoses found.

† The definitions of pelvic pain and especially chronic pelvic pain are being debated in several societies with a view to simplification and restructuring of the classification. The chronic (present for at least 3 months) pain syndromes have not been included till consensus is reached.

‡ The definitions of pelvic pain and especially chronic pelvic pain are being debated in several societies with a view to simplification and restructuring of the classification. The chronic (present for at least 3 months) pain syndromes have not been included till consensus is reached.

§ Commonly suggested criteria for (1) bacteriuria are >100,000 CFU/mL on voided specimen or >1000 CFU/mL on catheterized specimen and (2) pyuria are >10 WBC/mm^3. usually accompanied by symptoms such as increased bladder sensation, urgency, frequency, dysuria, urgency urinary incontinence, and/or pain in the lower urinary tract.

¶ Recurrent UTIs have not been consistently defined. There is the difficulty of balancing the practical clinical definition and the scientific one. Records of diagnostic tests are often inaccessible over the medium to longer term. With a bias toward the former category, a definition might be the presence of at least three medically diagnosed UTI over the previous 12 months. "Recur" strictly means to "occur again" or "be repeated." This would imply a minimum of (1) two or more or the more commonly accepted (2) three or more UTI in the previous 12 months. The previous UTIs should have resolved prior to a further UTI being diagnosed.

** Stress incontinence on prolapse reduction is a sign frequently alluded to but not properly defined to date. The means of reducing the prolapse will vary. The use of a Sims speculum is common. A pessary or ring might, at times, obstruct the urethra, giving a false negative for this sign.

* The ICS POP quantification system that describes the topographic position of six vaginal sites is the subject of a review by the IUGA Standardization and Terminology Committee with a view to simplification. These sites and the methodology behind the measurement format [15] have therefore not been included here. Consensus was not reached on inserting a valuation of the different prolapse stages into the report, though it will be subject to ongoing discussion, for example, considering stage 0 or 1 as different degrees of normal support and considering stage 2 or more, where the leading edge is at or beyond the hymen, as definite prolapse [17,18].

† Most gynecologists are generally comfortable with the terms cystocele, rectocele, vaginal vault prolapse, and enterocele. Coupled with the brevity of these terms and their clinical usage for up to 200 years [19], the inclusion of these terms is appropriate. Some regard it as important to surgical strategy to differentiate between a central cystocele (central defect with loss of rugae due to stretching of the subvesical connective tissue and the vaginal wall) and a paravaginal defect (rugae preserved due to detachment from the arcus tendineus fascia pelvis).

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* More than 20% (young adults) to 33% (over 65 years) has been suggested as excessive [3].

* The use of the word "sudden," defined as "without warning or abrupt," used in earlier definitions [2,8] has been subject to much debate. Its inclusion has been continued. Grading of "urgency" is being developed..

* The correlation between MUCP and ALPP may depend on the catheter type used.

* The use of the word "sudden," defined as "without warning or abrupt, used in earlier definitions [2,8] has been subject to much debate. Its inclu sion has been continued. Grading of "urgency" is being developed.

† In scientific studies, consideration should be given to standardization of the Valsalva strength, for example, by using an intrarectal pressure transducer.

‡ In scientific studies, consideration should be given to standardization of the Valsalva strength, for example, by using an intrarectal pressure transducer.

§ In scientific studies, consideration should be given to standardization of the Valsalva strength, for example, by using an intrarectal pressure transducer.

¶ In scientific studies, consideration should be given to standardization of the Valsalva strength, for example, by using an intrarectal pressure transducer.

* In scientific studies, consideration should be given to standardization of the Valsalva strength, for example, by using an intrarectal pressure transducer.

† In scientific studies, consideration should be given to standardization of the Valsalva strength, for example, by using an intrarectal pressure transducer. bladder contraction, or micturition.

‡ The use of transvaginal ultrasound with an empty bladder optimizes this assessment [39].

* The most common diagnoses are those where there is evidence for a prevalence of 10% or more in women presenting with symptoms of pelvic floor dysfunction.

† This is the most common urogynecological diagnosis, occurring in up to 72% patients presenting for the first time [48]. This diagnosis may be made in the absence of the symptom of stress (urinary) incontinence in women who have the sign of occult or latent stress incontinence.

‡ The prevalence of detrusor overactivity can vary widely between 13% [48] and 40% [49] of patients undergoing urodynamic studies at different centers.

§ The prevalence of the oversensitive bladder in urogynecology and female urology patients (from studies on the now obsolete term "sensory urgency") is around 10%–13% [51,52].

* Depending on definition, voiding dysfunction has a prevalence of 14% [54] to 39% [48], the latter figure making it either the third or fourth most common urodynamic diagnosis (after urodynamic stress incontinence, POP, and possibly detrusor overactivity).

† Approximately 2% of PVR measurements are over 200 mL [29]. This is a suggested cutoff.

‡ Around 61% [48] of women presenting for initial urogynecological assessment will have some degree of prolapse, not always symptomatic. Objective findings of prolapse in the absence of relevant prolapse symptoms may be termed "anatomic prolapse." Approximately half of all women over the age of 50 years have been reported to complain of symptomatic prolapse [55]. There is a 10% lifetime incidence for women of undergoing surgery to correct pelvic organ prolapse [56]. The presence of any such sign should correlate with relevant POP symptoms.

§ Using this definition, two or more and three or more UTIs can occur with a prevalence of 19% and 11% respectively in women presenting with symptoms of pelvic floor dysfunction [57]. This then becomes a significant, generally intercurrent, diagnosis likely to require treatment additional to that planned for the other diagnoses found..

Appendix D

Commentary on the 2009 IUGA/ICS Joint Report on the Terminology for Female Pelvic Floor Dysfunction

Rufus Cartwright

INTRODUCTION

Since 1976, the International Continence Society (ICS) has published a series of standardization reports relating to lower urinary tract function [1–12], pelvic floor dysfunction [13–15], and urodynamic technique [16–18]. These reports have had a huge impact on usage of terminology in the field, achieving an unprecedented degree of harmonization between researchers around the globe. Not all the recommendations, however, have been universally accepted [19], particularly for the 2002 lower urinary tract function terminology report [9], which made many controversial changes.

The 2009 International Urogynecological Association (IUGA)/ICS joint report [11] expands and updates this work, aiming to be comprehensive account of terminology for the signs, symptoms, and investigations of the whole range of female pelvic floor dysfunction. As in previous terminology reports, the description of each disorder is spread through multiple sections, separately describing the symptoms, examination findings, investigations, and holistic diagnoses. In order to maintain user-friendliness, the document is however extensively footnoted and cross-referenced both between sections and to previous standardization reports.

This commentary on the 2009 standardization report aims to highlight the major changes from previous reports and suggest areas of new controversy that may need to be addressed in future revisions.

Symptoms

Table D.1 compares the terminology and definitions for incontinence symptoms from the 2002 report with the now current 2009 recommendations. In each definition, the new report has replaced the term "involuntary urine leakage," with "involuntary urine loss," recognizing that leakage might be adequately contained by pads or other products, but still be a significant bothersome symptom. The 2002 report recommended that the term "urinary" be included when describing stress, urge, and continuous incontinence, to distinguish urine leakage from fecal or flatal incontinence. This has certainly been adopted to some extent, but in many contexts is unnecessary. The new report has therefore made the "urinary" qualifier optional.

The terms urge and urgency have always caused some confusion and certainly should not be interchangeable. A strong urge to void is a normal bladder sensation, whereas urge incontinence is a pathological symptom. Over recent years, the term "urgency urinary incontinence" had been recommended to resolve this ambiguity (241) and has now been approved by the new report. Encouragingly, it has already gained some usage in the literature [20]. Three "new" subtypes of incontinence have been introduced: "postural," "insensible," and "coital incontinence." In each case, the underlying pathophysiology is less clear than for stress and urge incontinence, and hopefully formal recognition of these problems will stimulate further research.

Table D.2 again compares the terminology and definitions for bladder storage symptoms from the 2002 to 2009 reports. The definitions of urgency and overactive bladder (OAB) syndrome have attracted more attention than almost any other items in the 2002 report. Critics attacked the definition of OAB, suggesting that the simplistic framing created clinical and intellectual confusion [21–24], and new experimental evidence suggested that the onset of urgency was not necessarily "sudden" [25,26]. In the absence of consensus, the 2009 report has elected to leave both definitions largely unchanged.

Increased, reduced, and absent bladder sensation now have their own section in the report and exactly match their cystometric counterpart signs. The prognostic significance of symptomatic altered bladder sensation is however unclear. Even in healthy volunteers, there is a wide variation in the volumes at which bladder sensations occur [27]. The reliability of reporting of sensations at differing bladder volumes is variable with many groups reporting poor results [28,29], and others finding near perfect reliability [27,30]. There are even conflicting results regarding sensations associated with sham cystometry [31,32]. These new definitions should help researchers reach new understanding regarding the relationships between symptoms and signs.

Bernard Haylen, who spearheaded the joint report, has been a pioneer in the objective assessment of voiding symptoms in women. Not surprisingly, this section has been extensively updated (Table D.3). The list of voiding symptoms has been expanded from 8 to 11, with the loss of "terminal dribble," a more characteristically male symptom, and the introduction of "need to immediately revoid" and "position-dependent micturition." Retention has been added as a symptom in its own right, although it can also be an examination finding and a diagnosis. "Dysuria" was discouraged by the 2002 report as part of a trend away from Latinate words. "Urethral pain" was suggested as a suitable alternative, but has not made any significant impact on the literature (Figure D.1). The present report now contains both terms, with dysuria being a special case of urethral pain associated with voiding.

Table D.1 Comparison of Incontinence Symptom Terminology and Definitions 2002–2009

Symptom terminology		**Symptom definition**	
2002	**2009**	**2002**	**2009**
Urinary incontinence	Urinary incontinence	Complaint of any involuntary leakage of urine	Complaint of involuntary loss of urine
Stress urinary incontinence	Stress (urinary) incontinence	Complaint of involuntary leakage on effort or exertion or on sneezing or coughing	Complaint of involuntary loss of urine on effort or physical exertion (e.g., sporting activities) or on sneezing or coughing
Urge urinary incontinence	Urgency (urinary) incontinence	Complaint of involuntary leakage of urine accompanied or immediately preceded by urgency	Complaint of involuntary loss of urine associated with urgency
n/a	Postural (urinary) incontinence	n/a	Complaint of involuntary loss of urine associated with change of body position, for example, rising from a seated or lying position
Nocturnal enuresis	Nocturnal enuresis	Complaint of loss of urine occurring during sleep	Complaint of involuntary urinary loss of urine that occurs during sleep
Continuous urinary incontinence	Continuous (urinary) incontinence	Complaint of continuous leakage	Complaint of continuous involuntary loss of urine
n/a	Insensible (urinary) incontinence	n/a	Complaint of urinary incontinence where the woman has been unaware of how it occurred
n/a	Coital incontinence	n/a	Complaint of involuntary loss of urine with coitus

Abbreviation:n/a, not applicable

Table D.2 Comparison of Storage Symptom Terminology and Definitions 2002–2009

Symptom terminology		**Symptom definition**	
2002	**2009**	**2002**	**2009**
Increased daytime frequency	Increased daytime urinary frequency	Complaint by the patient who considers that he/she voids too often by day	Complaint that micturition occurs more frequently during waking hrs than previously deemed normal by the woman
Nocturia	Nocturia	Complaint that the individual has to wake at night one or more times to void	Complaint of interruption of sleep one or more times because of the need to micturate
Urgency	Urgency	Complaint of sudden	Complaint of sudden compelling desire to pass urine, which is

		compelling desire to pass urine, which is difficult to defer	difficult to defer (unchanged)
Overactive bladder syndrome	Overactive bladder syndrome	Urgency with or without urge incontinence, usually with frequency and nocturia	Urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of urinary tract infection or other obvious pathologies

The 2009 report includes short sections on sexual dysfunction, defining superficial and deep dyspareunia, and an expanded description of prolapse symptoms. Despite the successful dissemination of the Pelvic Organ Prolapse Quantification (POPQ) system for objective assessment of prolapse, there has remained huge heterogeneity in subjective assessment. Five core symptoms are now listed, namely, vaginal bulging, pelvic pressure, bleeding/discharge/infection, splinting/digitation, and low backache. The symptoms of vaginal bulging [33] and pressure [34] are usually thought to be most important. It would, however, be useful for future unified standardization documents to include cross-references to other key symptom areas affected by prolapse, including sexual dysfunction, incontinence, voiding symptoms, and anorectal dysfunction, as in the previous pelvic floor standardization report [15].

The section on anorectal dysfunction is entirely new in keeping with the expanded remit. Most anorectal symptoms are now couched in terms that exactly match their corresponding urinary symptom. For example, fecal (rectal) urgency is a “sudden compelling desire to defecate that is difficult to defer,” and a feeling of incomplete (bowel) evacuation is the “complaint that the rectum does not feel empty after defecation.” This approach could be extended to diminished rectal sensation, and rectal prolapse, to bring them in line with reduced bladder sensation and POP, respectively.

The new section on lower urinary tract infection (UTI) suggests increased bladder sensation, urgency, frequency, dysuria, urgency urinary incontinence, and pain as the likely symptoms of infection. Since none of these are sensitive or specific for UTI and each of these occurs elsewhere in the report, it might have been clearer to include UTI only in the section on diagnoses.

Table D.3 Comparison of Voiding Symptom Terminology 2002–2009

Symptom terminology		**Symptom definition**	
2002	**2009**	**2002**	**2009**
Hesitancy	Hesitancy	Difficulty in initiating micturition resulting in a delay in the onset of voiding after the individual is ready to pass urine	Complaint of a delay in initiating micturition
Slow stream	Slow stream	Perception of reduced urine flow usually compared to previous performance or in comparison to others	Complaint of a urinary stream perceived as slower compared to previous performance or in comparison with others
Intermittent stream (intermittency)	Intermittency	Urine flow that stops and starts, on one or more occasions, during micturition	Complaint of urine flow that stops and starts on one or more occasions during voiding
Straining	Straining to void	Muscular effort used to either initiate, maintain, or improve the urinary stream	Complaint of the need to make an intensive effort (by abdominal straining, Valsalva, or suprapubic pressure) to either initiate, maintain, or improve the urinary stream
Splitting or spraying	Spraying (splitting) of urinary stream	n/a	Complaint that the urine passage is a spray or split rather than a single discrete stream
Feeling of incomplete emptying	Feeling of incomplete (bladder) emptying	Self-explanatory term for feeling experienced by the individual after passing urine	Complaint that the bladder does not feel empty after micturition
n/a	Need to immediately revoid	n/a	Complaint that further micturition is necessary soon after passing urine

Postmicturition dribble	Postmicturition leakage	Involuntary loss of urine immediately after he or she has finished passing urine	Complaint of a further involuntary passage of urine following the completion of micturition
n/a	Position-dependent micturition	n/a	Complaint of having to take specific positions to be able to micturate spontaneously or to improve bladder emptying
n/a	Dysuria	n/a	Complaint of burning or other discomfort during micturition
n/a	(Urinary) retention	n/a	Complaint of the inability to pass urine despite persistent effort

Abbreviation:n/a, not applicable

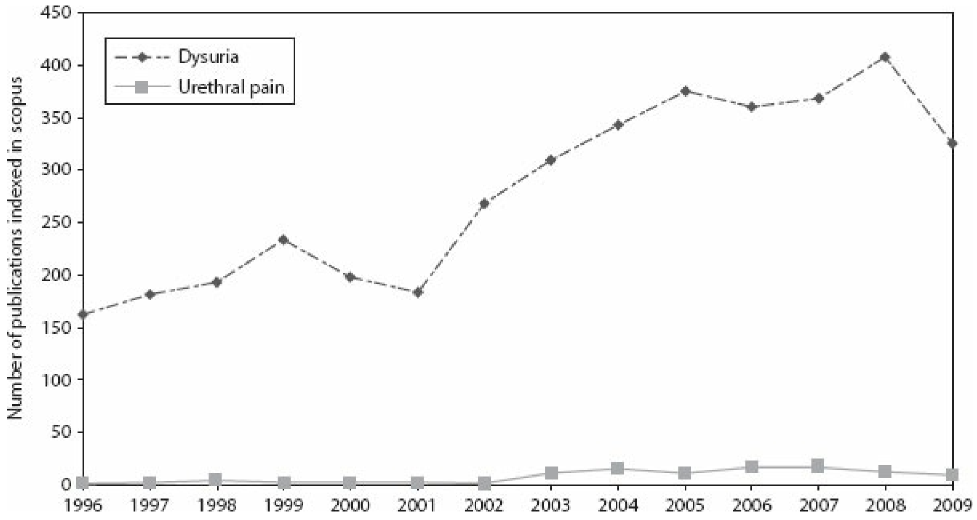

Figure D.1 Publications indexed in Scopus 1996–2009, using the terms “dysuria” or “urethral pain.”

Signs

The new report specifies that stress (urinary) incontinence and urge (urinary) incontinence can each be a sign as well as a symptom. Although assessment of stress (urinary) incontinence, with a cough test, has an extensive supporting literature, some sources have cast doubt on the validity of patient reports of a “sudden compelling desire to void” [25,35], as a useful indicator of urgency. For the first time, occult or latent stress incontinence is formally defined and properly termed “stress incontinence on prolapse reduction.” Treatment of coexisting prolapse and incontinence is considered a priority area in pelvic floor research [36]. Although “stress incontinence on prolapse reduction” may be found in half of women considering prolapse surgery [37], current evidence is inconclusive [38,39] about optimal treatment.

The POPQ system has had excellent uptake in research settings, facilitating comparisons between studies, but the complexity of the system has limited its use in clinical practice [40]. A simplified version of the POPQ [41] is currently subject to ongoing validation work. At present, the joint report gives only a brief overview of staging and compartments, but in the future might serve as one route for the dissemination of this important aspect of standardization.

Uniquely among assessments of lower urinary tract symptom severity and frequency, volume charts are found to be both highly reliable [42] and cost-effective [43]. The 2009 report, along with other major guidance [44], stresses their importance in the initial assessment of women with incontinence. The description of frequency volume charts and bladder diaries has been simplified by removing the category of “micturition time charts.” The definitions given specify cutoffs for polyuria and nocturnal polyuria, but not for frequency and nocturia themselves. Recent longitudinal and cross-sectional population-based studies, using questionnaires or diaries, have provided accurate estimates of the distribution of day- and nighttime voids in men and women [45–47]. It is to be hoped that these estimates can be incorporated into future revisions of the standardization document.

Urodynamics and Imaging

Urodynamics has always formed a core part of the ICS standardization reports. As the 2009 report covers only women, there are presently three current ICS documents on the standardization of urodynamics [9,11,16]. There are new recommendations for the assessment of average flow rate during free uroflowmetry and for calculation of bladder compliance. The section on detrusor function during filling has been extensively updated, and changes are described in Table D.4. Some clarification may be required regarding the status of terms that do not appear in the current report, including "phasic detrusor overactivity," "terminal detrusor overactivity," and "detrusor overactivity incontinence." Detrusor function during voiding is largely unchanged although the description of normal function in women describes a new sequence "initial (voluntary) relaxation in intraurethral pressure (urethral relaxation) … generally followed by continuous detrusor contraction that leads to complete bladder emptying within a normal time span."

The inclusion of a section on diagnoses has led to some inconsistencies. Urodynamic stress incontinence (USI) is defined in the urodynamics section solely as "the involuntary leakage of urine during filling cystometry, associated with increased intra-abdominal pressure, in the absence of detrusor contraction," but appears later as a combination of the stress urinary incontinence symptom and sign, with this cystometric finding. "Dysfunctional voiding" is defined as "an intermittent and/or fluctuating flow rate due to involuntary intermittent contractions of the peri-urethral striated or levator muscles during voiding," while the very similar "voiding dysfunction" is "abnormally slow and/or incomplete micturition." This seems liable to lead to some confusion, particularly if these terms need to be translated.

Table D.4 Filling Detrusor Function Terminology and Definitions 2002–2009

Filling detrusor function terminology		**Filling detrusor function definitions**	
2002	**2009**	**2002**	**2009**
Normal detrusor function	Normal (previously "stable") detrusor function	Allows bladder filling with little or no change in pressure. No involuntary phasic contractions occur despite provocation.	There is little or no change in detrusor pressure with filling. There are no involuntary phasic contractions despite provocation with activities such as postural changes, coughing, hearing the sound of running water, and hand washing.
Detrusor overactivity	Detrusor overactivity	A urodynamic observation characterized by involuntary detrusor contractions during the filling phase, which may be spontaneous or provoked.	The occurrence of involuntary detrusor contractions during filling cystometry. These contractions, which may be spontaneous or provoked, produce a waveform on the cystometrogram or variable duration and amplitude.
Phasic detrusor overactivity	n/a	Defined by a characteristic waveform and may or may not lead to urinary incontinence.	n/a
Terminal detrusor overactivity	n/a	A single involuntary detrusor contraction occurring at cystometric capacity, which cannot be suppressed, and results in incontinence, usually resulting in bladder emptying.	n/a
Detrusor overactivity incontinence	n/a	Incontinence due to an involuntary detrusor contraction.	n/a

Abbreviation:n/a, not applicable

At a little over one page, and with only two figures, the new section on pelvic imaging can provide only the briefest overview of the roles of ultrasound, radiography, and MRI in the evaluation of pelvic floor dysfunction. At present, it provides key references for further reading, and as the validity of each methodology is developed, this section can clearly be expanded.

DIAGNOSES

The final section on diagnoses addresses six common conditions that make up a majority of clinical practice in urogynecology or female urology. The report stresses that the diagnoses should be based on symptoms, signs, and investigation findings. Although this may sound uncontroversial, in practice in each case, the appropriate diagnostic criteria are very much a matter of ongoing research and debate.

The report recommends USI as a diagnosis requiring cystometry. The best available current evidence does not however suggest additional prognostic benefit from the observation of "involuntary leakage during filling cystometry, associated with increased intra-abdominal pressure, in the absence of a detrusor contraction," as opposed to a simple cough test [48–50]. Other evidence-based guidance has specifically recommended against cystometry for uncomplicated stress incontinence [51]. The decision to reaffirm the role of cystometry effectively means the diagnosis can only be made in secondary care settings, which might limit patient access to appropriate community-based care.

The 2002 report revised detrusor overactivity from a diagnosis to a urodynamic observation on the basis that no available evidence supported the additional benefit of cystometry over noninvasive symptom assessment [52]. New research in the intervening years has supported that decision. It is a retrograde step to have divided patients with urgency and frequency symptoms into "detrusor overactivity" and the new "bladder oversensitivity" on the basis of "involuntary detrusor muscle contractions during filling cystometry." Recent studies have suggested that detrusor overactivity is a poor prognosticator of treatment outcome for a wide variety of incontinence interventions, including stress incontinence surgery [48,53], anticholinergic treatment [54,55], with or without behavioral modification [56], and sacral neuromodulation [57,58]. Further threats to the validity of detrusor overactivity as a measure of urgency have come from studies demonstrating unacceptably poor interrater reliability [59,60] and no significant association between individual contractions and reporting of increased sensation [61,62]. The consensus process for drafting the 2009 report would therefore seem to have reiterated the conventional wisdom regarding cystometry, in the face of the best evidence. The concept of OAB has, however, gained enormous popularity in the years since the 2002 report [63], including with EU and U.S. regulatory bodies. It seems unlikely that these new suggested diagnoses "detrusor overactivity" and "bladder oversensitivity" will supplant OAB. In some quarters, "voiding dysfunction" has become a catchall term for lower urinary tract symptoms. This report specifies however that the term refers only to "abnormally slow and/or incomplete micturition." The 2002 standardization report did not give a standardized urodynamic definition for voiding dysfunction, reflecting a lack of consensus. The new report suggests a 30 mL residual as the upper limit of normal and a 200 mL residual as representing chronic retention [64]. Although usage of the Liverpool nomogram for average flow rate is recommended, the report recognizes that this is an area requiring further validation studies, with poorly defined relationships between symptoms and pathology [65,66]. The report specifies that the diagnosis requires both subjective symptoms and objective findings. It is not entirely clear which term is intended to represent objective voiding dysfunction but without symptoms.

CONCLUSIONS

The 2009 report truly represents a landmark in the development of terminology for female pelvic floor dysfunction. For the first time, it provides unifying coverage of urogynecology and female urology. It should be an invaluable reference both for researchers planning and reporting studies and for clinicians who need to map the research evidence base onto the myriad of individual complaints and symptoms reported by patients. This commentary, however, identifies some sections that would benefit from greater depth and other areas where recommendations substantially diverge from recent evidence. Future reports should consider incorporating systematic reviews of current evidence, such as those provided by the International Consultation on Incontinence [44], and use of a formal Delphi method to achieve better balance of coverage.

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Appendix E

Standardization of Terminology of Female Pelvic Organ Prolapse and Pelvic Floor Dysfunction*

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INTRODUCTION

The International Continence Society (ICS) has been at the forefront in the standardization of terminology of lower urinary tract function since the establishment of the Committee on Standardization of Terminology in 1973. The committee's efforts over the past two decades have resulted in the worldwide acceptance of terminology standards that allow clinicians and researchers interested in the lower urinary tract to communicate efficiently and precisely. While female pelvic organ prolapse and pelvic floor dysfunction are intimately related to lower urinary tract function, such accurate communication using standard terminology has not been possible for these conditions.

There is no universally accepted system for describing the anatomic position of the pelvic organs. Many reports use terms for the description of pelvic organ prolapse, which are undefined; none of the many aspiring grading systems has been adequately validated with respect either to reproducibility or to the clinical significance of different grades. The absence of standard, validated definitions prevents comparisons of published series from different institutions and longitudinal evaluation of an individual patient. A primary goal of this report is to introduce a system that will allow the accurate, quantitative description of pelvic support findings in individual patients.

This document is a first effort toward the establishment of standard, reliable, and validated descriptions of female pelvic anatomy and function. The subcommittee acknowledges a need for well-designed reliability studies to evaluate and validate various descriptions and definitions. We have tried to develop guidelines that will promote new insights rather than existing biases. Acknowledgment of these standards in written publications and scientific presentations should be indicated in the methods section with the following statement: "Methods, definitions, and descriptions conform to the standards recommended by the ICS, except where specifically noted."

DESCRIPTION OF PELVIC ORGAN PROLAPSE

The clinical description of pelvic floor anatomy is determined during the physical examination of the external genitalia and vaginal canal. Although the specifics of the examination technique are not dictated by this document, authors should describe their specific technique precisely. Segments of the lower reproductive tract will replace such terms as "cystocele, rectocele, enterocele, or urethrovesical junction" because these terms may imply an unrealistic certainty as to the structures on the other side of the reproductive tract bulge, particularly in women who have had previous prolapse surgery.

Conditions of the Examination

Many variables of examination technique may influence findings in patients with pelvic organ prolapse. It is critical that the examiner sees and describes the maximum protrusion noted by the individual subject during her daily activities. Therefore, the criteria for the end point of the examination and the full development of the prolapse must be specified in any report.

Suggested criteria for demonstration of maximum prolapse should include one or all of the following:

- Any protrusion of the vaginal wall has become tight during straining by the patient.
- Traction on the prolapse causes no further descent.

- The subject confirms that the size of the prolapse and extent of the protrusion seen by the examiner is as extensive as the most severe protrusion that she has experienced. The means of this confirmation should be specified. For example, the subject may use a small handheld mirror to visualize the protrusion.
- A standing, straining examination confirms that the full extent of the prolapse was observed in other positions used.

Other variables of technique that should be specified during the quantitative description and the ordinal staging of pelvic organ prolapse include the following:

- The position of the subject (e.g., supine lithotomy, lateral Sims' position, specified degrees of upright, erect sitting, standing)
- The type of examination table or chair used
- The type of standard vaginal specula, retractors, or tractors used
- Diagrams of any customized retraction, traction, or measuring devices used
- The type (e.g., Valsalva maneuver, cough) and, if measured, intensity (e.g., vesical or rectal pressure rise) of straining used to develop the prolapse maximally
- Fullness of the bladder and, if the bladder was empty, whether this was by spontaneous voiding or by catheterization
- Content of the rectum
- The method by which any quantitative measurements were made (e.g., estimation by visualization or palpation, direct measurement with a calibrated device)

There is a critical need to define the importance of all variables of technique as they relate to the ease of assessment and reproducibility of measurements. Researchers should determine the intra- and interobserver reliability of measurements made with their assessment techniques before utilizing them as baseline and outcome variables. Manuscript descriptions of assessment techniques should include sufficient detail to ensure that other researchers can replicate them precisely.

Quantitative Description of Pelvic Organ Position

This description system is a tandem profile in that it contains a series of component measurements grouped together in combination, but listed separately in tandem, without being fused into a distinctive new expression or "grade." It allows for the precise description of an individual woman's pelvic support without assigning a "severity value." Second, it allows accurate site-specific observations of the stability or progression of prolapse over time by the same or different observers. Finally, it allows similar judgments as to the outcome of surgical repair of prolapse. For example, noting that a surgical procedure moved the vaginal apex from 0.5 cm beyond the hymeneal ring to 0.5 cm above the hymeneal ring denotes more meager improvement than stating that the prolapse was reduced from grade 3 to grade 1 as would be the case using some current grading systems.

Definition of Anatomic Landmarks

Prolapse should be evaluated by a standard system relative to clearly defined anatomic points of reference. There are two types of points of reference: fixed reference points and defined points for measurement.

Fixed Point of Reference

Prolapse should be evaluated relative to a fixed anatomic landmark that can be consistently and precisely identified. The hymen will be the fixed point of reference used throughout this system of quantitative prolapse description.

Visually, the hymen provides a precisely identifiable landmark for reference. Although it is recognized that the plane of the hymen is somewhat variable depending upon the degree of levator ani dysfunction, it remains the best landmark available. "Hymen" is preferable to the ill-defined and imprecise term "introitus." The anatomic position of the six defined points for measurement (see section "Defined Points for Measurement") should be centimeters above or proximal to the hymen (negative number) or centimeters below or distal to the hymen (positive number) with the plane of the hymen being defined as zero (0). For example, a cervix that protruded 3 cm distal to the hymen would be +3 cm.

Palpably, the ischial spines provide precisely identifiable landmarks. In the sitting or standing position, or in situations with limited viability due to obesity or limited ability for hip abduction, the position of the cervix or the leading point of the prolapse relative to the ischial spines may be measured by palpation. Measurements so obtained should be normalized to the level of the hymen by noting the distance between the ischial spines and the plane of the hymen. For example, a cervix that is 3 cm distal to the ischial spines would be at −2 cm if the spines were 5 cm above the plane of the hymen.

Defined Points for Measurement

Anterior Vaginal Wall. Because the only structure directly visible to the examiner is the surface of the vagina, anterior prolapse should be discussed in terms of a segment of the vaginal wall rather than the organs that lie behind it. Thus, the term “anterior vaginal wall prolapse” is preferable to “cystocele” or “anterior enterocele” unless the organs involved are identified by ancillary tests.

- *Point Aa*: A point located in the midline of the anterior vaginal wall 3 cm proximal to the external urethral meatus. This corresponds to the approximate location of the “urethrovesical crease,” a visible landmark of variable prominence that is obliterated in many patients. By definition, the range of position of point Aa relative to the hymen is −3 to +3 cm.
- *Point Ba*: A point that represents the most distal (i.e., most dependent) position of the upper portion of the anterior vaginal wall from the vaginal cuff or anterior vaginal fornix to point Aa. By definition, point Ba is at −3 cm in the absence of prolapse and would have a positive value equal to the position of the cuff in women with total posthysterectomy vaginal eversion.

Vaginal Apex. These points represent the most proximal locations of the normally positioned lower reproductive tract.

- *Point C*: A point that represents either the most distal (i.e., most dependent) edge of the cervix or the leading edge of the vaginal cuff scar in a woman who has undergone total hysterectomy.
- *Point D*: A point that represents the location of the posterior fornix (or pouch of Douglas) in a woman who still has a cervix. It represents the level of uterosacral ligament attachment to the proximal posterior cervix. It is included as a point of measurement to differentiate suspensory failure of the uterosacral–cardinal ligament complex from cervical elongation. When the location of point C is significantly more positive than the location of point D, this is indicative of cervical elongation, which may be symmetrical or eccentric (e.g., involving only the anterior lip of the cervix due to a prior laceration). Point D is omitted as a point for measurement in the absence of the cervix.

Posterior Vaginal Wall. Analogous to anterior prolapse, posterior prolapse should be discussed in terms of segments of the vaginal wall rather than the organs that lie behind it. Thus, the term “posterior vaginal wall prolapse” is preferable to “rectocele” or “enterocele” unless the organs involved are identified by ancillary tests. If small bowel appears to be present in the rectovaginal space, the examiner should comment on this fact and should clearly describe the basis for this clinical impression (e.g., by observation of peristaltic activity in the distended posterior vagina, by palpation of loops of small bowel between an examining finger in the rectum and one in the vagina). In such cases, a “pulsion” addendum to the point Bp position should be noted (e.g., Bp = +5 [pulsion]) (see section “Supplementary Physical Examination Techniques,” points A and B).

- *Point Bp*: A point that represents the most distal (i.e., most dependent) position of the upper portion of the posterior vaginal wall from the vaginal cuff or posterior vaginal fornix to point Ap. By definition, point Bp is at –3 cm in the absence of prolapse and would have a positive value equal to the position of the cuff in a woman with total posthysterectomy vaginal eversion.
- *Point Ap*: A point located in the midline of the posterior vaginal wall 3 cm proximal to the hymen. By definition, the range of position of point Ap relative

Other Landmarks and Measurements

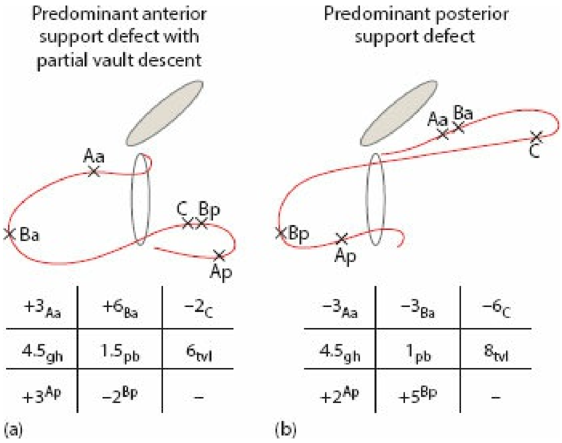
The *genital hiatus* is measured from the middle of the external urethral meatus to the posterior midline hymen. If the location of the hymen is distorted by a loose band of skin without underlying muscle or connective tissue, the firm palpable tissue of the perineal body should be substituted as the posterior margin for this measurement.

The *perineal body* is measured from the posterior margin of the genital hiatus (as just described) to the midanal opening. Measurement of the genital hiatus and perineal body is expressed in centimeters.

The total *vaginal length* is the greatest depth of the vagina in centimeters when point C or D is reduced to its full normal position. (*Note*: Eccentric elongation of a prolapsed anterior or posterior vaginal wall should not be included in the measurement of total vaginal length [see Figure E.1a and accompanying discussion].) The points and measurements discussed in this section are presented in Figure E.2.

Making and Recording Measurements

The position of points Aa, Ba, Ap, Bp, C, and (if applicable) D with reference to the hymen should be measured and recorded. Positions are expressed as centimeters above or proximal to the hymen (negative number) or centimeters below or distal to the hymen (positive number) with the plane of the hymen being defined as zero (0). While an examiner may be able to make measurements to the nearest half (0.5) cm, it is doubtful that further precision is possible.


Predominant anterior support defect with partial vault descent
Aa
Ba
C
Bp
Ap
(a)
Predominant posterior support defect
Aa
Ba
C
Bp
Ap
(b)

$+3_{Aa}$	$+6_{Ba}$	-2_{C}
4.5_{gh}	1.5_{pb}	6_{tvl}
$+3^{Ap}$	-2^{Bp}	–

-3_{Aa}	-3_{Ba}	-6_{C}
4.5_{gh}	1_{pb}	8_{tvl}
$+2^{Ap}$	$+5^{Bp}$	–

Figure E.1 (a) Predominant anterior prolapse and (b) predominant posterior prolapse. *Abbreviations*: gh, genital hiatus; pb, perineal body; tvl, total vaginal length.

All reports should clearly specify how measurements were derived. For example, were direct measurements made using a probe, ruler, glove, speculum, or other device marked in centimeters, were indirect measurements made with the examiner’s fingers and then measured off a centimeter tape, were measurements estimated by the examiner without using a graduated device, or were combinations of techniques used? If customized measuring devices were used, diagrams of such should be included in any manuscript or presentation.

Measurements may be recorded as a simple line of numbers (e.g., −3, −3, −7, −9, −3, −3, 9, 2, 2 for points Aa, Ba, C, D, Bp, Ap, total vaginal length, genital hiatus, and perineal body, respectively). Note that the last three numbers have no sign (i.e., − or +) attached to them because they denote lengths and not positions relative to the hymen. Alternatively, a three-by-three “tic-tac-toe” grid can be used to organize concisely the measurements as noted in Figure E.3. If point D is not applicable due to a prior hysterectomy, this should be noted as such with “NA” or “—” either in the line of numbers or in the grid.

Figure E.4 is a line diagram contrasting measurements indicating normal support to those of posthysterectomy vaginal eversion.

In the example of normal support (Figure E.4a), points Aa and Ba and points Ap and Bp are all −3 since there is no anterior or posterior wall descent. The lowest point of the cervix is 8 cm above the hymen (−8) and the posterior fornix is 2 cm above this (−10). The vaginal length is 10 cm and the genital hiatus and perineal body measure 2 and 3 cm, respectively.

In the example of complete eversion (Figure E.4b), the most distal point of the anterior wall (point Ba), the vaginal cuff scar (point C), and the most distal point of the posterior wall (point Bp) are all at the same position (+8) and points Aa and Ap are maximally distal (both at +3). The fact that the total vaginal length equals the maximum protrusion reflects the fact that the eversion is total.

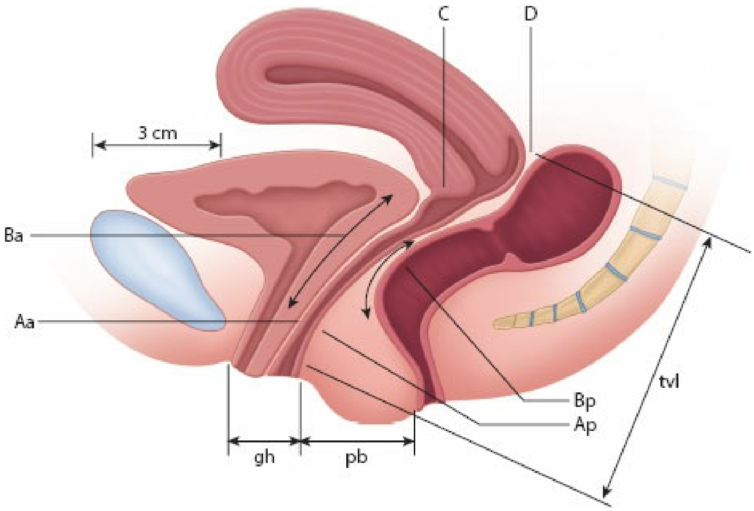
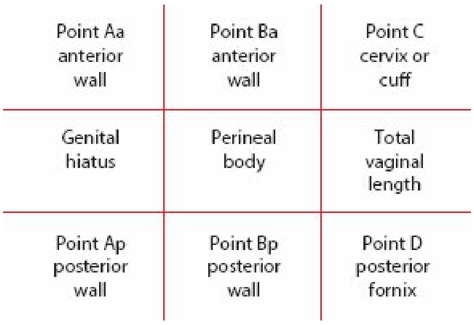
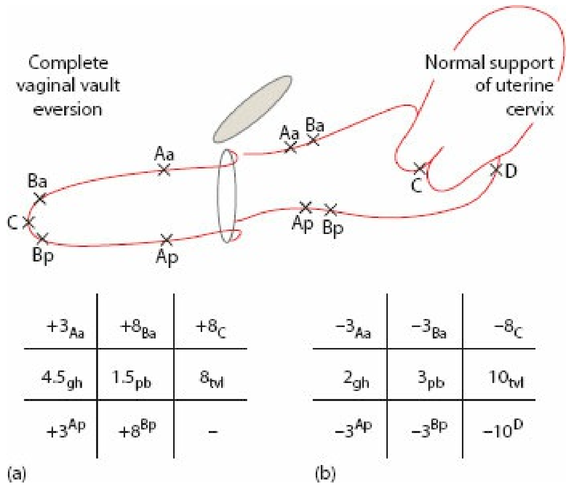


Figure E.2 Six points, genital hiatus (gh), perineal body (pb), and total vaginal length (tvl) used for prolapse quantitation.



Point Aa anterior wall	Point Ba anterior wall	Point C cervix or cuff
Genital hiatus	Perineal body	Total vaginal length
Point Ap posterior wall	Point Bp posterior wall	Point D posterior fornix

Figure E.3 A three-by-three grid for recording the quantitative description of pelvic organ prolapse.


Complete vaginal vault eversion
Normal support of uterine cervix
Aa
Ba
C
Bp
Ap
Aa
Ba
C
D
Ap
Bp

$+3_{Aa}$	$+8_{Ba}$	$+8_{C}$
4.5_{gh}	1.5_{pb}	8_{tvl}
$+3^{Ap}$	$+8^{Bp}$	–

(a)

-3_{Aa}	-3_{Ba}	-8_{C}
2_{gh}	3_{pb}	10_{tvl}
-3^{Ap}	-3^{Bp}	-10^{D}

(b)

Figure E.4 (a) Complete eversion and (b) normal support. *Abbreviations*: gh, genital hiatus; pb, perineal body; tvl, total vaginal length.

Figure E.1 is a line diagram representing predominant anterior and posterior vaginal wall prolapse with partial vault descent.

In the example of a predominant anterior support defect (Figure E.1a), the leading point of the prolapse is the upper anterior vaginal wall, point Ba (+6). Note that there is significant elongation of the bulging anterior wall. Point Aa is maximally distal (+3) and the vaginal cuff scar is 2 cm above the hymen (C = −2). The cuff scar has undergone 4 cm of descent since it would be at −6 (the total vaginal length) if it were perfectly supported. In this example, the total vaginal length is not the maximum depth of the vagina with the elongated anterior vaginal wall maximally reduced, but rather the depth of the vagina at the cuff with point C reduced to its normal full extent as specified in section "Other Landmarks and Measurements."

In the example of the predominant posterior support defect (Figure E.1b), the leading point of the prolapse is the upper posterior vaginal wall, point Bp (+5). Point Ap is 2 cm distal to the hymen (+2) and the vaginal cuff scar is 6 cm above the hymen (−6). The cuff has undergone only 2 cm of descent since it would be at −8 (the total vaginal length) if it were perfectly supported.

Ordinal Staging of Pelvic Organ Prolapse

The tandem profile for quantifying prolapse just described provides a precise description of anatomy for individual patients. However, because of the many possible combinations, such profiles cannot be directly ranked; the many variations are too numerous to permit useful analysis and comparisons when populations are studied. Consequently, they are analogous to other tandem profiles such as the tumor–node–metastasis (TNM) index for various cancers. For the TNM description of individual patients' cancers to be useful in population studies evaluating prognosis or response to therapy, they are clustered into an ordinal set of stages. Ordinal stages represent adjacent categories that can be ranked in an ascending sequence of magnitude, but the categories are assigned arbitrarily and the intervals between them cannot actually be measured.

While the committee is aware of the arbitrary nature of an ordinal staging system and the possible biases that it introduces, we conclude that such a system is necessary if populations are to be described and compared, if symptoms putatively related to prolapse are to be evaluated, and if the results of various treatment options are to be assessed and compared.

Stages are assigned according to the most severe portion of the prolapse when the full extent of the protrusion has been demonstrated according to the criteria in section "Conditions of the Examination." In order for a stage to be assigned to an individual subject, it is essential that her quantitative description be completed first. The 2 cm buffer related to the total vaginal length in stages 0–IV is an effort to compensate for vaginal distensibility and the inherent imprecision of the measurement of total vaginal length. The 2 cm buffer around the hymen in stage II is an effort to avoid confusing a stage to a single plane and to acknowledge practical limits of precision in this assessment.

Stage 0

No prolapse is demonstrated. Points Aa, Ap, Ba, and Bp are all at −3 cm and either point C or D is between −X cm and – (X – 2) cm, where X is the total vaginal length in centimeters (i.e., the quantitation value of point C or D is ≤ – (X – 2) cm). Figure E.4a represents stage 0 pelvic organ prolapse.

Stage I

The criteria for stage 0 are not met but the most distal portion of the prolapse is more than 1 cm above the level of the hymen (i.e., its quantitation value is <−1 cm). stage I can be subgrouped according to which portion of the lower reproductive tract is the most distal part of the prolapse using the following letter qualifiers: a, anterior vaginal wall; p, posterior vaginal wall; C, vaginal cuff; Cx, cervix; and Aa, Ap, Ba, Bp, and D for the points of measurement already defined (e.g., I-Cx if the cervix is the most distal, I-Bp if the upper posterior wall is most distal, or I- if the junction of the distal and proximal anterior wall is the most distal part of the prolapse).

Stage II

The most distal portion of the prolapse is 1 cm or less proximal to or distal to the plane of the hymen (i.e., its quantitation value is ≥−1 cm but ≤+1 cm). Stage II can be subgrouped according to the scheme described under stage I (e.g., II-a, II-C, or II-Bp).

Table E.1 International Continence Society Pelvic Organ Prolapse Ordinal Staging System

Stage 0	Points Aa, Ap, Ba, and Bp are all at −3 cm and either point C or D is at ≤–(X – 2) cm.
Stage I	The criteria for stage 0 are not met and the leading edge of prolapse is <–1 cm.
Stage II	Leading edge of prolapse is >–1 cm but ≤+1 cm.
Stage III	Leading edge of prolapse is >+1 cm but <+(X – 2) cm.
Stage IV	Leading edge of prolapse is ≥+(X – 2) cm

Notes:X = total vaginal length in centimeters in stages 0, III, and IV. Stages I through IV can be subgrouped according to which portion of the lower reproductive tract is the leading edge of the prolapse using the following qualifiers: a, anterior vaginal wall; p, posterior vaginal wall; C, vaginal cuff; Cx, cervix; and Aa, Ba, Ap, Bp, and D for the defined points of measurement (e.g., IV-Cx, II-a, or III-Bp).

Stage III

The most distal portion of the prolapse is more than 1 cm below the plane of the hymen but protrudes no further than 2 cm less than the total vaginal length in centimeters (i.e., its quantitation value is >+1 cm but <+(X − 2) cm where X is the total vaginal length). stage III can be subgrouped according to the scheme described under stage I. For example, Figure E.1a represents stage III-Ba and Figure E.1b represents stage III-Bp prolapse.

Stage IV

Essentially, complete eversion of the total length of the lower genital tract is demonstrated. The distal portion of the prolapse protrudes to at least (X − 2) cm where X is the total vaginal length in centimeters (i.e., its quantitation value is ≤+(X − 2) cm). In most instances, the leading edge of stage IV prolapse will be the cervix or vaginal cuff scar. Rare exceptions to this can be noted according to the subgrouping scheme described under stage I. Figure E.4b represents stage IV-C prolapse. Table E.1 summarizes the staging system.

ANCILLARY TECHNIQUES FOR DESCRIBING PELVIC ORGAN PROLAPSE

This series of procedures may help to further characterize pelvic organ prolapse in an individual patient. They are considered ancillary either because they are not yet standardized or validated or because they are not universally available to all patients.

Authors utilizing these procedures should include the following information in their manuscripts:

- Describe the objective information they intended to generate and how it enhanced their ability to evaluate or treat prolapse
- Describe precisely how the test was performed, any instruments that were used, and the specific testing conditions (see section “Conditions of the Examination”) so that other authors can reproduce the study
- Document the reliability of the measurement obtained with the technique

Supplementary Physical Examination Techniques

Many of these techniques are essential to the adequate preoperative evaluation of a patient with pelvic organ prolapse. While they do not directly affect either the tandem profile or the ordinal stage, they are important for the selection and performance of an effective surgical repair. These techniques include, but are not necessarily limited to, the following:

1. Performance of a digital rectal–vaginal examination while the patient is straining and the prolapse is maximally developed to differentiate between a high rectocele and an enterocele
2. Digital assessment of the contents of the rectal–vaginal septum during the examination (noted in (1)) to differentiate between a “traction” enterocele (the posterior cul-de-sac is pulled down with the prolapsing cervix or vaginal cuff but is not distended by intestines) and a “pulsion”

enterocele (the intestinal contents of the enterocele distend the rectal–vaginal septum and produce a protruding mass)
3. Q-tip testing for the measurement of urethral axial mobility
4. Measurements of perineal descent
5. Measurements of the transverse diameter of the genital hiatus or of the protruding prolapse
6. Measurements of vaginal volume
7. Description and measurement of rectal prolapse
8. Examination techniques for differentiating between various types of defect (e.g., central vs. paravaginal defects of the anterior vaginal wall)

Endoscopy

Cystoscopic visualization of bowel peristalsis under the bladder base or trigone may identify an anterior enterocele in some patients. The endoscopic visualization of the bladder base and rectum and observation of the voluntary constriction and dilation of the urethra, vagina, and rectum has, to date, played a minor role in the evaluation of pelvic floor anatomy and function. When such techniques are described, authors should include the type, size, and lens angle of the endoscope used; the doses of any analgesic, sedative, or anesthetic agents used; and a statement of the level of consciousness of the subject in addition to a description of the other conditions of the examination.

Photography

Still photographic documentation of prolapse beyond stage II may be utilized both to document serial changes in individual patients and to illustrate findings for manuscripts and presentations. Photographs should contain an internal frame of reference such as a centimeter ruler or tape.

Imaging Procedures

Different imaging techniques have been used to visualize pelvic floor anatomy, support defects, and relationships among adjacent organs.

These techniques may be more accurate than physical examination in determining which organs are involved in pelvic organ prolapse. However, they share the limitations of the other techniques in this section, that is, a lack of standardization, validation, and/or availability. For this reason, no specific technique can be recommended, but guidelines for reporting various techniques will be considered.

General Guidelines for Imaging Procedures

Landmarks should be defined to allow comparisons with other imaging studies and the physical examination. The lower edge of the symphysis pubis should be given high priority as a landmark. Other examples of bony landmarks include the superior edge of the pubic symphysis, the ischial spine, the obturator foramen, and the promontory of the sacrum.

All reports on imaging techniques should specify the following:

- Position of the patient including the position of her legs (images in manuscripts should be oriented to reflect the patient's position when the study was performed and should not be oriented to suggest an erect position unless the patient was erect)
- Specific verbal instructions given to the patient
- Bladder volume and content and bowel content, including any prestudy preparations
- The performance and display of simultaneous monitoring such as pressure measurements that might be used to document that exposures were made at the most appropriate moment

Ultrasonography

Continuous visualization of dynamic events is possible. All reports using ultrasound should include the following information:

- Transducer type and manufacturer (e.g., sector, linear, MHz)
- Transducer size
- Transducer orientation

- Route of scanning (e.g., abdominal, perineal, vaginal, rectal, urethral)

Contrast Radiography

Contrast radiography may be static or dynamic and may include voiding colpocystourethrography, defecography, peritoneography, and pelvic fluoroscopy, among others. All reports of contrast radiography should include the following information:

- Projection (e.g., lateral, frontal, horizontal, oblique).
- Type and amount of contrast media used and sequence of opacification of the bladder, vagina, rectum and colon, small bowel, and peritoneal cavity.
- Any urethral or vaginal appliance used (e.g., tampon, catheter, bead chain).
- Type of exposure (e.g., single exposure, video).
- Magnification—an internal reference scale should be included.

Computed Tomography and Magnetic Resonance Imaging

These techniques do not allow for continuous imaging under dynamic conditions. Currently available equipment usually dictates supine scanning. Details of the technique should be specified including

- The specific equipment used, including the manufacturer
- The plane of imaging (e.g., axial, sagittal, coronal, oblique)
- The field of view
- The thickness of sections and the number of slices
- The scan time
- The use and type of contrast
- The type of image analysis

Surgical Assessment

Intraoperative evaluation of pelvic support defects is intuitively attractive but as yet of unproven value. The effects of anesthesia, diminished muscle tone, and loss of consciousness are of unknown magnitude and direction. Limitations due to the position of the patient must also be evaluated.

PELVIC FLOOR MUSCLE TESTING

Pelvic floor muscles are voluntarily controlled, but selective contraction and relaxation necessitate muscle awareness. Optimal squeezing technique involves contraction of the pelvic floor muscles without contraction of the abdominal wall muscles and without a Valsalva maneuver. Squeezing synergists are the intraurethral and anal sphincteric muscles. In normal voiding, defecation, and optimal abdominal-strain voiding, the pelvic floor is relaxed, whereas the abdominal wall and the diaphragm may contract. With coughs and sneezes and often when other stresses are applied, the pelvic floor and abdominal wall are contracted simultaneously.

Evaluation and measurement of pelvic floor muscle function includes (1) an assessment of the patient’s ability to contract and relax the pelvic muscles selectively (i.e., squeezing without abdominal straining and vice versa) and (2) measurement of the force (strength) of contraction.

There are pitfalls in the measurement of pelvic floor muscle function because the muscles are invisible to the investigator and because patients often simultaneously and erroneously activate other muscles. Contraction of the abdominal, gluteal, and hip adductor muscles, Valsalva maneuver, straining, breath holding, and forced inspirations are typically seen. These factors affect the reliability of available testing modalities and have to be taken into consideration in the interpretation of these tests.

The individual types of test cited in this report are based on both the scientific literature and current clinical practice. It is the intent of the committee neither to endorse specific tests or techniques nor to restrict evaluations to the examples given. The standards recommended are intended to facilitate comparison of results obtained by different investigators and to allow investigators to replicate studies precisely.

For all types of measuring technique, the following should be specified:

- Patient position, including the position of the legs

- Specific instructions given to the patient
- The status of the bladder and bowel fullness
- Techniques of quantification or qualification (estimated, calculated, directly measured)
- The reliability of the technique

Inspection

A visual assessment of muscle integrity, including a description of scarring and symmetry, should be performed. Pelvic floor contraction causes inward movement of the perineum and straining causes the opposite movement. Perineal movements can be observed directly or assessed indirectly by movement of an externally visible device placed into the vagina or urethra. The abdominal wall and other specified regions might be watched simultaneously. The type, size, and placement of any device used should be specified as should the state of undress of the patient.

Palpation

Palpation may include digital examination of the pelvic floor muscles through the vagina or rectum as well as assessment of the perineum, abdominal wall, and/or other specified regions. The number of fingers and their position should be specified. Scales for the description of the strength of voluntary and reflex (e.g., with coughing) contractions and of the degree of voluntary relaxation should be clearly described and intra- and interobserver reliability documented. Standardized palpation techniques could also be developed for the semiquantitative estimation of the bulk or thickness of pelvic floor musculature around the circumference of the genital hiatus. These techniques could allow for the localization of any atrophic or asymmetric segments.

Electromyography

Electromyography from the pelvic floor muscles can be recorded alone or in combination with other measurements. Needle electrodes permit visualization of individual motor unit action potentials, while surface or wire electrodes detect action potentials from groups of adjacent motor units underlying or surrounding the electrodes. Interpretation of signals from these latter electrodes must take into consideration that signals from erroneously contracted adjacent muscles may interfere with signals from the muscles of interest. Reports of electromyographic recordings should specify the following:

- Type of electrode
- Placement of electrodes
- Placement of reference electrode
- Specifications of signal processing equipment
- Type and specifications of display equipment
- Muscle in which needle electrode is placed
- Description of decision algorithms used by the analytic software

Pressure Recording

Measurements of urethral, vaginal, and anal pressures may be used to assess pelvic floor muscle control and strength. However, interpretations based on these pressure measurements must be made with a knowledge of their potential for artifact and their unproven or limited reproducibility. Anal sphincter contractions, rectal peristalsis, detrusor contractions, and abdominal straining can affect pressure measurements. Pressures recorded from the proximal vagina accurately mimic fluctuations in abdominal pressure. Therefore, it may be important to compare vaginal pressures to simultaneously measured vesical or rectal pressures. Reports using pressure measurements should specify the following:

- The type and size of the measuring device at the recording site (e.g., balloon, open catheter)
- The exact placement of the measuring device
- The type of pressure transducer
- The type of display system
- The display of simultaneous control pressures

As noted in the section “Inspection,” observation of the perineum is an easy and reliable way to assess for abnormal straining during an attempt at a pelvic muscle contraction. Significant straining or a Valsalva maneuver causes downward/caudal movement of the perineum; a correctly performed pelvic muscle contraction causes inward/cephalad movement of the perineum. Observation for perineal movement should be considered as an additional validation procedure whenever pressure measurements are recorded.

DESCRIPTION OF FUNCTIONAL SYMPTOMS

Functional deficits caused by pelvic organ prolapse and pelvic floor dysfunction are not well characterized or absolutely established. There is an ongoing need to develop, standardize, and validate various clinimetric scales such as condition-specific quality-of-life questionnaires for each of the four functional symptom groups (described in the following texts) thought to be related to pelvic organ prolapse.

Researchers in this area should try to use standardized and validated symptom scales whenever possible. They must always ask precisely the same questions regarding functional symptoms before and after therapeutic intervention. The description of functional symptoms should be directed toward four primary areas: (1) lower urinary tract, (2) bowel, (3) sexual, and (4) other local symptoms.

Urinary Symptoms

This report does not supplant any currently approved ICS terminology related to lower urinary tract function [1]. However, some important prolapse-related symptoms are not included in the current standards (e.g., the need to manually reduce the prolapse or assume an unusual position to initiate or complete micturition). Urinary symptoms that should be considered for dichotomous, ordinal, or visual analog scaling include, but are not limited to, the following:

- Stress incontinence
- Frequency (diurnal and nocturnal)
- Urgency
- Urge incontinence
- Hesitancy
- Weak or prolonged urinary stream
- Feeling of incomplete emptying
- Manual reduction of the prolapse to start or complete voiding
- Positional changes to start or complete voiding

Bowel Symptoms

Bowel symptoms that should be considered for dichotomous, ordinal, or visual analog scaling include, but are not limited to, the following:

- Difficulty with defecation
- Incontinence of flatus
- Incontinence of liquid stool
- Incontinence of solid stool
- Fecal staining of underwear
- Urgency of defecation
- Discomfort with defecation
- Digital manipulation of the vagina or perineum to complete defecation
- Feeling of incomplete evacuation

Sexual Symptoms

Research is needed to attempt to differentiate the complex and multifactorial aspects of “satisfactory sexual function” as it relates to pelvic organ prolapse and pelvic floor dysfunction. It may be difficult to distinguish between the ability to have vaginal intercourse and normal sexual function. The development of satisfactory tools will require multidisciplinary collaboration. Sexual function symptoms that should be considered for dichotomous, ordinal, or visual analog scaling include, but are not limited to, the following:

- Is the patient sexually active?
- If she is not sexually active, why?
- Does sexual activity include vaginal coitus?
- What is the frequency of vaginal intercourse?
- Does the patient experience pain with coitus?
- Is the patient satisfied with her sexual activity?
- Has there been any change in orgasmic response?

Other Local Symptoms

We currently lack knowledge regarding the precise nature of symptoms that may be caused by the presence of a protrusion or bulge. Possible anatomically based symptoms that should be considered for dichotomous, ordinal, or visual analog scaling include, but are not limited to, the following:

- Vaginal pressure or heaviness
- Vaginal or perineal pain
- Sensation or awareness of tissue protrusion from the vagina
- Low back pain
- Abdominal pressure or pain
- Observation or palpation of a mass

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Appendix F

Good Urodynamic Practices: Uroflowmetry, Filling Cystometry, and Pressure–Flow Studies*

Werner Schaefer, Paul Abrams, Limin Liao, Anders Mattiasson, Francesco Pesce, Anders Spangberg, Arthur M. Sterling, Norman R. Zinner, and Philip van Kerrebroeck

INTRODUCTION

A good urodynamic practice comprises three main elements:

1. A clear indication for, and appropriate selection of, relevant test measurements and procedures
2. Precise measurement with data quality control and complete documentation
3. Accurate analysis and critical reporting of results

The aim of clinical urodynamics is to reproduce symptoms while making precise measurements in order to identify the underlying causes for the symptoms and to quantify the related pathophysiological processes. By doing so, it should be possible to establish objectively the presence of a dysfunction and understand its clinical implications. Thus, we may either confirm a diagnosis or give a new, specifically urodynamic, diagnosis. The quantitative measurement may be supplemented by imaging (videourodynamics).

Urodynamic measurements cannot yet be completely automated, except for the most simple urodynamic procedure—uroflowmetry. This is not an inherent problem of the measurement itself but is due to the current limitations of urodynamic equipment and the lack of a consensus on the precise method of measurement, signal processing, quantification, documentation, and interpretation. With the publication of this International Continence Society (ICS) standardization document on good urodynamic practice, it is expected that the necessary technological developments in automation will follow.

Urodynamics allows direct assessment of lower urinary tract (LUT) function by the measurement of relevant physiologic parameters. The first step is to formulate the "urodynamic question or questions" from a careful history, physical examination, and standard urologic investigations. The patient's recordings of micturitions and symptoms on a frequency volume chart, and repeated free uroflowmetry with determination of postvoid residual volume, provide important, noninvasive, objective information that helps to define the specific urodynamic question(s) prior to invasive urodynamics such as filling cystometry and pressure–flow studies.

Recommendations for good urodynamic practice are bullet pointed.

RECORDING MICTURITIONS AND SYMPTOMS

A micturition time chart records the time of each micturition. The usefulness of such a record is significantly enhanced when the voided volumes are recorded in a frequency volume chart. The bladder diary adds to this the relevant symptoms and events such as urgency, pain, incontinence, episodes, and pad usage. Recording for a minimum of 2 days is recommended. From the recordings, the average voided volume, voiding frequency, and, if the patient's time in bed is recorded, day/night urine production and nocturia can be determined. This information provides objective verification of the patient's symptoms, together with key values for plausibility control of subsequent urodynamic studies, for example, in order to prevent overfilling of the patient's bladder.

UROFLOWMETRY

Uroflowmetry is noninvasive and relatively inexpensive. Therefore, it is an indispensable, first-line screening test for most patients with suspected LUT dysfunction. Objective and quantitative information, which helps in the understanding of both storage and voiding symptoms, is provided by this simple urodynamic measurement.

Adequate privacy should be provided and patients should be asked to void when they feel a “normal” desire to void. Patients should be asked if their voiding was representative of their usual voiding and their view should be documented. Automated data analysis must be verified by inspection of the flow curve, artifacts must be excluded, and verification must be documented. The results from uroflowmetry should be compared with the data from the patient’s own recording on a frequency/volume chart. Sonographic estimation of postvoid residual volume completes the noninvasive assessment of voiding function.

Normal Uroflow

Normal voiding occurs when the bladder outlet relaxes (is passive) and the detrusor contracts (is active). An easily distensible bladder outlet with a normal detrusor contraction results in a smooth arc-shaped flow rate curve with high amplitude. Any other shapes—such as curves that are flat, asymmetric, or have multiple peaks (fluctuating and/or intermittent)—indicate abnormal voiding, but are not specific for its cause.

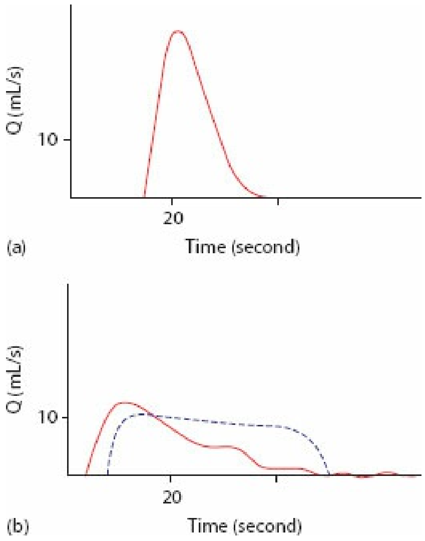


Figure F.1 (a) Typical normal flow; (b) constrictive flow curve (dotted line), compressive flow curve (solid line).

It is assumed that it is normal for the mechanical properties of a relaxed outlet to be constant, and that the properties can be defined by the dependency of the cross-sectional area of the urethral lumen on the intraurethral pressure at the flow rate controlling zone (FRCZ). Typically, below the minimum urethral opening pressure, the urethral lumen is closed. The lumen then opens widely with little additional pressure increase. With normal detrusor contractility and low intraurethral pressure, the normal flow curve is arc shaped with a high maximum flow rate (Figure F.1a).

A normal flow curve is a smooth curve without any rapid changes in amplitude because the shape of the flow curve is determined by the kinetics of the detrusor contraction that—arising from smooth muscle—does not show rapid variations. A decreased detrusor power and/or a constant increased urethral pressure will both result in a lower flow rate and a smooth flat flow curve. A constrictive obstruction (e.g., urethral stricture) with reduced lumen size results in a plateaulike flow curve (Figure F.1b, dotted line).

A compressive obstruction with increased urethral opening pressure (e.g., benign prostatic obstruction) shows a flattened asymmetric flow curve with a slowly declining end part (Figure F.1b, solid line).

The same pattern may also originate from a weak detrusor in aging males and females. Fluctuations in detrusor contractility or abdominal straining, as well as variable outlet conditions (e.g., intermittent sphincter activity), will lead to complex flow rate patterns.

Rapid changes in flow rate may have physiological or physical causes that are due either to changes in outlet resistance (e.g., sphincter/pelvic floor contraction or relaxation, mechanical compression of the urethral lumen, or interference at the meatus) or to changes in driving energy (e.g., abdominal straining). These intracorporeal causes lead to true flow rate changes. Rapid changes in flow rate may also be artifacts, when the flow rate signal is extracorporeally modified through interference between the stream and the collecting funnel (the flowmeter), movement of the stream across the surface of the funnel, or patient movements (see flow curves in Figures F.2 through F.7).

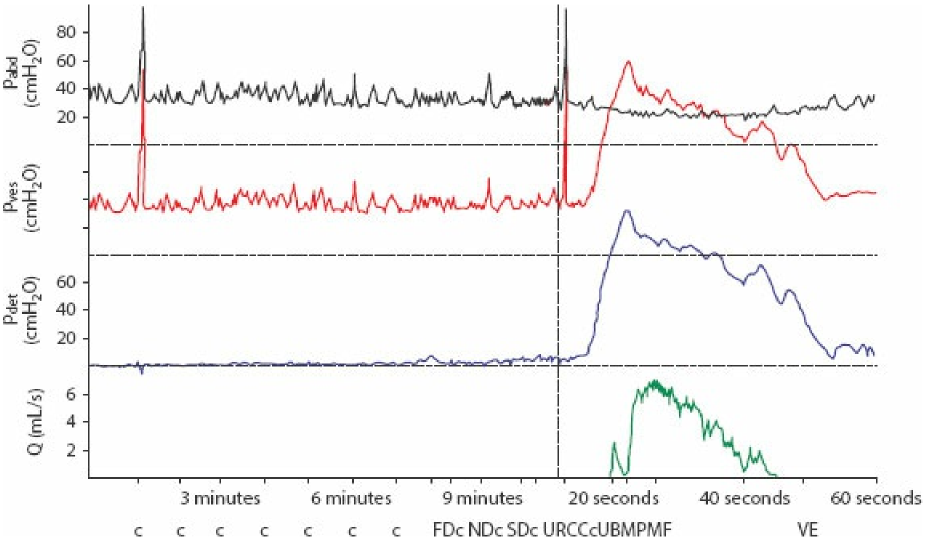


Figure F.2 Full recording of filling and voiding. Starting with initial values for p_{ves}, p_{abd} of 32 cmH_2O in the typical range for a standing patient with zero p_{det}; testing signal quality with a vigorous cough at the beginning, and regularly repeated (here less strong) coughs. Additionally, the pressure recordings show the typical pattern of a talking patient, while the p_{det} trace is unaffected; a weak contraction at first desire (FD); another vigorous cough before voiding; beginning of flow shows dyssynergic sphincter activity as proven by a decrease in flow with an increase in p_{det}.

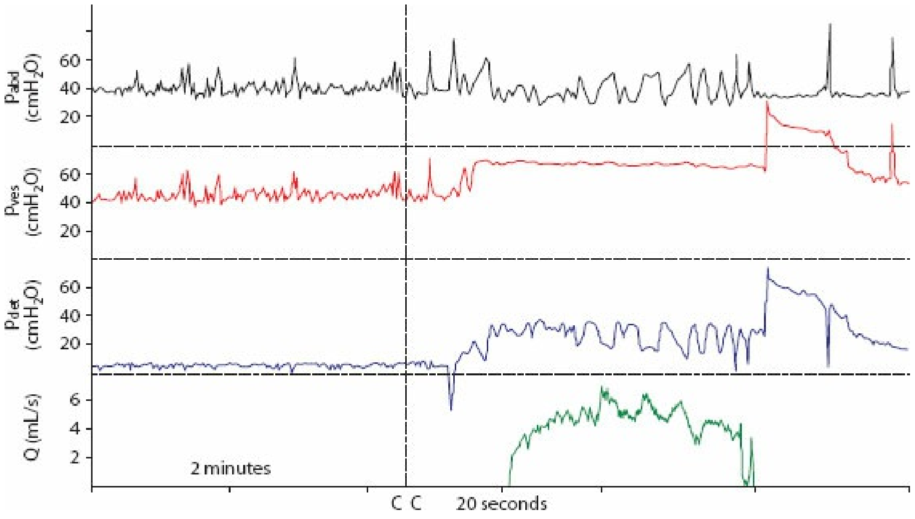


Figure F.3 Good recording quality until cystometric capacity is reached; at second cough before voiding the intravesical signal is lost (no response in p_{ves}, negative spike in p_{det}). Dead p_{ves}—signal during voiding, which is “live” again only at the second cough after voiding. Thus, pressure–flow study is lost. Careful observation of signals would have made it possible to interrupt the study immediately the signal failed and to correct this problem before voiding started.

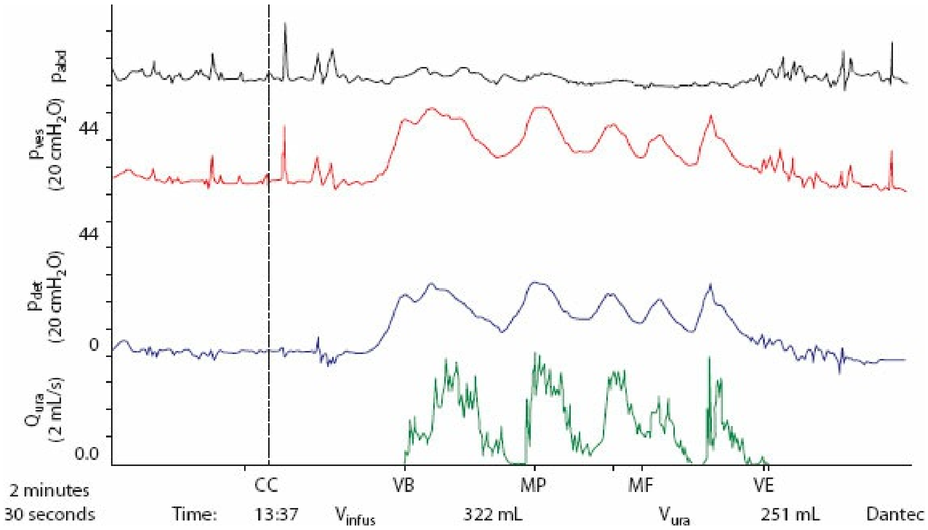


Figure F.4 Variable flow rate due to varying detrusor contraction strength (VO ID: 7/250/70). *Abbreviations*: CC, cystometric capacity; VB, void begins; MP, maximum pressure; MF, maximum flow; VE, void ends.

Accuracy of Uroflowmeters

Uroflowmetry measures the flow rate of the external urinary stream as volume per unit time in milliliters per second. The ICS Technical Report [1] made recommendations with respect to uroflowmetry, but did not compare different flowmeters by specific testing. There are, however, differences in the accuracy and precision of the flow rate signals that depend on the type of flowmeter, on internal signal processing, and on the proper use and calibration of the flowmeter. The desired and actual accuracy of uroflowmetry should be assessed in relation to the potential information that could be obtained from the urinary stream compared to the information actually abstracted for clinical and research purposes. Some relevant aspects of the physiological and physical information contained in the urinary stream are outlined here.

The desired clinical accuracy may differ from the technical accuracy of a flowmeter. The ICS Technical Report recommended the following standards: a range of 0–50 mL/s for Q_{max} and 0–1000 mL for voided volume, maximum time constant of 0.75 second, and an accuracy of ±5% relative to full scale, although a calibration curve representing the percentage error over the entire range of measurement should be made available. However, technical specifications from the manufacturers are rare and often not in accordance with ICS recommendations; this situation should be rectified.

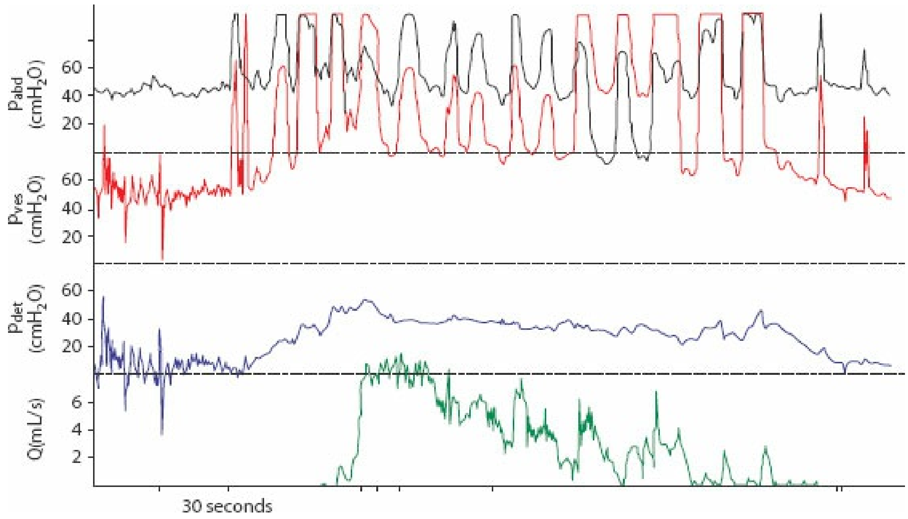


Figure F.5 The first part of the traces shows typical biphasic movement artifacts. The two coughs before voiding prove good recording quality. The typical picture of an unobstructed voiding: a weak detrusor

contraction with pdet of 40 cmH_2O and a Q_{max} of 9 mL/s is supported by vigorous straining, which causes some variability in flow (VO ID: 9/380/100).

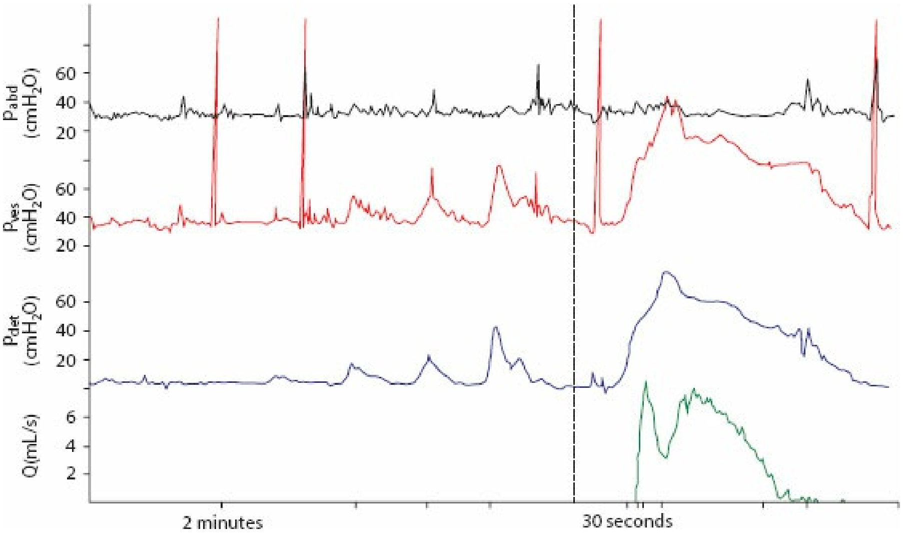


Figure F.6 A good recording showing the typical pattern of increasing detrusor overactivity and a dyssynergic event during voiding.

Furthermore, as most flowmeters are mass flowmeters (e.g., a weight transducer or rotating disk), variations in the specific gravity of the fluid will have a direct influence on the measured flow rate. For example, urine of high concentration may increase apparent flow rate by 3%. With x-ray medium, the flow rate may be overestimated by as much as 10%. These effects should be corrected by calibration software.

Thus, since the overall accuracy of flow rate signals will not be better than ±5%, it would not be meaningful to report a maximum flow rate of a resolution better than a full milliliter per second. Under carefully controlled research conditions, a better resolution may be possible by flowmeter calibration and instrument selection. However, such improvements in resolution may not be required for routine clinical applications. The dynamic properties of most flowmeters will be good enough for free uroflowmetry. When pressure–flow data are analyzed, however, the limitation in signal dynamics should be taken into account because pressure will be different from flow. Flow signals have a much slower response and are less accurate than pressure signals.

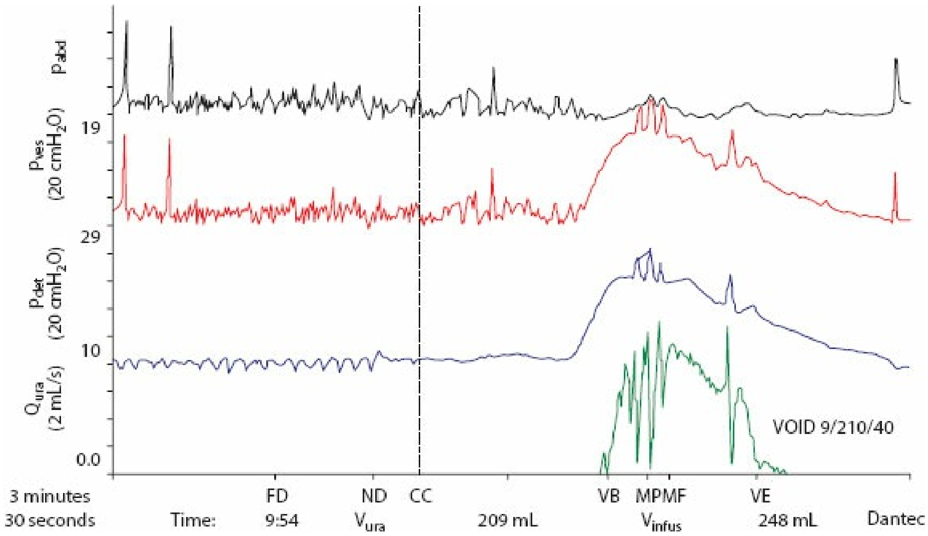


Figure F.7 High-quality recordings allow detailed interpretation. The typical pattern of rectal activity becomes clearly visible in p_{det}. The flow artifacts can be identified as dyssynergic events and manually

corrected from $Q_{max.raw}$ = 11.2 mL/s to Q_{max} = 9 mL/s. *Abbreviations*: CC, cystometric capacity; FD, first desire; ND, normal desire; MP, maximum pressure; MF, maximum flow; VB, void begins; VE, void ends.

Problems in Urine Flow Rate Measurement

The problems in measurement, as well as the information that can be abstracted from the flow rate signal, are rather different for free uroflowmetry compared to combined pressure–flow recordings.

In free uroflowmetry, the shape of the flow curve may suggest specific types of abnormality; however, reliable, specific, and detailed information about the cause of abnormal voiding cannot be derived from a flow curve alone. Only when uroflowmetry is combined with intravesical and abdominal pressure (p_{abd}) recordings does it become possible, from the pressure–flow relationship, to analyze separately the contributions of detrusor contractility and bladder outlet function to the overall voiding pattern (Figures F.2 through F.7).

Urine flow rate measurement is affected by a number of important factors.

Detrusor Contractility

As the voiding function reflects the interaction between the relaxed outlet and the contracting detrusor, variation of both will affect the flow. For steady outflow conditions, all variations in flow rate are related to changes in detrusor activity alone. The detrusor contraction strength varies neurogenically and myogenically, and can cause significant variability in urine flow rate measurements (Figure F.4).

Bladder Outflow Resistance

If detrusor contractility is constant, then changes in outflow resistance will lead to changes in flow rate, for example, in patients with detrusor–sphincter dyssynergia (Figures F.2, F.6, and F.7).

Bladder Volume

As the bladder volume increases and the detrusor muscle fibers become more stretched, there is an increase in the potential bladder power and work associated with a contraction. This is most pronounced in the range from empty up to 150–250 mL bladder filling volume. It appears that, at volumes higher than 400–500 mL, the detrusor may become overstretched and contractility may decrease again. Therefore, Q_{max} is physiologically dependent on the bladder volume. This dependency will vary between individuals and with the type and degree of pathology; for example, in constrictive obstruction, Q_{max} is almost independent of volume, and in compressive obstruction, the dependency becomes weaker with increasingly obstructed outlet conditions and lower flow rate.

Technical Considerations

The flow rate signal is influenced by the technique of measurement and by signal processing. The external urinary stream should reach the flowmeter unaltered and with minimal delay. However, any funnel or collecting device, as well as the flowmeter, will inevitably introduce modifications to the flow rate recording. Physically, the external urinary stream breaks into drops not far from the meatus. This fine structure of the stream has a high frequency, which can be assessed by drop spectrometry, and contains interesting information. For standard uroflowmetry, however, such high frequencies should be eliminated by signal processing.

For free uroflowmetry, all intracorporeal modulations of the flow rate are physiologic artifacts and should be minimized (e.g., by asking the patient to relax and not to strain). Nevertheless, certain dynamic patterns of intracorporeal modulations can provide information about functional obstruction (e.g., typical patterns of detrusor–sphincter dyssynergia or abnormal straining). This information may be lost by excessive filtering or during analog to digital (A/D) conversion with a filter speed of <10 Hz. The precise interpretation of dynamic variations in the flow rate signal is only possible when the flow rate is viewed together with the simultaneously recorded pressure signals. Thus, only in combined pressure–flow recordings can the details of the flow signal be fully understood.

For the determination of the “true” maximum flow rate value, particularly during free flow, such high-frequency signal variations are more likely to be misleading, and consequently they should be suppressed electronically.

Recommendations for Uroflowmetry

In order to facilitate the recording of urine flow rate and pattern recognition of flow curves, it is recommended that graphical scaling should be standardized as follows: 1 millimeter should equal 1 second on the x-axis and 1 mL/s and 10 mL voided volume on the y-axis.

With respect to the technical accuracy of uroflowmeters, it is meaningful for routine clinical measurements to read flow rate values only to the nearest full milliliters per second and volumes to the nearest 10 mL.

In order to make electronically read Q_{max} values more reliable, comparable, and clinically useful, we recommend internal electronic smoothing of the flow rate curve. It is recommended that a sliding average over 2 seconds should be used to remove positive and negative spike artifacts.

If curves are smoothed by hand, the same concept should be applied. That is, when reading Q_{max} graphically, the line should be smoothed by eye into a continuous curve so that in each period of 2 seconds, there are no rapid changes. Such a smoothed, clinically meaningful maximum free flow Q_{max} will be different (lower) from the peak value in the flow rate recording of electronic instruments currently available (Figures F.4, F.5, F.7, and F.8).

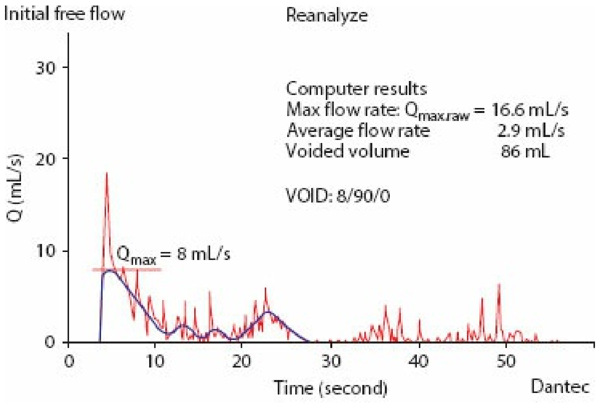
It is recommended that only flow rate values that have been “smoothed,” either electronically or manually, should be reported.

If a maximum flow value is determined electronically by simple signal peak detection without the recommended electronic smoothing, it should be labeled differently—$Q_{max.raw}$. Such raw data have meaning only if a detailed specification of the type of flowmeter used is given.

The interpretation of any dynamic variation (signal patterns) in free flow will rely on personal experience, can be only descriptive, and in general will remain speculative.

For the documentation of the results of uroflowmetry, the following recommendations are made:

- Maximum (smoothed) urine flow rate should be rounded to the nearest whole number (a recording of 10.25 mL/s would be recorded as 10 mL/s).
- Voided volume and postvoid residual volume should be rounded to the nearest 10 mL (a recording of a voided volume of 342 mL would be recorded as 340 mL).



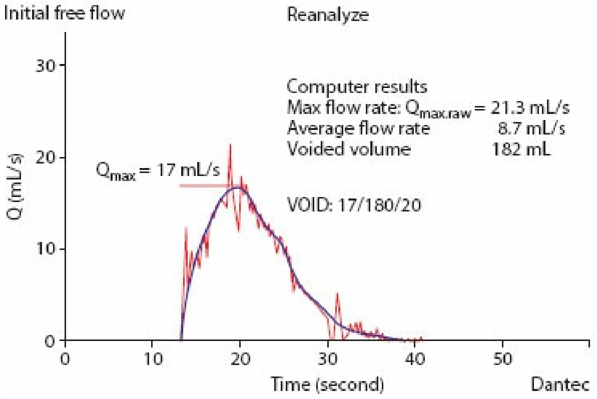


Figure F.8 Exclusion of artifactual spikes in the flow curve, $Q_{max.raw}$, and determination of a clinically relevant maximum flow rate, Q_{max}, by manual smoothing. The results from uroflowmetry should be reported in the standard format: $Q_{max}/V_{void}/V_{res}$.

- The maximum flow rate should always be documented together with voided volume and postvoid residual volume using a standard format (VOID: maximum flow rate/volume voided/postvoid residual volume).

For example, the automatically detected flows, $Q_{max.raw}$, are 16.6 and 21.3 mL/s with voided volumes of 86 and 182 mL, respectively. The smoothed Q_{max} values are 8 and 17 mL/s and should be reported with voided volumes of 90 and 180, respectively, and the estimated residuals as VOID1 = 8/90/0 and VOID2 = 17/180/20 (Figures F.4, F.5, and F.8).

The adoption of these standards will aid the interpretation of uroflowmetry results. If data are not available, then a minus sign should be used;, for example, if only the voided volume is known, VOID = −/340/−, or if the voided volume was missing, VOID = 10/−/90.

- If a flow/volume nomogram is used, this should be stated and referenced.

Uroflowmetry data from other than free flow (e.g., measured in combination with intravesical pressure) should be reported with an additional descriptive index, p, that is, Q_{maxp}, for pressure–flow recording.

INVASIVE URODYNAMICS: FILLING CYSTOMETRY, PRESSURE–FLOW STUDY OF VOIDING

Introduction

Invasive urodynamic procedures should not be performed without clear indications and the formulation of specific urodynamic question(s). This process will usually be aided by the a priori completion of a frequency volume chart and free uroflowmetry. There are certain key recommendations that will lead to the performance of a successful urodynamic study: First, a good urodynamic investigation should be performed interactively with the patient. It should be established by discussion with the patient that the patient's symptoms have been reproduced during the test. Second, there should be continuous and careful observation of the signals as they are collected, and the continuous assessment of the qualitative and quantitative plausibility of all signals. Third, artifacts should be avoided, and any artifacts that occur should be corrected immediately. It is always difficult and is often impossible to correct artifacts during a retrospective analysis. Furthermore, it is more time-consuming than if the signals are continuously observed and tested at regular intervals and artifacts recognized during the urodynamic study and corrected.

At present, ambulatory urodynamic monitoring has to rely on retrospective quality control and artifact corrections. However, in principle, the same quality criteria apply for ambulatory urodynamic monitoring as for standard urodynamics [2]. This makes a consensus on quality even more important, because only when such criteria are precisely defined can they be implemented in an "automated intelligent" ambulatory system.

Quality control relies on pattern recognition and a knowledge of normal values as well as prior identification of useful information obtained from noninvasive urodynamics and all other sources relevant for the urodynamic question. Thus, before invasive urodynamics, a frequency volume chart should be completed. Useful information obtained from noninvasive testing includes typical voided volumes and postvoid residual volumes as well as the expected values for Q_{max}. This information should be used for the control of subsequent invasive studies. Only by good preparation can it be ensured that (1) the proper answers to the urodynamic questions will be obtained before the study is terminated and (2) essential modifications, additions, or repetitions of measurements will have been performed in order to derive the necessary information.

The effective practice of urodynamics requires (1) a theoretical understanding of the underlying physics of the measurement, (2) practical experience with urodynamic equipment and procedures, (3) an understanding of how to ensure quality control of urodynamic signals, and (4) the ability to analyze critically the results of the measurements. Because urodynamics deals largely with mechanical measurements such as pressure and volume and their related changes in time, and because many analytical models use mechanical concepts such as resistance to flow or contraction power, it is essential that the nature of these measurements and concepts, in particular for pressure and flow rate, are understood. Therefore, in addition to a comprehensive understanding of anatomy and physiology, some basic knowledge of biomechanics and physics is required.

The quality control of urodynamic measurements must be approached on a holistic basis. Different types and levels of data quality and plausibility control should be used (1) on a physical and technical level, (2) on a biomechanical level, and (3) on a pathophysiological clinical level. A common problem in urodynamics is that clinicians often proceed immediately to a clinical interpretation, that is, to level 3, without a critical analysis of the potential pathophysiologic information content, without considering the plausibility of the signals (level 1), without considering the biomechanical context of the measurements (level 2), and without taking into account the physical properties of the parameters, technical limitations, and accuracy of the signals. Therefore, it is recommended that invasive urodynamics should not be performed without precise indications and well-defined "urodynamic questions" that are to be answered by the results of the urodynamic study.

Measurement of Urine Flow Rate during Pressure–Flow Studies

The usefulness of the concept of a FRCZ for data analysis requires that the recorded pressure and flow rate signal be synchronized with respect to the FRCZ [3]. Normally, no measurable time delay will exist between the intravesical pressure signal and the actual flow at the FRCZ. However, a significant delay is to be expected for the typical urodynamic flow rate recorded extracorporeally. This delay will vary with anatomy, pathology, flow rate, and the setup for measurement. Our understanding of the actual dynamics of flow rate changes is limited, and the relatively slow response of most flowmeters may not be sufficient to match the dynamics of the much faster pressure signal. The actual time difference may be from 0.5 to 2 seconds; the time delay between urethral closure and the end of any flow recording may be much longer, particularly in prostatic obstruction and terminal dribbling than between the opening of the urethra and the start of a flow rate signal. Therefore, we recommend the use of more descriptive terminology for synchronizing pressure and flow values, such as $p_{det.Qbeg}$ for the pressure at which flow begins instead of $p_{det.open}$, and $p_{det.Qend}$ when flow ends instead of $p_{det.close}$. The time delay correction needs to be considered when analyzing pressure–flow studies [3].

On average, the maximum flow rate recorded during pressure–flow studies ($Q_{max.p}$) is lower than during free flow (Q_{max}). This, however, is not due simply to a mechanical increase of outflow resistance by the intraurethral catheter, because such a difference is also found in suprapubic pressure–flow studies. A difference has also been reported between $Q_{max.p}$ during conventional and ambulatory urodynamics. This indicates more complex causes, possibly psychogenic, but also physiologic, for example, that a difference in detrusor contraction strength may be involved, and that the fast filling rate used in clinical studies may lead to reduced contractility. This could also explain the difference in results between conventional and ambulatory studies.

Measurement of Intravesical and Abdominal Pressure

It is recommended that there is strict adherence to the ICS standardization of zero pressure and reference height. Only then can pressure recordings be compared between patients and centers.

Zero pressure and reference height are concepts that are often confused in urodynamics, for example, by use of the misleading term "zero reference height." As both are independent features of pressure, they must be considered separately, and both must follow recommended ICS methodology:

- Zero pressure is the surrounding atmospheric pressure. Zero pressure is the value recorded when a transducer is open to the environment when disconnected from any tubes or catheters, or when the open end of a connected, fluid-filled tube is at the same vertical level as the transducer. Only then can a "set zero" or "balance" be performed.
- The reference height is defined as the upper edge of the symphysis pubis. The reference height is the level at which the transducers must be placed so that all urodynamic pressures have the same hydrostatic component. It is often argued that it does not make a difference for the most relevant parameter, p_{det}, if the same error is introduced to p_{ves} and p_{abd}, as they tend to cancel each other out. This is not an acceptable argument. The hydrostatic pressure is real and important, and

inevitably plays a role in any intracorporeal pressure recording. Many important aspects of quality and plausibility control, such as typical resting value ranges at different patient positions, are based on the proper recording of pressures, and will not apply if pressures are not recorded according to ICS standards. Also, it is only meaningful to subtract one pressure from the other—for example, ($p_{ves} - p_{abd} = p_{det}$)—when both are recorded to the same reference level.

Pressure Transducers

Urodynamic techniques are developed using external pressure transducers connected to the patient with fluid-filled lines, allowing easier compliance with the standards of correct zero and reference height. Catheter-mounted pressure transducers, so-called microtip transducer catheters, have become popular due to their apparent higher accuracy, better dynamic resolution, and their apparent independence from hydrostatic pressure. A catheter-mounted pressure transducer is an advantage for dynamic recordings of urethral pressures during coughing (stress profiles) as well as for ambulatory urodynamics in mobile patients. Here, only the application of catheter-mounted pressure transducers for intravesical and p_{abd} recordings will be discussed as urethral pressures are dealt with in a separate report [4].

All aspects of urodynamic pressure recording outlined in the preceding section are valid and independent of transducer type. It is impossible to define the precise position of an intravesical and a rectal catheter-mounted pressure transducer as to place them at any common level, and impossible to position them at the standard level of the upper border of the symphysis pubis. It has become popular to circumvent this problem by setting the catheter-mounted pressure transducer to zero pressure when inside the body at the start of pressure recording. This, however, means that both the standard zero pressure as well the reference level are ignored, so that such recorded pressure cannot be compared between patients or centers. The fact is that the initial intravesical and abdominal resting pressures are real, are different between patients, and depend significantly on the patient's position. Thus, there are significant potential errors: By ignoring the correct atmospheric zero pressure, an error of up to 50 cmH_2O can occur, and as the reference height of catheter-mounted pressure transducers is usually undetermined, another potential error of 10 cmH_2O is possible for a full bladder. In addition, when a study starts with zero p_{abd}, then the commonly observed p_{abd} decrease at pelvic floor relaxation during voiding will result in negative p_{abd} values, and thus in p_{det} being higher than p_{ves}.

The same problem of apparent independence from the existing hydrostatic pressure also applies to air-filled catheters and/or connection tubings. Due to the absence of a water column between the balloon-covered opening on the catheter and the external transducer, the reference height in an air-filled system will refer to the position of the sensing balloon on the catheter and not to the external transducer.

It is recommended that external transducers connected to fluid-filled tubings and catheters be used for intravesical and p_{abd} recording. If microtip or air-filled catheters are used, any deviation from standard zero and reference level should be minimized and taken into account at the time of data analysis.

Urodynamic Catheters

Comparison between patients and urodynamic studies performed in different centers would be facilitated by the use of standard catheters. It is recommended that for the measurement of intravesical pressure and for bladder filling, the standard catheter for routine urodynamics is a transurethral double-lumen catheter.

Only in small children and patients with severe constrictive obstruction (stricture) does suprapubic pressure recording have clear advantages. Intraurethral catheters should be as thin as possible, limited only by the practicality of insertion and by internal lumen sizes, which should be sufficiently large to avoid excessive damping of pressure transmission and to achieve the desired filling rate with standard pumps. A 6 Fr double-lumen catheter is the smallest practical size at present.

The major advantage of a double-lumen catheter is that the fill/void sequence can be repeated without the need for recatheterization. Note that the use of a 6 Fr double-lumen catheter can limit the infusion rate during cystometry to 20–30 mL/min, as a typical roller pump may not manage to transport a higher perfusion rate through such a small lumen. This can result in an incorrect filling volume being indicated by the machine when the filling volume is calculated from the pump setting. For example, with a filling rate set at 60 mL/min and an actual filling rate of 30 mL/min, the machine will show double the filling volume. Thus, after voiding, a high calculated residual will occur. With some equipment, higher filling rates are possible; it is essential that any system should be critically tested to (1) measure the maximum filling rate that can be achieved by a particular catheter attached to an individual pump and (2) correct or calibrate the indicated infused volume.

The use of two separate tubes for filling and recording is less convenient. Removing the larger filling tube for voiding may appear to be an advantage because only a single small tube is left in the urethra. However, there are no data to suggest that, for example, in a compressive obstruction such as benign prostatic obstruction, a 6 Fr catheter has a detrimental influence on the pressure or flow data. There are, however, data suggesting that results from a single study may be misleading. A double-lumen catheter facilitates a second fill/void study to establish reproducibility. Reintroduction of the separate filling tube for a repeated study is more invasive and complicated.

- The use of rectal balloon catheter is recommended for the measurement of p_{abd}.

Although there are various methods for the successful recording of p_{abd}, a flaccid, air-free balloon in the rectal ampulla gives a suitable signal for p_{abd} to determine a meaningful p_{det} when p_{ves} is measured synchronously ($p_{det} = p_{ves} - p_{abd}$). In females, vaginal recording may be more acceptable and provides comparable results. The recording of p_{abd} allows the measurement of any abdominal (i.e., perivesical) pressure component during changes in intravesical pressure. The role of the balloon is to maintain a small fluid volume at the catheter opening and to avoid fecal blockage, which can prevent or impair pressure transmission to the transducer. Additionally, as the rectal ampulla and the vagina are not homogeneously fluid-filled spaces, the balloon prevents pressure artifacts arising from contact between the catheter opening and the wall tissue. The balloon serves this function best when it is filled to only 10%–20% of its unstretched capacity. Overfilling and elastic distension of the balloon is the most common mistake in p_{abd} recording. The resultant high balloon (not abdominal) pressure will produce a misleading pressure reading. Such an artificially elevated balloon distention pressure can be avoided by making a small hole in the balloon, although this is unnecessary if the balloon is filled properly as described earlier. It is also possible to record reliable p_{abd} with a very slowly perfused (<2 mL/min) open-ended catheter. However, excessive fluid volume in the rectal ampulla may cause problems.

Equipment: Minimum Requirements for Filling Cystometry and Pressure–Flow Studies of Voiding

The ICS has not yet specified definite technical standards in respect of minimum requirements for filling cystometry and pressure–flow studies beyond the ICS Technical Equipment Report [1] and the appendix to the ICS document on pressure flow [3], where a data exchange software standard is recommended. Some further aspects will be discussed in more detail here.

Equipment Recommendations

The minimum recommended requirements for a urodynamic system are as follows:

- Three measurement channels—two for pressure and one for flow.
- A display (on printer and/or monitor) and secure storage of three pressures (p_{abd}, p_{ves}, p_{det}) and flow (Q) as tracings against time.
- Infused volume and voided volume may be shown graphically or numerically.
- Online display of pressures and flow, with adequate scale and resolution; scales must be clearly given on all axes; no information should be lost electronically when tracings go off-scale on display.
- Possibilities to record standard information about sensation and additional comments (event recordings).

Meaningful plausibility assessment and quality control are possible only when the measured and derived signals are displayed continuously as curves over time, without delay (in real time), as the examination proceeds. Each displayed curve and number should be labeled according to ICS standards, with clear scaling of amplitudes and the time axis. The following sequential position of tracings is suggested: p_{abd} at the top, then p_{ves}, p_{det}, and Q (Figures F.2 through F.7). It is least important when p_{abd} goes off-scale and is cut off (Figure F.5). Additional parameters such as electromyography (EMG), bladder filling, and voided volumes can be displayed either as curves or digitally as numbers.

The following minimum technical specifications are recommended:

- Minimum accuracy should be ±1 cmH_2O for pressure and ±5% full scale for flow and volume.
- Ranges of 0–250 cmH_2O, 0–25 (50) mL/s, and 1000 mL for pressure, flow, and volume, respectively.
- The software must ensure that no information for pressures up to 250 cmH_2O and for flow rates up to 50 mL/s is lost internally, even when not displayed, and that off-scale values are clearly identified.
- An A/D frequency of 10 Hz per channel as the lower limit for pressure and flow.
- A higher frequency (minimum 20 kHz) is necessary for recording EMG.
- Calibration of all measurements should be possible.

The scalings should be kept unchanged as much as possible, because urodynamic data quality control is based on pattern recognition, and the recognition of patterns depend on scaling. Therefore, it is recommended that during recording and for analysis, minimum scaling for pressure should be of 50 cmH_2O/cm, for flow 10 mL/s/cm, and for the time axis 1 min/cm or 5 s/mm during filling and 2 s/mm during voiding.

To enable a retrospective judgment of the curves, urodynamic measurements should be documented as curves over time with comments and explanations. It is usually insufficient to document urodynamic measurements by a few numerical values alone. The same amplitude of scaling should be used for all documentation, although the time axis may be compressed. Only if there is no relevant information to be lost by reducing resolution (e.g., during filling), the time scale can be compressed.

For a printout, maximum full-scale deflections of 200 cmH_2O, 50 mL/s, and 1000 mL are sufficient for pressure, flow, and volume, respectively. In most cases, half the maximum full scale will be sufficient to show all relevant parts of curves. Line resolution should be better than 0.10 mm.

During interventions (e.g., interruption of bladder filling or manipulation of catheters), the continuation of both measurement and recording must always be possible.

Online recording of comments should be possible, to complete the documentation.

Calibration of Equipment

The need to calibrate pressure transducers, flowmeters, and pumps cannot be stated simply as “yes” if there is a need or “no” if there is not. The specification of the manufacturer should be studied. Two aspects must be considered: the intended accuracy of the system and the investigator’s experience with the system. If a new system is installed or new transducers are being used, it is recommended that regular calibration be carried out. If experience with daily calibration shows that the potential error is small (e.g., <2 cmH_2O), then it will be sufficient to calibrate once a month. However, calibration should not be ignored and good urodynamic equipment makes it technically possible to perform a calibration. Calibration should not be confused with simple “zero balancing,” which is only one part of calibration. In addition to setting the zero, it must be possible to check and adjust the amplitudes of all measurement channels, that is, to calibrate all signals.

Calibration of a flowmeter can be achieved by pouring a precisely measured volume at a constant flow into the flowmeter, typically 400 mL in 20–30 seconds (at 15–20 mL/s), and checking the recorded volume. Special constant flow rate bottles are available for flow calibration. Similarly, one can test a pump by measuring the time to deliver a known volume (e.g., 100 mL) into a measuring cylinder. It is recommended that pump calibration be performed with the filling catheter connected. Such a pump calibration can only be as good as the cylinder used, which needs to have good resolution and be accurate. Some measuring beakers usually available in clinics are not accurate.

Pressure Signal Quality Control: Qualitative and Quantitative Plausibility

It is very important to observe and to test signals carefully and to correct any problems before starting the urodynamic study. If the signals are perfect at the beginning of the study, they usually remain so without the need for major intervention. If the signals are not perfect, remedial action must be taken. If a quality problem does not disappear at once, when filling commences, it will usually deteriorate further during the study.

Conscientious observation of the patient and of the signals, in particular p_{det}, during all parts of the study, together with continuous signal testing, are the keys to high-quality urodynamics. The first aim is to avoid artifacts and the second to correct the source of all artifacts immediately they occur.

The following three criteria form the minimum recommendations for ensuring quality control of pressure recordings:

1. Resting values for abdominal, intravesical, and detrusor pressure are in a typical range (see in the following text).
2. The abdominal and intravesical pressure signals are “live,” with minor variations caused by breathing or talking being similar for both signals; these variations should not appear in p_{det}.
3. Coughs are used (every 1 minute or, for example, 50 mL filled volume) to ensure that the abdominal and intravesical pressure signals respond equally. Coughs immediately before voiding and immediately after voiding should be included.

When standards are followed, that is, with the transducer zeros set to atmospheric pressure and the transducers placed at the level of the upper edge of the symphysis, the typical ranges for initial resting pressure values for p_{ves} and p_{abd} are as follows (Schäfer, unpublished communications):

- Supine 5–20 cmH_2O
- Sitting 15–40 cmH_2O
- Standing 30–50 cmH_2O

Usually both recorded pressures are almost identical, so that the initial p_{det} is zero, or close to zero, that is, 0–6 cmH_2O in 80% of cases and in rare cases up to 10 cmH_2O [5].

All initial pressure values should be verified and the patient’s position should be documented on the urodynamics trace.

All negative pressure values, except when caused by rectal activity, should be corrected immediately. It should always be kept in mind that p_{abd} is recorded not in order to ascertain the actual rectal pressure but to eliminate the impact of (abdominal) pressure changes on p_{ves}. The principal aim is to determine the p_{det}, which is the pressure in the bladder without the influence of p_{abd}. Therefore, p_{det} cannot be negative.

By talking to the patient during the study, the proper dynamic response in the pressure signals can be observed and is “automatically” documented (Figures F.2, F.3, and F.7).

Problem Solving

If either detrusor or rectal contractions occur, the recorded pressures in p_{ves} and p_{abd} will be different. Such changes can be identified and interpreted with sufficient accuracy and reliability only when the patient is observed and the relation between signal changes and patient sensation/activity are checked for plausibility and documented. Any pressure change caused by smooth muscle contractions will show a “smooth” pattern (Figures F.4, F.6, and F.7), that is, there should be no rapid (“stepwise”) changes (Figure F.3). If pressures increase or decrease stepwise, or with a constant slope over a long period of time, a nonphysiologic cause, such as catheter movement, should be considered.

If a sudden drop or increase occurs in either the p_{ves} or the p_{abd} signal, the usual cause is the movement, blockage (Figure F.3), or disconnection of a catheter. When the patient changes position, sudden changes in resting values occur and are seen equally in both pressure signals. If p_{ves} (without change in p_{abd}) increases slowly—as is typical for a low-compliance bladder—it is important to test for any other possible cause for a slow pressure increase. One cause could be a problem with the intravesical catheter measurement; for example, the hole for the pressure conducting lumen is slowly moving into the bladder neck region. This should be assessed by asking the patient to cough, if there is no other apparent artifact. Furthermore, it is recommended that bladder filling is stopped if the filling rate is above a physiological limit of 10 mL/min. If the value of p_{ves} drops after filling is stopped, it is likely that “low compliance” was, at least in part, related to fast filling.

There are several common problems that must be solved before the study is started or when observed during a study:

- *Problem*: Initial resting p_{det} is negative, for example, −5 cmH_2O.
    - *Possible explanation*: The p_{abd} is too high.
    - *Solution*: If p_{ves} is in the typical range, and both pressures are “live,” open the valve in the abdominal line and drain one or two drops from the rectal balloon filling volume. This will usually cause p_{abd} to fall to a proper value. If not, gently reposition the rectal balloon and/or make a small hole in the balloon.
    - Because p_{ves} is too low.
    - *Solution*: This may be due to air bubbles trapped in the catheter, the catheter not being in the bladder, or the catheter being blocked/kinked. Gently flush through the p_{ves} line (maximum 10 mL). It is very important to flush slowly while observing the pressure signal because pressures above 300 cmH_2O may damage the transducer. If this does not solve the problem, add some more volume to the bladder via the filling lumen. If resistance to filling is high and it does not drain easily when opened, it will be necessary to check the catheter position, and to reposition the catheter, if necessary.
- *Problem*: Initial p_{det} is too high, for example, 15 cmH_2O.
    - *Possible explanations*: (1) The key problem here is indicated by the measurement of 15 cmH_2O. The situation is different from the clear statement that “p_{det} cannot be negative” as we do not have a definite upper limit for the normal maximum “resting” value for p_{det}. Thus, we can only follow the present guidelines that, in most tests in an empty bladder, p_{det} is between 0 and 5 cmH_2O, and in some 90%, it is between 0 and 10 cmH_2O. For any higher value, stringent plausibility checking must be applied. If the patient has no detrusor overactivity, a p_{det} of 15 cmH_2O is unlikely to be valid and there may be a signal problem. First check if p_{abd} and p_{ves} are in the expected ranges. For example, if, in a standing patient, initial p_{ves} is 30 cmH_2O and p_{abd} is 15 cmH_2O, then by experience the value of p_{abd} is too low (because p_{abd} is too low). If in a supine patient p_{abd} is 10 cmH_2O and p_{ves} is 25 cmH_2O, then the value of p_{ves} is too high (because p_{ves} is too high). Check the zero balance and proper signal response to coughing for both signals. (2) The p_{abd} is too low.
    - *Solution*: Very slowly flush the rectal balloon with 1 or 2 mL. o Because p_{ves} is too high.
    - *Solution*: This problem can be related to a misplaced catheter, a kink in the catheter, or contact with the bladder wall in an empty bladder, which occludes the eyehole(s) of the catheter. Proceed according to the solution of p_{ves} being too high, in the first aforementioned example.
    - If no signal problems can be identified, the clinical study may be started, but the p_{det} signal deserves particular attention. If compliance is normal and the bladder normal at filling, then it is very important to record and check, for some period after the micturition, the postvoiding resting value of p_{det}. Only if an elevated p_{det} is perfectly reproducible for repeated filling and voiding studies can it be accepted. However, it is most likely that a high resting p_{det} will not be reproducible and will be corrected by the measures described earlier.
    - In summary, if any resting value or cough response does not fit the usual values or patterns, it should be corrected before bladder filling is started. If this is not possible, the signals must be observed even more carefully and every effort made to reveal the potential source of error or artifact during the study.

Retrospective Artifact Correction

In principle, a good p_{det} signal requires only that p_{ves} and p_{abd} show the same fine structure and quality of signals before filling, during filling, and after a voiding (Figures F.2, F.3, F.6, and F.7). Both p_{ves} and p_{abd} must have the same zero and reference level. The most common mistake is to set (balance) the initial pressure values of p_{ves} and p_{abd} to zero with the catheters connected to the patient instead of setting zero to atmospheric pressure. This results in incorrect p_{ves} and p_{abd}. If this is done, urodynamic studies cannot be compared between centers and between patients. Although it may seem convenient and easy to start with a value of p_{det} as zero, this practice will lead to problems later in the test. As soon as pelvic floor relaxation occurs, which is particularly common during voiding, the value of p_{abd}, if starting at zero, becomes negative. With a negative pabd, p_{det} will be higher than p_{ves}, a conceptually meaningless result. Furthermore, it will then be impossible to correct a negative p_{abd}. Cough tests at regular intervals, particularly before and after voiding, document the dynamic response of the pressure channels and are fundamentally important.

A typical physiological artifact that can be easily recognized is a rectal contraction. Rectal contractions are usually of low amplitude and may or may not be felt by the patient (Figure F.7). The value of p_{abd} shows a phasic rise with no change in the p_{det} signal—a potentially confusing fall in p_{det} results from the electronic subtraction, but this is, of course, an artifact. Usually, rectal contractions are relevant only because they may be misinterpreted as detrusor overactivity (Figure F.7); they have no relevance to voiding.

Biphasic spikes as a response to cough tests are another example of artifacts that are easy to correct. However, any other artifacts—such as a signal that is nonresponding (dead), has stepwise changes in pressure, or has negative pressures—often cannot be corrected or can be corrected only with extensive speculation about the underlying causes of the problem. Studies with such artifacts should be repeated (see the next section).

Retrospective corrections require the same strategies for plausibility control as during recording, but are then much more difficult and less successful to perform.

A few common artifacts (e.g., rectal activity, biphasic spikes at cough tests, or insufficient p_{abd} response during straining) can be accepted during the study as they can be corrected retrospectively. Usually, this is easier to do manually than through a computerized system.

Urodynamic Computer Software

Computer applications should allow the easy use of even the most complicated analytical algorithms. However, most of the software offered by the urodynamic equipment industry is neither original nor validated. The software may, in fact, not do what the original developer(s) of the algorithm intended. Therefore, it is recommended that when analytical urodynamic software is used to perform data analysis according to any published concept, the source of the software should be specified. It should also be clearly stated if the software has been validated, that is, proven to provide results consistent with the algorithms to which the analyses are attributed.

STRATEGY FOR REPETITION OF URODYNAMIC TESTS

- It is recommended that a urodynamic test should be repeated if the initial test suggests an abnormality, leaves the cause of troublesome LUT symptoms unresolved, or if there are technical problems preventing proper analysis.

It may not be necessary, however, to repeat a study that, beyond any doubt, confirms the expected pathology, for example, detrusor overactivity that correlates with the patient’s symptoms. However, if the study is inconclusive, then the consequences of not finding a clear answer to the urodynamic question(s) should be considered. If an invasive therapy is planned, the urodynamics should be repeated. Therefore, it is necessary to analyze the signals during the study and document the study immediately upon its conclusion. Only then is it possible to be sure that the urodynamic study is of a quality that answers the urodynamic question and provides an understanding about the patient’s clinical problem. Therefore, it is recommended that the urodynamic findings and the interpretation of the results should be documented immediately after the study is finished, that is, before the patient has left the urodynamic laboratory, thus allowing for a second test if required.

The analysis of a good study is easy and straightforward. Indeed, an easy analysis is actually the key criterion for good urodynamics. A good study is one that is easy to read and one from which any experienced urodynamicist will abstract the same results and come to the same conclusions. For computerized analyses, high data quality is even more important than for manual graphical data analysis. The future development of urodynamic equipment and software should force investigators to conduct proper online data quality control. Analysis of ambulatory studies will remain problematic, as it is less easy to conduct online assessment of quality, and analysis is time-consuming. Hence, it will be necessary to ask the patient to return, on another occasion, should the investigation require repeating, for whatever reason.

CONCLUSIONS

This is the first report of the ICS Standardization Committee of Good Urodynamic Practice. The authors are well aware that this is just a first step and many more will have to follow. Only the essential aspects are considered, but if these basic standards are followed, the quality of urodynamic studies will be significantly improved.

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Appendix G

Developing Evidence-Based Standards for Diagnosis and Management of Lower Urinary Tract or Pelvic Floor Dysfunction*

Peter F.W.M. Rosier, Dirk de Ridder, Jane Meijlink, Ralph Webb, Kristene Whitmore, and Marcus J. Drake

INTRODUCTION

One of the most recognized activities of the International Continence Society (ICS) has been the publication of standardizations of terminology for diagnosis and testing in functional urology. This work started in 1976, with subsequent updates.

The 1988 [1] and the 2002 [2] reports, with ±1000 and ±2500 citations, respectively, are among the most widely quoted publications in urology.

There have been two particularly important categories of publication. The first is the standardization of terminology, such as the "Standardization of Terminology of Lower Urinary Tract Function" [2]. Standardized definitions of key medical terms with international consensus are increasingly needed as analysis and registration in health care become ever more automated and communication increasingly global. The establishment of the International Health Terminology Standards Development Organization (http://www.ihtsdo.org/index.php?id¼502) signifies the increasing weight attached to the agreed definitions of terminology to describe conditions at a fundamental level in medicine. The second category deals with the provision of guidelines for quality control and improvement of standards, which serve as a benchmark for professional activity, exemplified by the "Good Urodynamic Practice" document [3].

ICS standards and standardization have led the way and have been widely accepted. The process by which they have been produced has been based on intensive expert discussion and consensus with input from the ICS membership, but without inclusion of the published evidence in a systematically weighed and transparent manner. The most recent report, a joint report with the International Urogynecological Association [4,5], was developed in a similar manner. Ease of modern electronic communication has allowed more experts to monitor the content of draft editions of newer documents. This has meant that expert opinions were included in a "numerically" more balanced manner. However, no "methods" paragraph was given to explain explicitly how decisions on topics to include were made nor how evidence and expert opinion were prioritized, included, or excluded beyond acknowledgement of the commenting experts in a final paragraph.

Ideally, only "genuine evidence" is included in standards and guidelines. Where genuine evidence is lacking or conflicting, it is preferable that expert opinion is separately added to recommendations in a transparent and explicit manner. In the mid-1980s, a group led by David Sackett, a key figure in evidence-based medicine (EBM) [6], developed a systematic approach to evaluate published evidence, after he analyzed the problem of "observer error" in the interpretation of medical literature [7]. "EBM is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of EBM means integrating individual clinical expertise with the best available external clinical evidence from systematic research" [8]. Standards to produce evidence-based clinical practice guidelines have been developed [9], with guidance manuals [10].

EBM as a strategy to improve health care is not disputed, but the implications in a rapidly expanding field of knowledge are substantial [11]. In the modern era of information technology, transparency, accountability, and complex multidisciplinary responsibilities cannot be ignored; expert opinion is only acceptable where evidence is lacking and must be clearly marked and explained as being expert opinion.

The ICS Standardization Committee recognized the importance of adhering to EBM principles. In

2010, a reorganization took place from which the renamed Standardization Steering Committee (SSC) emerged. A key difference between the new SSC and the old Standardization Committee is that the SSC does not itself deliver standardization documents; instead, it oversees ad hoc working groups (WGs) (see in the succeeding text) that deliver the documents, aiming to ensure transparency, balance, and adherence to the methods and principles of EBM. The SSC chairman is elected from the ICS membership according to the ICS articles and bylaws. The chairman and the SSC members serve for a term of 3 years, once renewable.

The ICS SSC aims to ensure ongoing development of high-quality terminology and/or practice standards, for guidance of professionals dealing with the basic scientific investigation, diagnosis, and management of lower urinary tract, pelvic floor, genital, and anal function and dysfunction. Developing these standards requires transparency and integrity; the SSC's process and expectations for modern-day development of some of the most important ICS documents are described in the succeeding text and illustrated in Figure G.1.

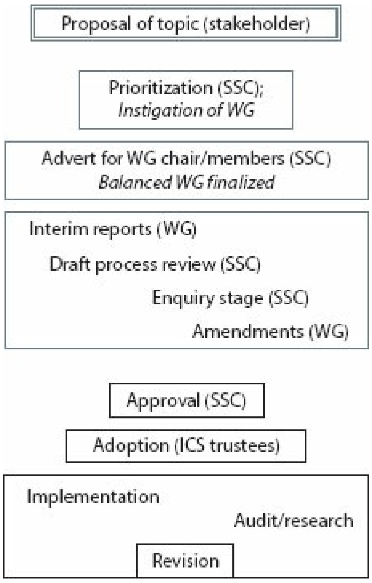

Figure G.1 Summary diagram of the key stages in the development of an International Continence Society standard (SS C, Standardization Steering Committee; WG, working group).

PROCESS OF DEVELOPING AN ICS STANDARD

Topics selected by the SSC for development or revision of standardization reports will be based on areas of priority need, whether identified by the SSC itself or in response to stakeholder suggestions. The delivery of a standardization document on a selected topic will be the remit of a specifically created ad hoc WG, which will focus on that specific subject (see Table G.1). The SSC's role is to agree the scope of the WG's activity, instigating and steering activity, checking compliance with suitable working practices, monitoring progress, ensuring adequate stakeholder input, and evaluating the end result.

Once the need for a new or revised standard has been identified, the SSC will invite applications from ICS members wishing to chair the relevant WG. The person selected will have submitted the proposal with the best strategy for developing the document in the opinion of the majority of SSC members. The SSC will evaluate proposals according to key criteria (Table G.2).

WG Composition

The selected chairperson will establish a WG of interested and knowledgeable individuals from a multinational and interdisciplinary background, representing all key stakeholder groups. Technical expertise relevant to the WG's remit will be taken into consideration in the selection of members. The WG will also be permitted or asked by the SSC to invite input from outside consultants where this is needed. This will typically be applicable in specialist contexts that are not widely represented within the ICS, such as engineering, computer sciences, or data handling. It may also be relevant in other fields, such as consumer perspectives or economic issues.

The SSC will ensure a transparent process for selection of WG members and will evaluate and adapt the composition to ensure a balance between different viewpoints (professional, patient, and other stakeholders’ perspectives). Once agreed, the proposal and the names of the WG’s members will be published on the ICS website. If a member of the SSC is also a member of a WG, he/she will not be included in SSC decisions related to that particular WG. All (potential) conflicts of interest will be published on the ICS website.

Table G.1 Structure and Function of Standardization Document Working Group

- The composition needs to be multidisciplinary and multinational, representing the most important stakeholders (including, e.g., patient representatives, health economists, and others as appropriate).
- Non-ICs members can be part of the WG as experts or representatives of specific stakeholders.
- The WG should generally not include more than 15 people.
- Selection of WG members should follow a transparent process, which is recorded and publically available.
- Additional contributions to a WG’s deliberations can be received from outside individuals.
- The WG should not receive any sponsorship from industry and the members should disclose all relationships.
- All members of the WG will be responsible for the entire content of the document as a group.
- The WG has a chairman who
    - Will propose the key question or topics of discussion to the SSC, together with a strategic plan
    - Will keep a digital working log of the WG activities
    - Will make sure that the composition of the WG is well balanced and that the process of standardization is transparent
    - Will use web-based and e-mail exchange of information and monitor the execution of assignments within the assigned timeline
    - Will adhere to EBM principles, where appropriate
    - Will report to the SSC
    - Will be responsible for production of a first draft of the report within a stipulated time frame (generally 18 months)
    - Will be responsible for submission for publication and dissemination
- After publication of the standard, the WG will be dissolved.
- A typical lifespan for an ad hoc WG will maximally be 36 months. If the WG fails to be productive, the SSC dissolves the WG.
- The ICS or ICS SSC will not provide financial budget for face-to-face meetings of any ad hoc WG.

Table G.2 SSC Criteria for Assessing WG Proposals

- Title of the project
- Name of applicant
- Description of the topic: The arguments for creating the WG are (explain why one or more of the following arguments are relevant)
    - Area of clinical uncertainty or “debate” exists
    - Evidence of better treatment is available
    - Evidence for renewal of the existing standard is available
    - Evidence of practice variation is available
    - Other clinical or scientific relevance
    - There is significant controversy in practice or literature
    - There is conflicting or incomplete evidence
    - There are cultural differences in practices or viewpoints
    - There is socioeconomic relevance
- List of proposed names (with CVs)
    - Confirmation that individuals have agreed to contribute
    - Evidence of multinational and interdisciplinary balance
    - Opportunity for ICS members to apply to join the WG and transparent, documented process for selection
    - Process to register contributions from individuals or groups not in the WG
- Description of the methodology and how it will be used:
    - Web-based approach
    - E-mail
    - Conference calls or webcasts
    - Face-to-face meeting (mainly during ICS international meetings)
    - Proposed timeline
- Description of topic, proposed WG composition, likelihood of
    - Implementation, likelihood of publication, innovation of approach, realistic timeline, use of electronic tools

Stages of a Standard

Stages through which a standardization document will progress are summarized in Table G.3. These will be listed in the project management-working log of the WG and the chairperson of the WG should report progress to the SSC. The SSC will provide a mentor for the WG, who will evaluate the progress at least every 6 months and be available if any problems arise. The mentor will keep a log of these contacts.

Table G.3 Development of an ICS Standard

	Timescale (months)	**WG**	**SSC**
Proposal stage	−6 to 0	Applications for chairmanship or membership	Call for applications. Review subject, chair, group, criteria, timeline, and starting date
Preparatory stage	0 to 18	WG constituted. Development of draft	Evaluate progress. Appoint mentor. Evaluation (at least every 6 months)
Committee stage	18 to 21	Draft submitted to SSC	Review of the process and document against criteria. Approval by consensus
Enquiry stage	21 to 24	Draft on ICS website	Internal and external review. Comments by ICS members and stakeholders
Approval stage	24 to 27	Submit final document to SSC	Process review, Submission to ICS Board of Trustees.
Publication	27 to 36	Final text to ICS office for web publication. Journal submissions	official ICS document. WG dissolved
Implementation stage	>36		Support implementation. Education (with ICS Education Committee). Register of comments. Identify research needs. Support health technology and economic assessment
Revision stage		Submit proposal to SSC	Start new process

Preparation of a Draft Report

The WG will prepare successive working drafts, circulating the drafts, and amending according to comments, until the group is satisfied that it has developed the best solution for the subject being addressed. Standards should adhere to EBM principles, where appropriate and possible. At an early stage, therefore, the WG has to devise a strategy for a comprehensive review of published literature and use an inclusive and transparent approach to derivation of expert opinion. It might sometimes be necessary to use the Delphi method [12]. Each WG will ensure a strategy for capturing and assimilating the views of all groups of stakeholders and criteria for inclusion or exclusion of these views in the finished document.

Throughout, the WG’s chairperson is responsible for

- Keeping a digital log of the WG’s activities
- Documenting the methods that were used to produce the draft document
- Promoting web-based and e-mail exchange of information and monitoring the execution of assignments within the agreed timeline
- Reporting to the SSC
- Producing a first draft of the report within 18 months

Committee Stage (Assessing the Process of Standardization)

As soon as a draft is available, the chairperson of the SSC will forward it to all the members of the SCC for internal process review. The process by which the draft standard was created will be evaluated according to preset criteria. The document requires SSC approval prior to progressing to the next stage of development. The SSC may require revisions or amendments that will need to be undertaken by the WG in a defined time frame. A document that fails to meet the objectives or was not developed in accordance with the appropriate approach will be rejected, and the WG will be dissolved.

Enquiry Stage (Wider Assessment of the Content of the Document)

The actual assessment of the content of the document will be undertaken by internal and external experts (invited by the SSC) and the ICS membership. The draft standard will be circulated to all members by website publication for commenting over a period of 3 months.

Approval Stage

The WG should resubmit the final version based on the comments received. Explicit criteria for the inclusion or exclusion of comments should be developed and each comment should be accompanied by a narrative explaining the reason why it was either included in or excluded from the final version. All comments and accompanying narrative will be published on the relevant document web forum. The revised version should be resubmitted to the SSC for process review and assessment of the amendments. If approved, the document and the log of the development process will be sent to the ICS Board of Trustees for confirmation and adoption.

Publication

Once the board has confirmed and adopted the document and the process, the final text will be published on the ICS website and will then be referred to as the new ICS standard, superseding previous standards. Thus, the new report must outline where it differs from previous reports. The WG will be encouraged to submit the document as an ICS Standard to Neurourology and Urodynamics, and the SSC will advise in this process. Copublication with other journals can be considered if relevant, within copyright regulations. Publication of the respective ICS standard will conclude the WG's activities.

Implementation Stage

The ICS SSC will promote the implementation of the standards by publication, dissemination, and education and the proposing of new standards to its affiliate and collaborating societies and organizations. Additionally, the SSC will monitor the undertaking of clinical audit based on the ICS standards' recommendations as a key aspect of successful introduction of the documents into mainstream practice [13] and the undertaking of the research and development necessary for ongoing development of the evidence base.

Standards will be written in UK English. Translation into other languages will be supported; for terminology standards, this will require that appropriate linguistic validation procedures are followed (for an example of the application of linguistic validation in the context of translation of symptom assessment tools, see Acquadro et al., 2006).

Revision of Standards

The ICS SSC will also keep track of comments that are received for consideration during a future revision of the standard text, as well as identifying future research needs. A revision or update can be proposed by the SSC or any ICS member or group of ICS members when there is a perceived need, and the timescale for anticipated revision of a standard will be specified at the time of adoption—subject to future developments in the field. The SSC can discuss not to revise outdated documents and declare them obsolete.

CONCLUSIONS

In developing evidence-based standardization documents, the ICS SSC aims to ensure inclusiveness, responsiveness, transparency, accessibility, flexibility, and evolution. The ICS SSC presents a structured process for ad hoc WGs to develop ICS standards and a strategy to guide that process. Consequently, each WG will be responsible for several stages of development, each clearly documented, until a high-quality document has been approved as an ICS standard.

The presented structure and strategy place emphasis on the principles of EBM and transparency in the development of ICS standards. They also provide the flexibility necessary for the varied nature of the initiatives established by the ICS, where multiple stakeholders are generally present, and also circumstances in which the evidence base may be limited. ICS standards will continue to be adopted and promoted as the basis for good professional practice, suitable for the demands of the modern era of

EBM.

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Appendix H

Standardization of Dynamic Magnetic Resonance Imaging Measurements of Pelvic Organ Prolapse: Can the PICS Line Help?*

Diaa E.E. Rizk and Ralf Tunn

Dynamic magnetic resonance imaging (MRI) of the pelvis has been rapidly introduced into urogynecological research and practice in recent years mainly to address the shortcomings of clinical assessment systems in women with pelvic organ prolapse (POP). The primary objective was to better select candidates for surgical intervention and choose the appropriate procedure in order to reduce recurrences by allowing accurate identification and objective measurement of prolapse and simultaneous topographic assessment of the pelvis at rest and straining [1–5]. MRI is particularly indicated in women with multicompartment POP and in those who had undergone previous repair, as imaging can reveal more extensive prolapse than physical examination alone with detection rates similar to other conventional fluoroscopic and ultrasound methods [1,3,4]. Staging of POP using MRI has also been suggested by measuring the perpendicular distance between several reference points and lines in each compartment at rest and after straining [1–5]. The two most commonly used lines are one connecting the inferior aspect of the pubic symphysis to the last coccygeal joint, the pubococcygeal line (PCL), and one extending caudally along the long axis of the symphysis pubis, the midpubic line (MPL). Several MRI staging systems have been published for both of these lines [1,3,4].

Despite the widely accepted role of MRI in supplementing clinical evaluation and management of women with POP, this imaging modality has certain limitations. Most importantly, so far, there has been no standardized technique for performing MRI examination of the pelvis. Imaging protocols vary according to patient positioning, filling media, pelvic organ opacification, patient maneuvers (i.e., rest, Kegel, Valsalva, evacuation), and MRI sequences and planes [1–5]. Most of the available imaging systems are unable to demonstrate the full extent of POP because patients are examined in a supine position promoting current efforts to image patients in the sitting and upright position using open-magnet MRI units [1,3–5]. In fact, sagittal plane images of women with POP that are commonly displayed in the literature as if taken in the upright position had been made in the supine position [6]. A further major problem with MRI studies of the pelvis is the incomplete reproducibility and lack of standardization of the patient effort exerted during straining [3–5].

The anatomical landmarks used for pelvic measurements are easily identified in MRI, and this is expected to increase the validity of measurement [5]. The intra- and interobserver reliability of most MRI measurements is, however, rarely described in POP studies [2]. Furthermore, the reference line used for MRI interpretation of POP is not consistent in all studies as this is often based on radiologist experience and referring physician preference [1,5]. In a recent systematic review, seven different reference lines in relation to a wide variety of reference points have been used in different studies with imprecise definition or interchangeable use of some lines, e.g., “MPL/hymenal line” and “PCL/sacrococcygeal inferior pubic point line” [2]. Although the MPL corresponds anatomically to the level of the hymen on cadaveric dissection, the landmark used for clinical staging of POP, the reliability of MRI using the MPL versus clinical findings in women with POP was lower than that of the PCL in most reports [1,2].

It is obvious that we lack a proper validation system for interpreting MRI measurements of POP, and we urgently need to reach a consensus on a more standardized and scientifically robust MRI protocol for examination of the pelvis. Betschart et al. review this topic further in a seminal clinical opinion [6]. The authors discuss the strengths and weaknesses of the current pelvic reference systems for dynamic MRI studies of POP. They clearly demonstrate, after analyzing their database of pelvic MRI scans from 149 women with and without POP, that existing reference lines can produce different measurements because of the following three factors:

1. The distances measured to the reference line vary with anteroposterior location in oblique line systems.
2. The soft tissue–based reference lines can underestimate organ movement relative to the pelvic bones.
3. The systems defined relative to the scanner are affected by intra- and interindividual differences in the pelvic inclination angle at rest and strain.

Based on these findings, Betschart et al. propose a standardized MRI measurement system for POP called the pelvic inclination correction system (PICS), which allows standardized measurement of organ displacement in the direction of prolapse by controlling for variation in pelvic inclination, at rest or straining, bony structures, and the body axis [6]. The hypothesis is biologically plausible since variations in pelvic inclination alter the direction of intra-abdominal vector forces and the degree of transmission of abdominal pressure onto the pelvic floor, thereby influencing the development of pelvic floor weakness and subsequent prolapse [7].

The PICS line, a new reference line, is a significant novelty in the standardization of pelvic floor measurements using MRI. Classifications and reference systems are widely used in medicine and define groups by similar properties, e.g., the POP-Q system for the clinical staging of POP or the TNM system for the staging of cancer. The PICS line allows the determination of descent of any pelvic organ in a standardized way, independent of the location of the pelvis in the scanner, whether it is tilted, flexed, or extended, the size or shape of the pelvis, and the orientation between different examinations or individuals. The advantages of this new system are as follows:

1. It is capable of measuring the line of the body axis.
2. It results in reliable distance calculation independent of the anteroposterior midsagittal location of the organ because it is not oblique.
3. It is related to a bony landmark (pubic bone).
4. It follows the movements of the pelvis.

The most significant value, however, is that the PICS line measures the prolapse (or any organ of interest) in the line of gravity, that is, the natural vector/direction for urogynecological disorders.

The development of the PICS is a product of a fruitful and interdisciplinary collaboration of the Michigan Pelvic Floor Research Group, led by Dr. John DeLancey, which implemented the basic geometrical theorems to solve this measurement problem. Since the group published their first article about the standardized MRI investigation technique in 2001 [8], this contribution 12 years later shows how long the research process takes and how important the ongoing process of standardization of MRI measurements of POP is [6].

Introduction of the new PICS reference line and, hopefully in the future, a new reference plane to measure distances out of the midsagittal plane is an important step in the field of urogynecology toward obtaining standardized and comparable measurements for both clinical practice and research. Until more prospective data are available on the reproducibility of the PICS line in larger and more diverse populations of women with POP, imaging of the pelvic organs using error correction models would assist in establishing a uniform diagnostic and classification system for describing structural defects. It remains to be seen whether the PICS line could also be applied to ultrasound measurements of POP to support routine preoperative imaging of women with single-compartment prolapse, whether or not surgical treatment is contemplated. We also believe that the PICS line will improve our understanding of the pathogenesis and risks of global pelvic floor dysfunction in women by standardizing the reporting of anatomical variations of the levator ani muscle and endopelvic fascia and correlating this with supportive function.

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